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On the Constitution of Phenolphthalein Oxime and Related Compounds

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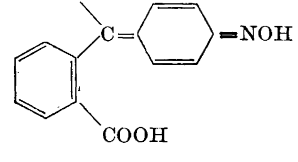
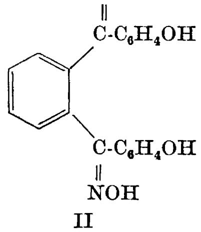
Phenolphthalein oxime is suggested to be a *p*-hydroxyanil of *o*-(*p*-hydroxybenzoyl)benzoic acid. Chemical evidence, infrared spectra, and polarographic data supporting the proposed constitution are presented. Structures for the "pseudoanilides" and "anilides" of *o*-benzoylbenzoic acids are suggested. According to the proposed constitution of phenolphthalein oxime a new rearrangement, which ressembles that of the Lossen degradation, occurs during the formation of the compound.

Phenolphthalein reacts in alkaline solution with hydroxylamine and a yellow, insoluble compound is obtained on acidifying with acetic acid[1]. Friedländer assumed that the compound was an oxime of the quinoid form of phenolphthalein and suggested formula I accordingly. The phenolphthalein oxime was found to be hydrolysed by mineral acid to *o*-(*p*-hydroxybenzoyl)-benzoic acid and *p*-aminophenol, and the latter was assumed to be obtained by a rearrangement of the supposed primarily formed phenylhydroxylamine. Shortly after, however, Friedländer[2] abandoned the structure I, as it did not explain the behaviour of the oxime of 3',5',3'',5''-tetrabromophenolphthalein, which on acid hydrolysis yielded 2,6-dibromo-4-aminophenol instead of 3,5-dibromo-4-aminophenol expected from I.


I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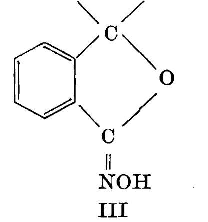
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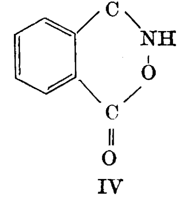
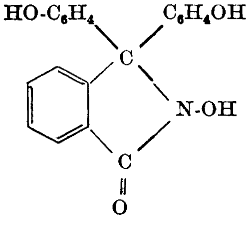
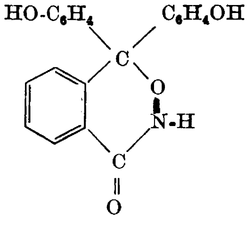
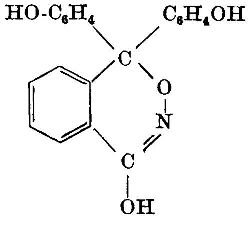

IV

Later H. Meyer [3] proposed formula II and R. Meyer [4] discussed the structures III and IV without deciding between them. Orndorff and Murray [5] adopted the formula V, which H. Meyer [6] previously had considered, and this seemed to be common accepted constitution for many years. Some inconsistencies of this formulation with the experimental facts were pointed out by Lund [7] who instead proposed the structures VI, which take in consideration the tautomerism found in this series of compounds.


V


VI a

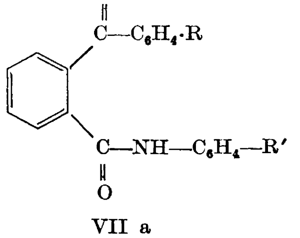

VI b

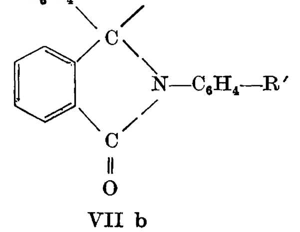
Although the proposed formulations are rather different, all but II assume that the *p*-hydroxyphenyl groups are bonded to the central carbon atom in the same manner as in phenolphthalein.

The purpose of the present investigation was to decide between the proposed structures of phenolphthalein oxime, and to this end a chemical, spectrophotometric, and polarographic investigation of the compound and derivatives thereof was undertaken.

CHEMICAL INVESTIGATION

It has long been known [8] that phenolphthalein oxime on reaction with dimethyl sulfate in alkaline solution yields a yellow trimethyl ether, which on boiling with alcoholic potassium hydroxide splits off one methyl group thus forming a dimethyl ether. This dimethyl ether can exist as a yellow and a colourless compound [7], which are readily interconvertible. On boiling with acetic anhydride it rearranges into 2-(4'-methoxybenzoyl)benz-*p*-anisidide (VIIa or VIIb, R = R' = OCH_3). On hydrolysis of the dimethyl ether with mineral acid *o*-(*p*-anisoyl) benzoic acid and *p*-anisidine are obtained.


VII a


VII b

As might have been expected the mixed anhydride made from *o*-(*p*-methoxybenzoyl) benzoic acid and ethyl chloroformate reacted with *p*-anisidine yielding *o*-(*p*-methoxybenzoyl)benz-*p*-anisidide. When *o*-(*p*-methoxybenzoyl)benzoic acid, however, was treated with excess of thionyl chloride and the resulting chloride, after removing the excess of thionyl chloride *in vacuo*, reacted with *p*-anisidine in dry benzene, a compound was obtained in high yield, which proved to be phenolphthalein oxime dimethyl ether.

If it is assumed that phenolphthalein oxime dimethyl ether has one of the structures previously proposed with the two *p*-methoxyphenyl groups bonded to the central carbon atom one of the anisyl groups must have come from the anisoylbenzoic acid and the other one by some rearrangement from the *p*-anisidine. It would, however, in the phenolphthalein oxime dimethyl ether be impossible to determine which group has come from the acid and which one from the amine. Only one compound would, therefore, be expected to be formed in the reaction between *o*-(*p*-anisoyl)benzoic acid chloride and aniline and in the reaction between *o*-benzoylbenzoic acid chloride and *p*-anisidine.

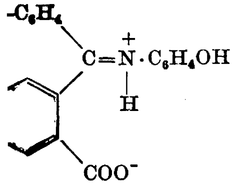
When *o*-(*p*-anisoyl)benzoic acid after treatment with thionyl chloride reacted with aniline an "*o*-(*p*-anisoyl)benz-pseudoanilide" was formed with properties similar to that of phenolphthalein oxime dimethyl ether. On hydrolysis with mineral acid only *o*-(*p*-anisoyl)benzoic acid and aniline were obtained. The compound rearranged on boiling with acetic anhydride to "*o*-(*p*-anisoyl)benzanilide" with a structure represented by VII a or b ($R = OCH_3$, $R' = H$).

o-Benzoylbenzoic acid, after treatment with thionyl chloride, reacted with *p*-anisidine yielding an "*o*-benzoylbenz-pseudo-*p*-anisidide", which, too, had properties very similar to those of phenolphthalein oxime dimethyl ether. This compound had previously been obtained by H. Meyer[9] by heating a mixture of *o*-benzoylbenzoic acid and *p*-anisidine. On boiling with mineral acid *o*-benzoylbenzoic acid and *p*-anisidine were obtained, and as found by Meyer it reacted with phenylhydrazine yielding "benzoylbenzoic acid phenylhydrazone", *i.e.* 2,4-diphenyl-phthalazin-1-one. On boiling with acetic anhydride the "*o*-benzoylbenz-pseudo-*p*-anisidide" rearranged into "*o*-benzoylbenz-*p*-anisidide" (VIIa or b, $R = H$, $R' = OCH_3$).

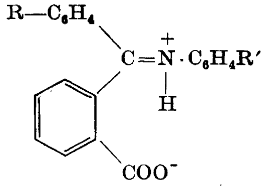
As the "*o*-(*p*-anisoyl)benz-pseudoanilide" is not identical with "*o*-benzoylbenz-pseudo-*p*-anisidide" it follows that the two *p*-anisyl groups in phenolphthalein oxime dimethyl ether are not bonded in the same manner to the central carbon atom. None of the previously suggested structures can account for this fact and must, therefore, be rejected.

Instead are proposed the following constitutions for phenolphthalein oxime (VIII), its dimethyl ether (IXa and b; $R = R' = OCH_3$), and trimethyl ether (XIV). Whether the compounds VIII and IXa exist in solution as zwitterions or with an undissociated carboxyl group is not known; in the solid state the oxime is assumed to possess the zwitterion structure.

