PHTHALONES AND THEIR STRUCTURAL ANALOGS (REVIEW)

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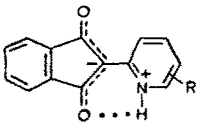
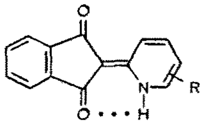
This review is devoted to research on the synthesis, reactivities, practical application, and structural problems of compounds of the phthalone series, primarily pyrophthalones and quinophthalones. The properties and peculiarities of the structures of the indicated compounds are compared with structural analogs that contain other heterocyclic substituents and other β-dicarbonyl systems and also with other betainelike derivatives of β-dicarbonyl compounds. Problems in the development of the chemistry of phthalones are discussed.

Indane-1,3-dione derivatives that contain a heterocyclic nitrogen-containing substituent, the nitrogen atom of which is in the α position with respect to the indanedione residue and consequently, in direct conjugation with the tautomeric β-dicarbonyl system, connected to the methylene group, are called phthalones. Substituents of the necessary type include 2-pyridyl (pyrophthalones), 2-quinolyl (quinophthalones), 2-benzimidazolyl, 2-benzothiazolyl, etc.

Several limiting structures — intraionic (betainelike) (A), aminovinylcarbonyl (with disruption of the cyclic delocalization of the π electrons i.e., the "aromaticity" of the heteroring)(B), and enol (C) — can be written for phthalones. An intramolecular hydrogen bond is formed in each of the three cases. Frequently, without going into the fine points of structures A, B, and C, phthalones with a stabilized "pseudoaromatic" enol chelate ring (D) are depicted. The problem of the greater or lesser contribution of the above-enumerated limiting structures to the real structure of the phthalones must be studied and discussed concretely in each case as a function of substituents R.



A



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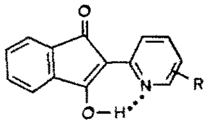

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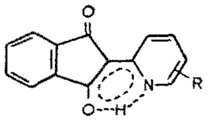

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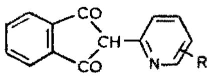

E

In most cases the data necessary for this are not yet available. For this reason, in those cases where the equation of the fine structure is not discussed, it seems simpler to use the conventional depiction of the dicarbonyl system (E).

In a broader sense, betainelike derivatives of any β-dicarbonyl compounds (with an onium heterocyclic substituent connected to the active methylene group) in which there is direct conjugation between the anionic portion of the β-dicarbonyl residue and the onium heteroatom acting counter to the total charge localization can be called compounds of the phthalone type. Heteroatoms can also be found in rings condensed with the aryl residue.

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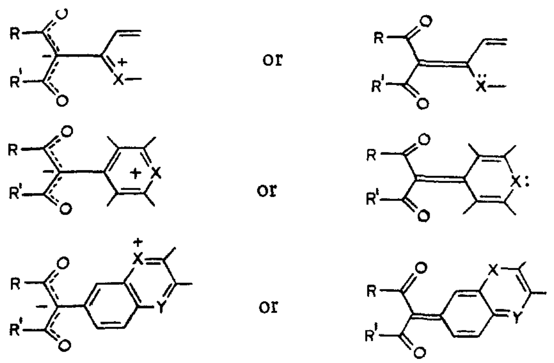


X = NH, NR, O, S, Se; Y = N, CH

Phthalones are interesting in that they absorb light intensively in the visible region (yellow and orange dyes). In addition to a study of the interrelationship between the structure and the color character, an essential problem in the chemistry of phthalones is their fine structure and the reactivities and electrophysical properties that depend on this problem. The possibility of obtaining not only dyes and organic semiconductors but also new biologically active substances on the basis of phthalones seems attractive.

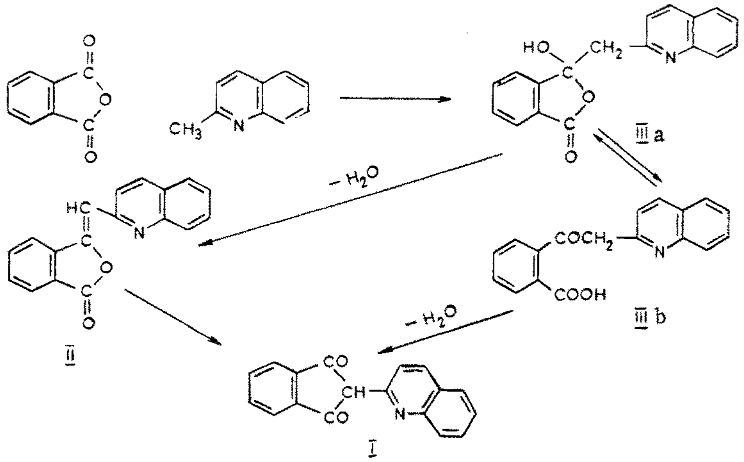
Syntheses of Phthalones

The principal method for the synthesis of phthalones is acylation of the reactive α-(or γ-)methyl groups of heterocyclic bases by derivatives of phthalic acid or its structural analogs. The "phthalone reaction" — direct condensation of heterocyclic bases with phthalic anhydride, which was first described in 1882 [1, 6] — is the simplest and most general method. Other synthetic methods are applicable only in unique cases.

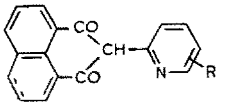
The quinophthalone formula proved in the first studies [5, 6] did not make it possible to make a choice between the isomeric quinaldylidenephthalide and quinolylindane-1,3-dione structures. The observation that, as in the bromination of arylidenephthalides, hydrogen bromide is not evolved in the reaction of bromine with quinophthalone led to the conclusion that phthalones have arylidenephthalide structures [7]. This sort of structure was in better agreement with the concepts of the reactivity of phthalic anhydride and the reasons for the chromaticity of the substances [8]. In a number of systematic investigations [8-21] phthalone condensation and the reactions of phthalones were studied, and isomeric side products were isolated in condensations with quinaldines ("isoquinophthalones"). A product (IIIa), which is probably in equilibrium with open form IIIb [ω-(2-quinolyl)acetophenone-o-carboxylic acid], is formed at up to 130°. When the addition product is heated to 160° water is split out to give quinaldylidenephthalide (isoquinophthalone) (II). The latter is soluble in alkali, and acidification of solutions of it gives acid IIIb, which does not form II reversibly on heating but is converted to 2-(2-quinolyl)indane-1,3-dionequinophthalone (I). Isoquinophthalone II decomposes above its melting point (187°) to give only very small amounts of quinophthalone I. Consequently, II is a side product rather than an intermediate in the phthalone condensation, and, like other arylidenephthalides, is converted to an indane-1,3-dione (quinophthalone) derivative only on reaction with alkoxide. Thus an indane-1,3-dione derivative structure was proved definitively for phthalones. Earlier studies of phthalones have been reviewed [22]. However, inaccuracies are encountered considerably later in the literature (for example, see [23, 24]). (See scheme on following page.)

The conditions of the phthalone condensation — heating phthalic anhydrides with quinaldines, picolines, and other heterocyclic bases containing active methylene groups at 180-250° in the presence of zinc chloride — were not improved to any great extent in the subsequent studies. It was ascertained that the use of a catalyst ($ZnCl_2$) does not affect the yields of quinophthalones [25]. It has been proposed that the condensation be carried out in high-boiling solvents (o-dichlorobenzene [26], trichlorobenzene [27], nitrobenzene [28, 29], 1-chloronaphthalene [28], diphenyl, diphenylmethane, and diphenyl ether [30]). Condensation to give quinophthalones also occurs in dimethylformamide (DMFA) [31]. Quinophthalones are not formed in inert solvents at the boiling point of DMFA (153°).

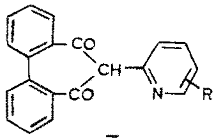
The phthalone condensation is an extremely general reaction and has been carried out successfully with substituted phthalic anhydrides containing halogens, a nitro group, and a carboxyl group, with pyromellitic dianhydride, with 3,6-dithia-3,4,5,6-tetrahydrophthalic