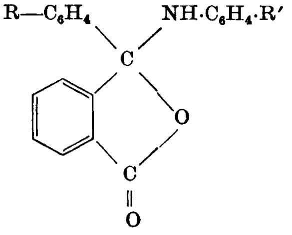
This formulation, where phenolphthalein oxime is a *p*-hydroxyanil of *o*-(*p*-hydroxybenzoyl)benzoic acid, requires that during the formation of the oxime a rearrangement, not previously described, of the type found in the Lossen degradation occurs.



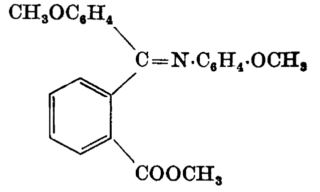
VIII



a



b



XIV

IX R = R′ = OCH_3
X R = OCH_3; R′ = H
XI R = H; R′ = OCH_3
XII R = R′ = H
XIII R = OCH_3; R′ = OH

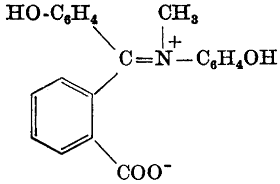
The constitution of the oxime assumed here is in accordance with the hydrolysis of the oxime in mineral acid and alkaline solution to *o*-(*p*-hydroxybenzoyl)benzoic acid and *p*-aminophenol. The formation of 2,6-dibromo-4-aminophenol on hydrolysis of the oxime of 3',5',3'',5''-tetrabromophenolphthalein is expected from this formulation. The solubility of the phenolphthalein oxime and its dimethyl ether in alkali, the insolubility in alkali of the trimethyl ether, the alkaline hydrolysis of the trimethyl ether to the dimethyl ether, and the hydrolysis of "*o*-(*p*-anisoyl)benz-pseudoanilide" (X) to *o*-(*p*-anisoyl) benzoic acid and aniline and the hydrolysis of "*o*-benzoylbenz-pseudo-*p*-anisidide" (XI) to *o*-benzoylbenzoic acid and *p*-anisidine are readily understood from the structures VIII to XIV. The difference in colour of the phenolphthalein oxime at pH 10 and 13 [1] is explained by the successive dissociation of the three acidic groups, and the yellow and the colourless form of the phenolphthalein oxime dimethyl ether [7] correspond to IXa and b, respectively.

A titration curve of phenolphthalein oxime has not been obtained due to the insolubility of the compound at pH-values lower than 7, but on rapid titration of the hydrochloride of the dimethyl ether in 50 % alcohol with 0.1 N NaOH a p*K*-value of 5.8 was found for the supposed carboxyl group under conditions, where the p*K*-value of *o*-(*p*-anisoyl)-benzoic acid was found to be 5.0.

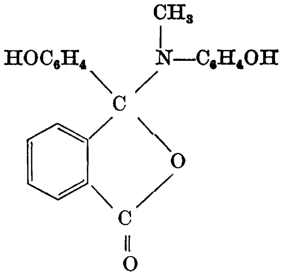
The solubility of phenolphthalein oxime and its ethers in mineral acid is assumed to be due to the presence of the azomethine group. Benzophenone anil and benzophenone *p*-hydroxyanil are soluble in mineral acid, and the latter is claimed by Reddelin [10] to require boiling with strong mineral acid for hydrolysis.

The phenolphthalein oxime contains one mole of water of crystallization which is not removed by drying in high vacuum at 100°C over phosphorus pentoxide for 18 h. On raising the temperature to 120°C for 18 h most of the water was removed, but still about 0.3 mole of water of crystallization was found by a Fischer-titration. This might explain the low values for carbon and high values for hydrogen reported by Friedländer[1] for the analysis of the phenolphthalein oxime.

Phenolphthalein reacts with N-methyl hydroxylamine analogously with the reaction with hydroxylamine yielding a compound similar to phenolphthalein oxime; the compound is hydrolysed to *o*-(*p*-hydroxybenzoyl)benzoic acid and N-methylaminophenol[7]. This ”phenolphthalein N-methyl-oxime” also contains one mole of water of crystallization which is difficult to remove. The yellow ”phenolphthalein N-methyl-oxime” is soluble in alkali and acid yielding a yellow solution, but the solution in ether or dioxane is colourless. The yellow form is assumed to possess the structure XVa, whereas the colourless form would be represented by XVb. None of the previously suggested formulations allow the ”phenolphthalein N-methyl-oxime” to exist in two forms.



XV a



XV b

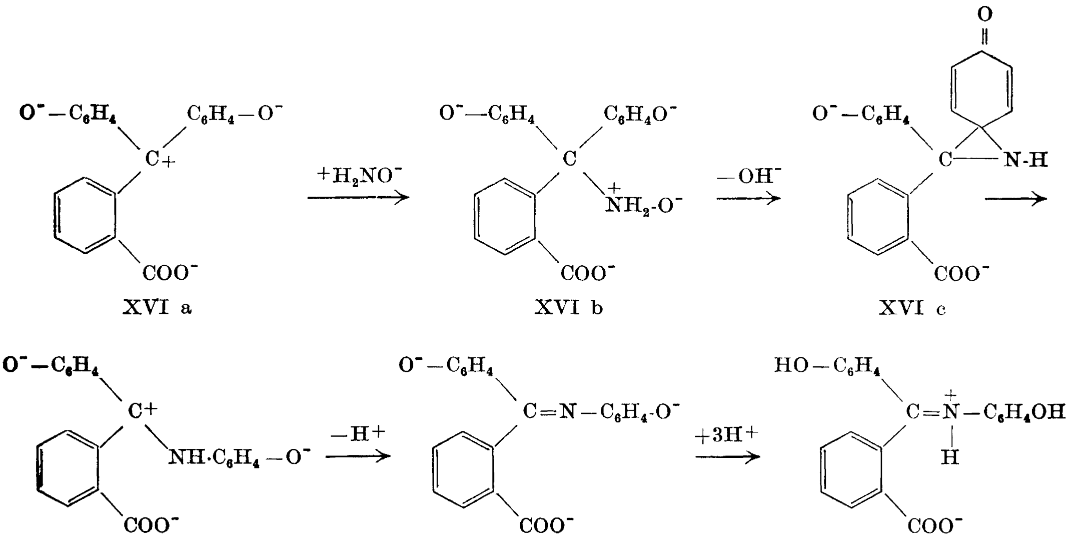
o-(*p*-Anisoyl)benzoic acid reacts after treatment with thionyl chloride with N-methylaniline yielding a white compound, which dissolves in acid with a yellow colour. The colourless form of ”*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide” is assumed to have a structure similar to XVb, whereas in acid solution a protonated form corresponding to XVa is likely.

From a similar reaction between the acid chloride of 2-benzoylbenzoic acid and N-methylaniline Wawzonek *et al.*[11] isolated a white compound which they assumed to be a non-cyclic normal N-methylanilide with the nitrogen bonded to the carboxyl carbon atom. In view of the similarities with the above mentioned ”*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide” it seems likely that the compound obtained by Wawzonek *et al.* is ”*o*-benzoylbenz-pseudo-N-methylanilide” with a structure similar to XVb.

Phenolphthalein monomethylether reacts with hydroxylamine yielding a ”phenolphthalein monomethylether oxime” (XIII), which is hydrolyzed on boiling with mineral acid to *o*-(*p*-anisoyl)benzoic acid and *p*-aminophenol. The same compound is formed by action of *p*-aminophenol on the chloride obtained from *o*-(*p*-anisoyl)benzoic acid on treatment with thionyl chloride.

On reaction with diazomethane in a mixture of ether and dioxane the phenolphthalein oxime yields a mixture of different methylated compounds from which phenolphthalein oxime trimethyl ether and a dimethyl ether were isolated. This dimethyl ether was different from IX as it was hydrolyzed by alcoholic potassium hydroxide to ”phenolphthalein monomethylether oxime” (XIII).

A mechanism of the postulated rearrangement, which proceeds during the formation of phenolphthalein oxime, is presented below.



XVI a XVI b XVI c

XVI d XVI e VIII

The structure XVIa is one of the resonance structures of phenolphthalein in alkaline solution. This carbonium ion is assumed to react with the anion of hydroxylamine forming a bond between carbon and nitrogen. The migration of the phenyl group requires the formation of a quinoid form of the phenyl group, and the plane of the migrating phenyl group is at a right angle to the plane of the three-membered ring. After completion of the migration the carbonium ion XVId loses a proton, and on addition of acid the phenolphthalein oxim (VIII) precipitates.

This mechanism is in agreement with many features found in the reaction between phenolphthalein and hydroxylamine. It has been found[12] that only phthaleines containing at least one *p*-hydroxyphenyl group are able to form oximes. The mechanism suggested above makes that requirement understandable. If, however, a nitro group is present *ortho* to the hydroxyl group it is found that the phthalein does not form an oxime; thus 3',3''-dinitrophenolphthalein forms no oxime, whereas 3',5'-dinitrophenolphthalein does[12]. This is explained by the formation of an *aci*-form of the nitro group in alkaline solution containing an *o*-quinoid structure, which excludes the possibility of a *p*-quinoid form of the phenyl group during the migration.

Furthermore, the formation of N-(*p*-hydroxyphenyl)phthalimide on reaction of phenolphthalein with excess of hydroxylamine can be explained by assuming that the carbonium ion XVId reacts with hydroxylamine analogously with the carbonium ion XVIa with the migration of the second *p*-hydroxyphenyl group. The compound formed would split off one mole of *p*-aminophenol and yield N-(*p*-hydroxyphenyl)phthalimide.

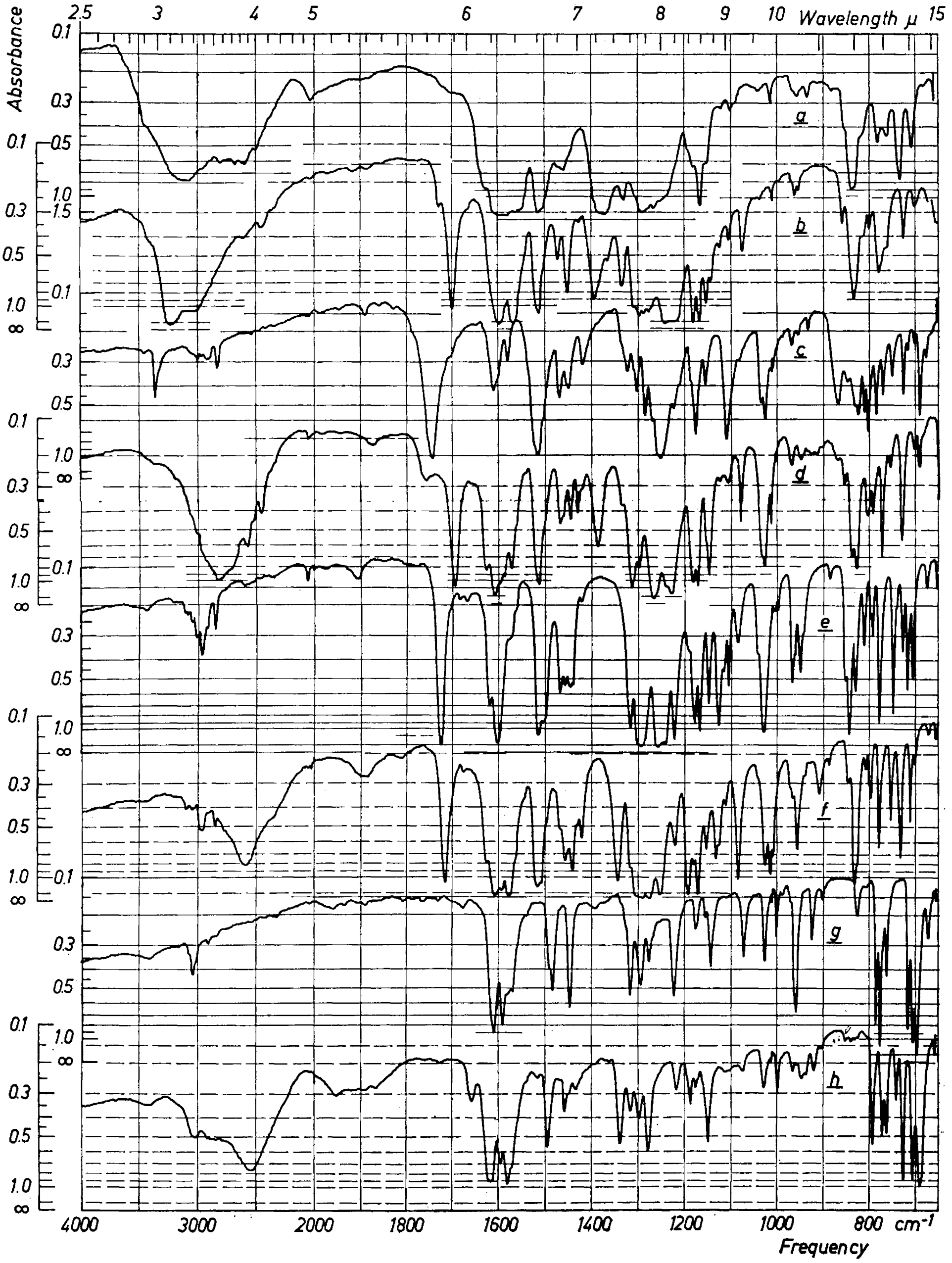


Fig. 1. Infrared spectra (potassium bromide) of phenolphthalein oxime (a), its hydrochloride (b), phenolphthalein oxime dimethyl ether (c), its hydrochloride (d), phenolphthalein oxime trimethyl ether (e), its hydrochloride (f), benzophenone anil (g), and its hydrochloride (h).

Fluorescein does not form an oxime on treatment with hydroxylamine which might be understood as a migration of one of the phenyl groups is hindered by the oxygen bridge between them. Hydroquinonephthalein [8] forms 3 "oximes" on reaction with hydroxylamine, but as they on hydrolysis with mineral acid yield hydroquinonephthalein [8] their constitution must be different from that of phenolphthalein oxime.

SPECTROPHOTOMETRIC INVESTIGATION

The infrared spectra were obtained using potassium bromide discs which had been kept at 100°C for 2—3 minutes before the spectra were recorded following the procedure of Buur Jensen [13].

The spectrum of phenolphthalein oxime (Fig. 1a) shows a strong absorption from 3 500 cm^{-1} to 2 300 cm^{-1}. The absorption between about 2 800 cm^{-1} and 2 300 cm^{-1} is believed to be an "ammonium band" [14] and the absorption about 2 040 cm^{-1} an "immonium band" [14], both of which would be expected from the structure VIII. The strong absorption from 1 615 cm^{-1} to 1 550 cm^{-1} is assumed to contain the phenyl bands and the bands of the carboxylate ion. In this respect the spectrum of the phenolphthalein oxime resembles those of many amino acids. A shoulder at 1 630 cm^{-1} may be due to the azomethine group. The absence of any absorption from 1 800 cm^{-1} to 1 640 cm^{-1} makes the structures I, II, IV, and V very unlikely, whereas III and VIb would not be expected to have absorption in this region; however, the presence of the "ammonium band" excludes III.

The hydrochloride of phenolphthalein oxime (Fig. 1b) has an absorption band at 1 700 cm^{-1} which is attributed to the presence of an unionized carboxyl group. It may be recalled [15] that the carboxyl group of the hydrochlorides of β- and γ-amino acids generally have a carbonyl absorption in the region 1 730 cm^{-1} to 1 700 cm^{-1} and aromatic carboxyl groups at 1 700 cm^{-1} to 1 680 cm^{-1}. This is in accordance with VIII, whereas it seems more difficult to accept that the hydrochloride of VIb would absorb about 1 700 cm^{-1}, when VIb as zwitterion does not do so.

The colourless form of phenolphthalein oxime dimethyl ether (Fig. 1c) has a sharp absorption peak at 3 390 cm^{-1} which is attributed to an N—H stretching frequency. A carbonyl absorption is found at 1 750 cm^{-1}, which also is present in phthalide and substituted phthalides as phenolphthalein and its dimethyl ether. Both the presence of the N—H stretching frequency and the phthalide ring is required by the suggested structure IXb and excludes the formulations I, II, III and V. The yellow form (IXa) has not been obtained free from the colourless dimethyl ether in the solid state, why no spectrum of this compound can be presented.

In the spectrum of the hydrochloride of phenolphthalein oxim dimethyl ether (Fig. 1d) a carbonyl absorption band is found at 1 700 cm^{-1} as in the hydrochloride of the oxime itself, which also would be expected from IXa.

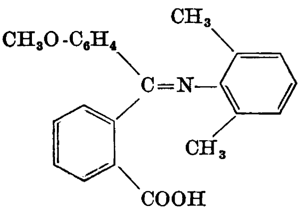
It might be mentioned that in all the compounds containing an aryl methyl ether a band of medium intensity is found between 1 040 cm^{-1} and 1 025 cm^{-1} besides the strong ether band about 1 250 cm^{-1}. A similar observation has been made by Colthup [16].

The carbonyl absorption of phenolphthalein oxime trimethyl ether (Fig. 1e) is at 1 726 cm^{-1}. This is in accordance with the structure XIV which contains an aryl ester group, and the normal frequency for aryl esters is in the region 1 730 cm^{-1} to 1 717 cm^{-1} [15]. A band of medium intensity at 1 620 cm^{-1} might be attributed to the presence of the azomethine group. In the hydrochloride (Fig. 1f) of the trimethyl ether a similar band is found at 1 625 cm^{-1}. The carbonyl frequency at 1 717 cm^{-1} is attributed to an ester group as in XIV. The "ammonium band" and "immonium band" required by the suggested structure is found about 2 600 cm^{-1} and 1 900 cm^{-1}, respectively.

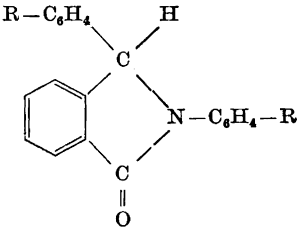
For comparison the spectra of benzophenone anil (Fig. 1g) and its hydrochloride (Fig. 1h) are presented, and the similarities in the spectra of the phenolphthalein oxime trimethyl ether and the benzophenone anil on the one hand and their hydrochlorides on the other support the proposed structures.

The spectra of "*o*-(*p*-anisoyl)benz-pseudoanilide" (X), "*o*-benzoylbenz-pseudo-*p*-anisidide" (XI) and "*o*-benzoylbenz-pseudoanilide" (XII) are similar to that of the colourless form of phenolphthalein oxime dimethyl ether in that they contain an N—H stretching frequency about 3 390 cm^{-1} and a carbonyl absorption about 1 750 cm^{-1}. They are, therefore, believed to possess structures similar to IXb in the solid state.

The yellow compound, *o*-(*p*-methoxybenzoyl)benz-pseudo-2,6-dimethylanilide, obtained from the action of 2,6-xylidine on the acid chloride from *o*-(*p*-anisoyl)benzoic acid and thionyl chloride, yields a spectrum without a N—H absorption about 3 400 cm^{-1} and with a carbonyl absorption at 1 711 cm^{-1}. This is attributed to an unionized carboxyl group, although the frequency is slightly higher than the usual one for aromatic carboxyl acids. The structure XVII is suggested for the compound in the solid state. The presence of the azomethine group is in accordance with the yellow colour. It is noteworthy that the two methyl groups in the xylidine nucleus prevent the formation of a phthalide structure or a zwitterion. However, the absorption from 2 800 cm^{-1} to 2 300 cm^{-1} attributed to the O—H stretching vibrations of the carboxyl group might contain an amount of "ammonium"-absorption.



XVII



XVIII

The spectrum of "phenolphthalein N-methyl-oxime" in potassium bromide is similar to that of the phenolphthalein oxime, but in a dioxane solution, which is colourless, the spectrum is quite different. In the dioxane solution the "phenolphthalein N-methyl-oxime" shows a strong carbonyl absorption at 1 760 cm^{-1} which suggests the presence of a phthalide ring. As some absorption about 1 750 cm^{-1} is found in the spectrum obtained in potassium bromide it is possible that a certain amount of the compound contains the lactone form in the solid state. The analysis seems to exclude that the presence of the absorption at 1750 cm^{-1} (in potassium bromide) is due to a small content of unreacted phenolphthalein. The spectra are thus in accordance with the structures XVa and b.

The white compounds, "*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide" and "*o*-(*p*-anisoyl)benz-pseudo-N-methyl-*p*-anisidide" contain a carbonyl absorption about 1 760 cm^{-1} and no other carbonyl absorption. A structure as that suggested by Wawzonek *et al.*[11] for "*o*-benzoylbenz-pseudo-N-methylanilide" containing a keto and an amide group is thus unlikely for these compounds, and a structure similar to XVb is suggested. This structure is also in accordance with the fact that the compounds are hydrolyzed by cold, dilute alkali, which would not be expected for a normal anilide.

The "*o*-(*p*-anisoyl)benz-*p*-anisidide", obtained from phenolphthalein oxime dimethyl ether on treatment with acetic anhydride [7], yields a spectrum containing a broad absorption around 3 250 cm^{-1}, which is attributed to the presence of a hydroxyl group. A carbonyl absorption is found at 1 675 cm^{-1} and a small shoulder is visible at 1 660 cm^{-1}. This suggests that in the solid state most of the compound is found in the cyclic form VIIb and a minor part possesses the open chain structure VIIa.

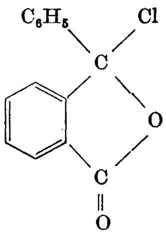
The compounds obtained on treatment of the "pseudoanilides" and "pseudoanisidides" with acetic anhydride yield similar spectra and are assumed to exist mainly in the cyclic form corresponding to VIIb with varying contents of the open chain structure. The presence of the methoxy groups seems to favour the cyclic form, and in *o*-benzoylbenzanilide the diaryl ketone group manifests itself as a band with medium intensity at 1 660 cm^{-1} indicating that an appreciable amount of this compound possesses the open chain structure.

Whereas the spectrum of *o*-(*p*-anisoyl)benz-N-*cyclo*hexylamide, obtained from the acid chloride and *cyclo*hexylamine, only suggests the presence of the cyclic structure of the amide, the *o*-benzoylbenz-N-ethylamide shows three carbonyl bands (1 689 cm^{-1}, 1 676 cm^{-1}, 1 660 cm^{-1}) indicating the presence of approximately equal amounts of both forms in the solid state.

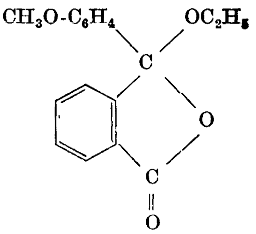
On controlled potential reductions of phenolphthalein oxime was obtained a compound with a carbonyl absorption at 1 645 cm^{-1} which is in accordance with the structure XVIII suggested by H. Meyer [17] for the reduction product obtained from the action of zinc on phenolphthalein oxime.

The spectrum in carbon tetrachloride of the acid chloride from thionyl chloride and *o*-benzoylbenzoic acid contains a carbonyl band at 1 790 cm^{-1} and no bands between 1 760 cm^{-1} and 1 620 cm^{-1}. As no diaryl ketone thus is present it is likely that the chloride exists in the cyclic form XIX, which supports the formulation of the reaction products of the chloride and aromatic amines.

The "*o*-(*p*-anisoyl)benz-pseudo-ethyl ester", formed on reaction between the acid chloride and ethanol, shows in potassium bromide and in chloroform solution a carbonyl band at 1 765 cm^{-1} indicating the presence of a phthalide ring and the spectrum contains no absorption corresponding to a diaryl ketone. The spectrum is thus in accordance with the structure XX.



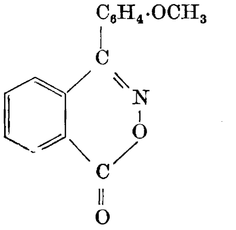
XIX



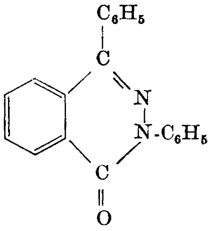
XX

The carbonyl absorption of the "α-oxime" of hydroquinonephthalein is found about 1 680 cm^{-1}. The formula proposed by Meyer [8] for this white compound contains a ring system similar to that (V) suggested by Orndorff and Murray [5] for the phenolphthalein oxime. The spectrum of the "α-oxime" seems not to exclude the structure proposed by Meyer.

The anhydride of the oxime of *o*-(*p*-anisoyl)benzoic acid, 4-(4'-methoxyphenyl)-2,3-benzoxazin-1-one, XXI has a spectrum containing a carbonyl absorption at 1 730 cm^{-1}, whereas the anhydride of the phenylhydrazone of 2-benzoylbenzoic acid, 2,4-diphenyl-phthalazin-1-one, XXII, absorbs at 1 660 cm^{-1}.



XXI



XXII

POLAROGRAPHIC INVESTIGATION

Phenolphthalein has been investigated polarographically by Kolthoff *et al.*[17,18] The compound was assumed to be reduced in a 2 electron reduction to phenolphthalin which in this investigation has been confirmed by controlled potential reduction. The wave showed in certain media a characteristic minimum, and at higher alcohol concentrations the height of the wave was dependent upon the alcohol concentration in such a way, that the wave height diminished at higher alcohol concentrations and became rate controlled [18]. It was assumed that the current below pH 7 was determined by the rate of the transformation of phenolphthalein through its anion into a quinoid form, which was reduced. Some experimental facts, however, seem to be incompatible with this assumption. It would be expected that the rate of the formation of the anion would be very much lower at pH 1 than at pH 7; furthermore, phenolphthalein dimethyl ether is reduced at potentials similar to those of phenolphthalein, and the wave is best defined in solutions more acid than pH 1; at higher pH-values minima are found. In this case no possibility of a transformation through an anion into a quinoid form exists, and it seems more likely that the rate of a reaction which involve some kind of protonization is determining for the height of the wave. This might also be the case for phenolphthalein but the mechanism of the reduction is still not clear.

The polarographic behaviour of 2-benzoylbenzoic acid, 2-(4'-hydroxybenzoyl)benzoic acid, and 2-(4'-methoxybenzoyl)benzoic acid resembles that of pyruvic acid[19] in that the acids and their anions are reduced at different potentials. In a certain pH-region the height of the more positive wave is determined by the rate of the recombination of the anion and the proton.

By controlled potential reduction of 2-(4'-methoxybenzoyl)benzoic acid it was found that the reaction was a two-electron reduction to 3-(4'-methoxyphenyl)-phthalide.

In Table 1 are given the polarographic data of phenolphthalein oxime (VIII), its monomethyl- (XIII), dimethyl-(IX), and trimethyl ether (XIV), "*o*-(*p*-anisoyl)benz-pseudoanilide" (X), "*o*-benzoylbenz-pseudo-*p*-anisidide" (XI), "*o*-benzoylbenz-pseudoanilide" (XII), "*o*-(*p*-anisoyl)-benz-pseudo-2,6-dimethylanilide" (XVII), "phenolphthalein N-methyl-oxime", and "*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide".

Table 1. Limiting currents in μA and half-wave potentials *vs* S.C.E. at different pH-values of phenolphthalein oxime (VIII), phenolphthalein monomethylether oxime (XIII), phenolphthalein oxime dimethyl ether (IX), phenolphthalein oxime trimethyl ether (XIV), "*o*-(*p*-anisoyl)benz-pseudoanilide" (X), "*o*-benzoylbenz-pseudo-*p*-anisidide" (XI), "*o*-benzoylbenz-pseudoanilide" (XII), "*o*-(*p*-anisoyl)benz-pseudo-2,6-dimethylanilide" (XVII), "phenolphthalein N-methyl-oxime" (XV), and "*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide" (XXIII). Concentration 10^{-3} M. 0.01 % gelatin added as maximum suppressor.

pH	1.0		3.5		5.5		7.5		9.8		13	
	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$
VIII	3.6	0.79	3.4	0.84	3.5	0.92	3.6	1.07	3.4	1.28	1.5	1.48
XIII	3.6	0.75	3.4	0.80	3.4	0.87	3.4	1.01	3.5	1.25	0.8	1.38
IX	3.8	0.75	3.8	0.79	3.7	0.87	3.9	1.00	3.9	1.25	1.2	1.37
											~1.0	~1.80
XIV[a]	3.3	0.78	3.3	0.93	3.5	1.04	3.5	1.12[b]	3.6	1.21[b]	0.5	1.37
									0.5	1.80	2.0	1.73
X	3.9	0.66	3.7	0.72	3.8	0.79	3.9	0.95	3.8	1.18[b]	0.6	1.31
			4.0	1.38					1.4	1.77	3.2	1.73
XI	4.0	0.59	4.1	0.66	4.0	0.74	4.0	0.93	4.0	1.16[b]	1.6	1.29[b]
											2.6	1.65
XII	3.7	0.53	3.7	0.64	3.6	0.71	3.8	0.89	4.1	1.09[b]	0.5	1.20
									0.6	1.65	3.4	1.54
XVII	3.7	0.78	3.6	0.87	3.6	0.95	3.7	1.08	2.9	1.30[b]	0	—
			5.8	1.28								
XV	3.4	0.77	3.4	0.82	3.6	0.90	3.6	0.99	3.9	1.17	[c]	~1.33
XXIII	4.0	0.66	3.2	0.75	3.3	0.84	3.4	0.92	3.5	1.03	[c]	~1.07

[a] 40 % dioxane. [b] Minimum. [c] The compound is hydrolyzed.

The phenolphthalein oxime yields below pH 11 a diffusion controlled, two-electron wave. The half-wave potentials are dependent upon pH with a slope of the $E_{\frac{1}{2}}$-pH curve of about 0.02 V/pH-unit below pH 5 and about 0.08 V/pH-unit between pH 5 and 10. The presence of the dissociable groups in the compound explains this behaviour. In strongly alkaline solution the height of the wave diminishes somewhat.

The half-wave potentials of phenolphthalein oxime are a little less negative than those of 2-(4'-hydroxybenzoyl)benzoic acid in accordance with the proposed structure VIII. This makes formula V very unlikely, as neither phenolphthalein imide nor benzoylhydroxamic acid are reducible in the medium used.

Controlled potential reduction in acid solution of phenolphthalein oxime showed that the reduction consumed 2 electrons per molecule, and the isolated product was 2-(4'-hydroxyphenyl)-3-(4''-hydroxyphenyl)-2,3-dihydro-2-*iso*-benzazol-1-one (XVIII, R = OH).

The compounds IX, X, XI, and XII behave below pH 10 similarly to the oxime. The ''*o*-benzoylbenz-pseudoanilide'' (XII) has previously been investigated by Wawzonek *et al.*[11] who from the polarographic data concluded, that the compound in acid solution contained the azomethine group in accordance with the assumption made here. In strongly alkaline solution the wave diminishes in height and another wave appears at more negative potentials. According to Wawzonek *et al.*[11] the second wave is due to the reduction of the compound with the form XIIb containing a phthalide ring. As the height of the first wave in strongly alkaline solution is almost independent of the height of the mercury reservoir it is assumed to be determined by the rate of some reaction. This might be the opening of the phthalide ring, but as IX, X, and XI are soluble in alkali yielding a yellowish solution, it is likely that the phthalide ring in these solutions is opened. It must thus be another reaction which determines the height of the first wave of these compounds.

Controlled potential reduction of phenolphthalein oxime dimethyl ether yielded both in acid and alkaline solution 2-(4'-methoxyphenyl)-3-(4''-methoxyphenyl)-2,3-dihydro-2-*iso*benzazol-1-one (XVIII, R = OCH_3). The reduction of the dimethyl ether is thus analogous with that of phenolphthalein oxime.

The reduction of the phenolphthalein oxime trimethyl ether is slightly different from that of the above mentioned compounds in that the slope of the $E_{\frac{1}{2}}$ /pH-curve is about 0.08 V/pH-unit from pH 1 to 10. This is due to the methylation of the carboxyl group; no dissociable groups are thus present in the molecule. In strongly alkaline solution two waves are found, and in this case no phthalide ring, whose reduction can be due to the occurrence of the more negative wave, is present. In the reduction of oximes and other azomethine compounds [20] minima are often found in alkaline solution and in some cases a second wave is found. It is generally assumed that the height of the first wave of the oxime is dependent upon the rate of the protonization of the oxime, and the second wave is due to the reduction of the unprotonated compound. The pH at which the first wave diminishes is in the case of phenolphthalein oxime trimethyl ether considerably higher than in the case of the oximes, but possibly not high enough to exclude the occurrence of such a protonization at the electrode surface, and at present no other explanation of the two waves in alkaline solution can be offered.

Controlled potential reduction at pH 3 and pH 5 of phenolphthalein oxime trimethyl ether yielded in a two-electron reduction the same compound (XVIII, $R = OCH_3$) as the reduction of the dimethyl ether. As anils generally are reduced to the aniline derivatives it is assumed that the primarily formed derivative of benzhydrylaniline reacts with the methyl ester yielding the lactam.

The *o*-(*p*-anisoyl)benz-pseudo-2,6-dimethylanilide (XVII) resembles phenolphthalein oxime dimethyl ether below pH 8. However, in the region pH 2 to 4 a second wave, probably catalytic, appeared; the nature of this wave was not investigated further. At higher pH-values the first wave diminishes in height and disappears completely in strongly alkaline solution without the appearence of a second wave. The reduction thus resembles that of many oximes, and the height of the wave is, too, in a certain pH-interval assumed to be governed by the rate of protonization of the azomethine compound at the electrode surface.

Controlled potential reduction of the "*o*-(*p*-anisoyl)benz-pseudo-2,6-dimethylanilide" at pH 0.5 showed the reduction to be a two-electron reduction. In the reaction medium was precipitated a compound, which was identified as 3-(4'-methoxyphenyl)-phthalide. Steric hindrance might be responsible for the failure to form a derivative of 2,3-dihydro-2-*iso*benzazol-1-one, analogously with the reduction product of phenolphthalein oxime dimethyl ether, and for the instability of the assumed, primarily formed, benzhydrylaniline derivative.

The "*o*-(*p*-anisoyl)benz-pseudo-N-methylanilide" (XXIII) is reduced from pH 1 to 10 in a single two-electron wave. The slope of the $E_{\frac{1}{2}}$ /pH-curve is about 0.04 V/pH-unit. In strongly alkaline solution the compound is hydrolyzed and the wave of *o*-(*p*-anisoyl)benzoic acid appears.

From a controlled potential reduction in acid solution of the compound 3-(4'-methoxyphenyl)-phthalide was isolated. The reduction thus results in a cleavage of the carbon-nitrogen bond. This might be a direct reduction of the single bond or a reduction of the carbon-nitrogen double bond resulting from an opening of the phthalide ring by forming a zwitterion. As the solution in the neutral region is colourless the compound predominantly exists with the phthalide ring intact, and if the zwitterion is the reducible species the ring opening is a fast reaction. This is likely as the opening of the phthalide ring just requires a displacement of electrons without the participation of hydrogen ions.

The polarographic data of *o*-(*p*-anisoyl)benz-*p*-anisidide (VII), *o*-benzoylbenz-*p*-anisidide (XXVI), *o*-benzoylbenzanilide (XXVII), and *o*-(*p*-anisoyl)-benz-N-*cyclo*hexylamide (XXVIII) are given in Table 2. In acid solution the wave is hardly visible, but at higher pH-values the wave grows and reaches at pH 13 for some of the compounds a height to be expected of a diffusion controlled wave. At lower pH-values the height of the wave is governed by the rate of some reaction. The compounds can exist in a cyclic (VIIb) and a non-cyclic (VIIa) form. From the infrared spectra it can be concluded that the compounds in the solid state to a high degree are found in the cyclic form. As the potentials at which the compounds are reduced are not much different

Table 2. Limiting currents in μA and half-wave potentials *vs* S.C.E. at different pH-values of *o*-(*p*-anisoyl)benz-*p*-anisidide (VII), *o*-benzoylbenz-*p*-anisidide (XXVI), *o*-benzoylbenzanilide (XXVII), *o*-(*p*-anisoyl)benz-N-*cyclo*hexylamide (XXVIII), *o*-benzoylbenz-N,N-diethylamide (XXIX), and *o*-(*p*-anisoyl)benz-2,6-dimethylanilide (XXX). Concentration 10^{-3} M. 0.01 % gelatin added as maximum suppressor.

pH	1.0		3.5		5.5		7.5		9.8		13	
	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$
VII	0.08	0.91	0.15	1.01	0.15	1.11	0.45	1.23	2.7	1.43	3.2	1.54
XXVI	<0.05	–	<0.05	–	<0.05	–	<0.05	–	0.9	1.49	1.7	1.60
XXVII	<0.05	–	<0.05	–	0.1	1.1	0.3	1.25	2.0	1.37	2.7	1.56
XXVIII	0.15	0.84	0.15	1.01	0.2	1.12	0.5	1.23	0.8	1.36	2.3	1.57
XXIX	4.4	0.86	4.6	1.02	4.3	1.12	4.2	1.17	4.4	1.29	4.3	1.43
XXX[a]	1.8	0.88	2.3	1.12	2.2	1.23	3.0[b]	1.36	4.2	1.54	4.1	1.56

[a] 45 % dioxane. [b] Drawn out wave.

from those of *o*-benzoylbenz-N,N-diethylamide, which from the infrared spectrum ($>\text{C} = \text{O}$, $\nu = 1\ 665\ \text{cm}^{-1}$; $-\text{CO}-\text{N}<$, $\nu = 1\ 620\ \text{cm}^{-1}$) can be shown to possess the non-cyclic structure, it is assumed that the wave is due to the reduction of the form containing a free keto group (VIIa). The wave height would thus be determined by the rate of the transformation of the cyclic into the non-cyclic form.

Controlled potential reduction in strongly alkaline solution of *o*-(*p*-anisoyl)-benz-*p*-anisidide showed the reduction to be a two electron reduction and the isolated product was 3-(4'-methoxyphenyl)-phthalide. If it is the non-cyclic form which is reduced the expected compound would be a benzhydrol derivative. It seems a little unexpected that the carbon-nitrogen bond in the amide group is broken under the influence of the primarily formed secondary alcohol group.

o-Benzoylbenz-N,N-diethylamide (XXIX) yields from pH 1 to 13 a diffusion controlled, two-electron wave (Table 2). Controlled potential reduction in 0.5 N sodium hydroxide showed the reduction product to be 3-phenylphthalide. In this case, too, the carbon-nitrogen bond in the amide group is cleaved.

The polarographic reduction of *o*-(*p*-anisoyl)benz-2,6-dimethylanilide (XXX) showed that the compound to a higher degree than, e.g. *o*-benzoylbenzanilide, possessed the non-cyclic structure, and/or the rate of the ring opening is higher.

Whereas phenolphthalein imide, phenolphthalein hydrazide, and hydroquinonephthalein-α-oxime are not polarographically reducible 4-(4'-methoxyphenyl)-2,3-benzoxazin-1-one (XXI) and 2,4-diphenyl-phthalazin-1-one (XXII) are (Table 3). The polarographic data of the oxime of 2-(4'-methoxyphenyl)-benzoic acid (XXIV) are also shown in Table 3.

The behaviour of the oxime XXIV resembles that of benzophenone oxime. In a region around the neutral point the wave due to the reduction of the compound protonated at the electrode surface diminishes in height and disappears, whereas a more negative wave becomes visible, which represents the reduction of the unprotonated oxime. In strongly alkaline solution this wave

Table 3. Limiting currents in μA and half-wave potentials *vs* S.C.E. at different pH-values for 4-(4′-methoxyphenyl)-2,3-benzoxazin-1-one (XXI), 2-(4′-methoxybenzoyl)-benzoic acid oxime (XXIV), and 2,4-diphenylphthalazin-1-one (XXII). Concentration 10^{-3} M. 0.01 % gelatin added as maximum suppressor.

pH	1.0		3.5		5.5		7.5		9.8		13	
	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$
XXI	4.4	0.46	4.4	0.64	8.8	0.89	8.9	1.09	8.7	1.19	0	—
	4.3	0.69	4.3	0.80								
XXIV	8.0	0.71	7.8	0.88	7.6	1.04	3.0	1.18	4.3	1.72	0	—
XXII	4.6	0.87	3.7	1.08	3.7	1.11	2.5	1.25[a]	3.4	1.74	0	—

[a] Minimum.

disappears, probably due to a loss of a proton from the oxime group. In strongly acid solution the compound loses water and is transformed to the 2,3-benzoxazin-1-one (XXI).

This compound is in acid solution reduced in two two-electron steps, but due to the low solubility of the compound no preparative reduction has been made. From pH about 5 to 10 a single four-electron wave is found. In alkaline solution the 2,3-benzoxazin-1-one ring is opened and the oxime XXIV is formed

The 2,4-diphenyl-phthalazin-1-one is in acid solution reduced in a single wave. At higher pH-values the height of the wave diminishes and a minimum on the curve is found as in the case of many oximes and phenylhydrazones [20]. About pH 9 the first wave has disappeared and a more negative wave is found. This wave disappears, however, in strongly alkaline solution. The height of the wave corresponds to a two-electron reduction, but due to the low solubility of the compound this could not be tested in a controlled potential reduction.

Hydroquinonephthalein (XXV) is reduced (Table 4) from pH 0 to 10 in a single, two-electron wave, which at least in acid solution is diffusion controlled. At pH about 9 the oscillations due to the mercury drops are abnormal from —0.8 to —1.1 V *vs* S.C.E.; when the alcohol concentration was raised to 65 % the height of the wave about —0.7 V diminished and another wave about —1.2 V appeared. In strongly alkaline solution two waves are found both of which become smaller with time, probably due to the formation of a carbinol as in the case of phenolphthalein. It seems somewhat unexpected that hydroquinonephthalein is reducible at such positive potentials, when the phthalide ring is assumed to be reduced at about —1.9 V *vs* S.C.E. as in 3,3-(4'-hydroxydiphenyl)phthalide [21]. An explanation similar to that given by Kolthoff for the reduction of phenolphthalein is not likely as no quinoid structure can be formed after removal of a proton; the only possible quinoid structure seems to be an *ortho* quinoid form with the oxygen bridge between the phenyl groups carrying a positive charge. However, the mechanism of the reduction is not clear.

2-(4'-Methoxybenzoyl)benzoic acid pseudoethylester XX shows (Table 4) a single two-electron wave from pH 1 to 10. In more alkaline solutions the compound is hydrolyzed. From pH about 7 minima are found as in the case of phenolphthalein. On the evidence from the infrared investigation the com-

Table 4. Limiting currents in μA and half-wave potentials *vs* S.C.E. at different pH-values for 2-(4′-anisoyl)benzoic acid pseudo-ethylester (XX) and hydroquinonephthalein (XXV). Concentration 10^{-3} M. 0.01 % gelatin added as maximum suppressor.

pH	1.0		3.5		5.5		7.5		9.8		13	
	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$	i_l	$-E_{\frac{1}{2}}$
XX	4.1	0.75	4.2	0.91	4.1	0.98	4.2	1.08[a]	4.1	1.14[a]	—[b]	1.14
XXV	3.5	0.35	3.5	0.43	3.5	0.50	3.4	0.58	3.5	0.73[c]	—[d]	0.79
											—[d]	1.30

[a] Minimum. [b] The compound is hydrolyzed. [c] Abnormal drop oscillations. [d] The wave height diminishes with time.

pound is assumed to possess the structure XX containing a phthalide ring. As a transformation to the normal, non-cyclic ester is unlikely under the conditions employed, and the presence of the phthalide ring also is suggested by the occurrence of the minima, which would not be expected for the non-cyclic ester, it seems likely that the compound in the solution has the assigned structure XX. It is, however, unexpected that this structure would be reducible below −1.0 V *vs* S.C.E. in view of the reduction of phthalide at −2.03 V *vs* S.C.E.[21]

Controlled potential reduction at −1.2 V *vs* S.C.E. in an acetate buffer showed that the wave was due to a two-electron reduction, and the isolated product was 3-(4'-methoxyphenyl)-phthalide.

o-Benzoylbenzoic acid pseudoethyl ester is reduced in the medium used (40 % ethyl alcohol containing buffer and 1 M potassium chloride) in the same manner as XX and different from the normal ester of *o*-benzoylbenzoic acid; in 50 % dioxane containing 0.1 M tetraethylammonium iodide Wawzonek *et al.*[21] found a pH-independent wave at a much more negative potential (about −1.9 V *vs* S.C.E.) for the pseudoester, and this was confirmed in the present investigation. However, in solutions containing less dioxane than about 40 % a wave is visible about −1.1 V *vs* S.C.E. which is the higher the lower the concentration of dioxane is. In 50 % dioxane containing potassium chloride the wave about −1.1 V is found, but on addition of tetraethylammonium iodide this wave disappears. This kind of influence of the supporting electrolyte where one wave is replaced by another one in the presence of capillary-active cations has apparently not been described before and will be discussed in a later communication.

EXPERIMENTAL

The polarograph was a recording polarograph Radiometer Type PO 3a. The capillary delivered 2.16 mg of mercury at a corrected mercury column height of 48.5 cm. The drop time 3.90 sec. (H_2O, open circuit). The capillary constant $m^{2/3}t^{1/6} = 2.13$ mg$^{2/3}$ sec$^{-\frac{1}{2}}$. The apparatus used for the controlled potential reductions was an electromechanical potentiostat of the Lingane-Jones type. The buffer solutions employed were from pH 2.5 to 8 a sodium phosphate-citric acid buffer and from pH 8 to 11 a sodium borate buffer. The medium generally used was 40 % aqueous alcohol containing 1 M potassium chloride and 0.01 % gelatin. In a few cases the alcohol was replaced by peroxide-free dioxane.

For the infrared measurements a Perkin-Elmer Model 21 infrared spectrophotometer was employed. The potassium bromide discs were heated to 100°C for 2—3 min before use[13].

Phenolphthalein oxime was prepared and purified according to Friedländer[1] and Lund[7]. The compound contained one mole water of crystallization. (Found: C 68.32; H 4.72; N 3.86; H_2O 4.43. Calc. for $C_{20}H_{15}NO_4$, H_2O: C 68.37; H 4.88; N 3.98; H_2O 5.13. After drying for 20 h at 120°C *in vacuo* was found: H_2O 1.82.) Infrared spectrum, Fig. 1a.

In a similar manner was prepared *phenolphthalein monomethyl ether oxime* from phenolphthalein monomethyl ether and hydroxylamine, m. p. 228°. (Found: C 72.24; H 4.97; N 3.94. Calc. for $C_{21}H_{17}NO_4$: C 72.16; H 4.93; N 4.03.) The same compound was prepared analogously to the phenolphthalein oxime dimethyl ether (below) from the acid chloride of 2-(4′-methoxybenzoyl)benzoic acid and *p*-aminophenol. (Found: C 72.31; H 4.91; N 4.12; OCH_3 8.72. Calc. for $C_{21}H_{17}NO_4$: C 72.16; H 4.93; N 4.03; OCH_3 8.93.)

Phenolphthalein oxime dimethyl ether: 5.0 g of *o*-(*p*-anisoyl)benzoic acid were refluxed with 15 ml redestilled thionyl chloride for 30 min. The excess of thionyl chloride was removed *in vacuo* from a water bath, $t < 80$°C. 20 ml dry benzene were added to the residue and evaporated *in vacuo*. The residue was dissolved in 40 ml dry benzene, and 5 g of *p*-anisidine + 5 g of triethylamine in 50 ml dry benzene were added. The mixture was warmed for 15 min and after cooling poured into water. By addition of acetic acid pH was lowered to about 4, and the aqueous layer was discarded. The reaction product was extracted from the benzene layer with N sodium hydroxide, and on addition of acetic acid a precipitate, 5.8 g, was obtained. It was dissolved in ether, from which a white compound, 4.0 g, precipitated, m. p. 156°—158°. It was identified as phenolphthalein oxime dimethyl ether (here suggested to be 3-(4′-methoxyphenyl)-3-(N-4″-methoxyphenylamino)-phthalide, IXb) as the infrared spectrum, the polarographic data and m. p. were identical with those of authentic phenolphthalein oxime dimethyl ether[7]. (Found: C 72.85; H 5.20; N 3.91; OCH_3 16.99. Calc. for $C_{22}H_{19}NO_4$: C 73.09; H 5.30; N 3.89; OCH_3 17.18.) Infrared spectrum, Fig. 1c.

In a similar manner were prepared the following compounds: "o-(p-*anisoyl)benz-pseudoanilide*" (3-(4′-methoxyphenyl)-3-(N-phenylamino)-phthalide, Xb), m. p. 161°. (Found: C 76.05; H 5.26; N 4.37; OCH_3 9.30. Calc. for $C_{21}H_{17}NO_3$: C 76.12; H 5.18; N 4.23; OCH_3 9.37.) "o-*Benzoylbenz-pseudo*-p-*anisidide*" (3-phenyl-3-(N-4′-methoxyphenylamino)-phthalide, XIb), m. p. 195° (198°[9]). (Found: C 76.02; H 5.25; N 3.98. Calc. for $C_{21}H_{17}NO_3$: C 76.12; H 5.18; N 4.23.) "o-*Benzoylbenz-pseudoanilide*" (3-phenyl-3-(N-phenylamino)-phthalide), m. p. 220°—221° (220°—221°[22]). (Found: C 79.49; H 4.96; N 4.51; Calc. for $C_{20}H_{15}NO_2$: C 79.72; H 5.02; N 4.65.) "o-*(p-Anisoyl)benz-pseudo-2,6-dimethylanilide*" (2,6-dimethylanil of 2-(4′-methoxybenzoyl)benzoic acid), m. p. 187°—189°. (Found: C 76.41; H 5.82; N 3.98. Calc. for $C_{23}H_{21}NO_3$: C 76.86; H 5.89; N 3.90.)

"o-(p-*Anisoyl)benz-pseudo-N-methylanilide*" (3-(4′-methoxyphenyl)-3-(N-methyl-N-phenylamino)-phthalide): 5.0 g of 2-(4′-methoxybenzoyl)benzoic acid was transformed to the acid chloride as described above. 10 ml N-methylaniline in 50 ml dry benzene were added. After reaction the mixture was poured into water. The benzene layer was washed with dilute acid (too concentrated acid extracts the compound) and dilute alkali. After drying the benzene was removed, and the residue crystallized spontaneously after some days. It was recrystallized from benzene-ligroin. M. p. 103°. (Found: C 76.52; H 5.39; N 4.13. Calc. for $C_{22}H_{19}NO_3$: C 76.50; H 5.54; N 4.07.)

In the same manner was prepared "o-(p-*Anisoyl)benz-pseudo-N-methyl*-p-*anisidide*" (3-(4′-methoxyphenyl)-3-(N-methyl-N-4″-methoxyphenylamino)-phthalide), m. p. 145°—146°. (Found: C 73.52; H 5.72; N 3.74. Calc. for $C_{23}H_{21}NO_4$: C 73.60; H 5.63; N 3.72.)

Phenolphthalein oxime trimethyl ether (4-methoxyanil of 2-(4′-methoxybenzoyl)benzoic acid methyl ester, XIV) was prepared according to Meyer and Spengler[8]. (Found: C 73.43; H 5.52; N 3.95; OCH_3 24.58. Calc. for $C_{23}H_{21}NO_4$: C 73.60; H 5.63; N 3.72; OCH_3 24.80.) Infrared spectrum, Fig. 1e.

"*Phenolphthalein N-methyl-oxime*": 10 g of phenolphthalein and 8 g of potassium hydroxide were dissolved in 40 ml water and heated to 70°. 3.0 g of N-methyl hydroxylamine oxalate in 20 ml water were added. After 5—10 min the blood-red solution was cooled, 100 ml ether added and the mixture acidified with acetic acid. The yellow precipitate dissolved in ether giving a colourless solution. The ether layer was extracted with a mixture of carbonate and bicarbonate, which was acidified with acetic acid. The yellow precipitate was recrystallized from dioxane-water. It smelted unsharply between 160°

and 165°. (Found: C 68.87; H 5.24; N 3.80. Calc. for $C_{21}H_{17}NO_4$, H_2O: C 69.03; H 5.24; N 3.83.)

o-(p-*Anisoyl)benz*-p-*anisidide* was prepared according to Lund[7] by boiling the "pseudo"-compound with acetic anhydride for 2 min., m. p. 175°—177°. In the same manner were prepared o-(p-*anisoyl)benzanilide*, m. p. 190°—192°, o-*benzoylbenz*-p-*anisidide*, m. p. 202° (204°[9]), o-*benzoylbenzanilide* m. p. 195° (195°[22]), o-(p-*anisoyl)benz-2,6-dimethylanilide*, m. p. 238°. (Found: C 76.83; H 6.16; N 3.82. Calc. for $C_{23}H_{21}NO_3$: C 76.86; H 5.89; N 3.90.)

2-(4′-*Methoxybenzoyl)benzoic acid pseudo ethyl ester:* 7 g of the acid was transformed to the acid chloride as described before and treated with excess of ethyl alcohol. The excess alcohol was removed under reduced pressure and the residue dissolved in ether, which was washed with bicarbonate solution; the ether was dried and removed. The residue crystallized spontaneously after some time and was recrystallized from alcohol, 3.5 g. M. p. 76°—78°. (Found: C 71.67; H 5.89. Calc. for $C_{17}H_{16}O_4$: C 71.83; H 5.67.)

Reduction of phenolphthalein oxime: 1.0 g of the compound was reduced at —0.8 V *vs* S.C.E. in a mixture of 15 ml 4 N hydrochloric acid, 10 g potassium chloride, 80 ml water, and 50 ml alcohol. The reduction consumed two electrons per molecule; the yellow colour disappeared during the reduction and some of the reduction product precipitated. After completion the reaction mixture was diluted with water and extracted with ether, which was washed with dilute acid and bicarbonate and dried. After removal of the ether the residue was recrystallized from alcohol, m. p. 254°—256°. It was identified as 2,3-bis-(*p*-hydroxyphenyl)-phthalimidine[3] (2-(4′-hydroxyphenyl)-3-(4″-hydroxyphenyl)-2,3-dihydro-2-*iso*benzazol-1-one). (Found: C 75.69; H 4.94; N 4.38. Calc. for $C_{20}H_{15}NO_3$: C 75.70; H 4.77; N 4.42.)

In a similar manner was performed the *reduction of phenolphthalein oxime dimethyl ether*. The reaction product was identified as 2-(4″-methoxyphenyl)-3-(4′-methoxyphenyl)-2,3-dihydro-2-*iso*benzazol-1-one from m. p. 130° (130°—131°[23]) and analysis. (Found: C 76.49; H 5.53; N 3.88. Calc. for $C_{22}H_{19}NO_3$: C 76.50; H 5.55; N 4.06.) The same compound was isolated from an alkaline reduction.

Reduction of phenolphthalein oxime trimethyl ether: The compound (1 g) was reduced in a mixture of 40 ml water, 100 ml methanol, 30 ml ethyl acetate, 15 ml glacial acetic acid, and 10 g potassium hydroxide. After completion of the reduction (two electrons per molecule) the reduction product was isolated as described above for the phenolphthalein oxime. The product was identical with that obtained above from the dimethyl ether as shown from the m. p. 128°—130° and infrared spectrum.

Reduction of "o-(p-*anisoyl)benz-pseudo-N-methylanilide*": A suspension of 1 g of the compound in 40 % alcoholic acetate buffer was reduced at —0.85 V *vs* S.C.E. consuming 2 electrons per molecule. The compound dissolved during the reduction. The reaction mixture was diluted with water and made acid with mineral acid. The reaction product precipitated (0.5 g); it was identified as 3-(4′-methoxyphenyl)-phthalide from the m. p. 116°—117° (117,5°—118.5°[24]) and an infrared spectrum identical with that of actual 3-(4′-methoxyphenyl)-phthalide.

Reduction of "o-(p-*anisoyl)benz-pseudo-2,6-dimethylanilide*": This compound was reduced at —0.85 V *vs* S.C.E. in 50 % alcohol containing hydrochloric acid and potassium chloride. The reduction required two electrons per molecule, and the product precipitated during the reaction. After dilution of the reaction mixture the product was filtered off and identified as 3-(4′-methoxyphenyl)-phthalide from its m. p. 117° and infrared spectrum.

Reduction of o-(p-*anisoyl)benz*-p-*anisidide:* 1 g of the compound was reduced at —1.6 V *vs* S.C.E. in 40 % dioxane containing 0.5 N potassium hydroxide. After completion of the reduction (two electrons per molecule) the reaction mixture was diluted and acidified with mineral acid. The product precipitated and was identified as 3-(4′-methoxyphenyl)-phthalide from its m. p. 117° and infrared spectrum.

Reduction of o-(p-*anisoyl)benzoic acid pseudo ethyl ester:* The compound was reduced at —1.2 V *vs* S.C.E. in 50 % alcohol containing acetate buffer. The reduction required 2 electrons per molecule, and after removing some of the alcohol the mixture was acidified with mineral acid. The product precipitated and was identified as 3-(4′-methoxyphenyl)-phthalide from the m. p. 117° and the infrared spectrum.

In a similar manner the normal ester *ethyl* o-*benzoylbenzoate* was reduced in a two-electron reduction, and the isolated product was 3-phenyl-phthalide, m. p. 115°, identified from the infrared spectrum.

Reduction of o-*benzoylbenz*-N,N-*diethylamide:* The compound was reduced in 50 % alcohol containing 0.5 N sodium hydroxide and 5 g of potassium chloride at -1.6 V *vs* S.C.E. During the electrolysis a blue colour was observed which, on interruption of the current, faded in the course of half a minute, but reappeared when electrolysis was continued. The reduction required two electrons per molecule, and on acidifying the colourless solution the product precipitated. It was identified as 3-phenyl-phthalide from the m. p. 115° and the infrared spectrum.

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