acid [32], etc. Naphthalic and diphenic anhydrides also react under the conditions of the phthalone condensation with quinaldines and 2-methylpyridines [17, 20, 27, 33-39]. The properties of the condensation products — naphthalones (IV) and diphenones (V) — are close to the properties of phthalones. Quinonaphthalone [2-(2-quinolyl)perinaphthindane-1,3-dione] and quinodiphenone [6-(2-quinolyl)-6,7-dihydro-5H-dibenzo[*a*,c]cycloheptene-5,7-dione] are distinguished by yellow luminescence in UV light. Condensation products VI and VII were also obtained from quinaldine and naphthalene-1,4,5,8- and perylenetetracarboxylic acids [27, 36, 40]. In contrast to phthalic anhydride, naphthalic and diphenic anhydrides react with methylpyridines with considerably greater difficulty than with quinaldines, and the reaction always requires the presence of a catalyst, a higher reaction temperature, and a longer condensation time, and the yields are low (20-30%). Dibenzoylquinaldine is obtained under the conditions of the phthalone condensation with benzoic anhydride [41].



IV



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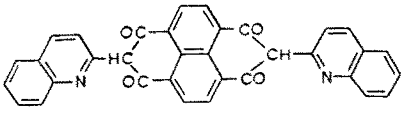
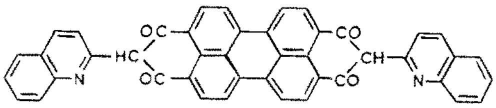


VI



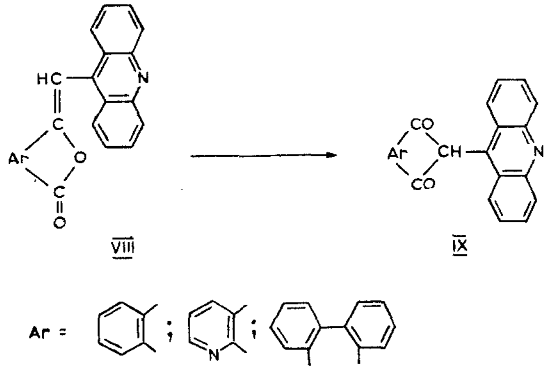
VII

The β-dicarbonyl structure for the yellow products of condensation of quinaldine with diphenylmaleic [7] and succinic anhydrides [8] cannot be considered to be proved.

Various alkyl-, aryl-, alkoxy-, hydroxy-, carboxy-, and haloquinaldines, as well as derivatives of angular benzoquinaldines, have been subjected to condensation with phthalic anhydride.

The reaction of α- and γ-picolines with phthalic anhydride commences only above 180°. A report of the isolation of α-isopyrophthalones [42] was found to be erroneous [16, 21]. The 2-methyl group in 2,4-lutidine and 2,4,6-collidine undergoes condensation [29, 43, 44]. The possibility of the condensation of both methyl groups in 2,6-lutidine [45] seems doubtful [18, 29, 46-48]. Lepidine reacts with phthalic anhydride, but the condensation product does not have the characteristic properties of phthalones [17], and an arylidenephthalide structure is likely for it.

It is possible that steric hindrance has a substantial effect on the course of the phthalone reaction. 3'-Methylpyrophthalone was obtained in 2.1% yield from 2,3-lutidine [48]. 9-Methylacridine does not react with phthalic anhydride in the presence of zinc chloride or sodium acetate, and in acetic anhydride in the presence of triethylamine at 100° it undergoes condensation to give only arylidenephthalide VIII, which is rearranged to an indane-1,3-dione derivative (IX) on reaction with sodium ethoxide [49].

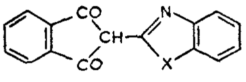


VIII

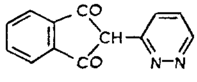
IX

It is known that steric factors have a pronounced effect on the formation of indane-1,3-diones from phthalic anhydrides and an active methylene component in acetic anhydride in the presence of triethylamine [50], but the analogy between the mechanisms of this reaction and the phthalone condensation is not evident and has not yet been discussed in the literature. The formation of a phthalone from 1-methylisoquinoline is unlikely for steric reasons. The relatively unreactive methyl group in 3-methylisoquinoline nevertheless undergoes condensation to give small amounts of 2-(3-isoquinolyl)indane-1,3-dione [48].

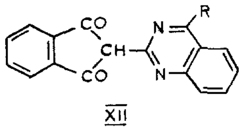
Indane-1,3-dione derivatives and a number of other heterocylic bases with activated methyl groups are formed under the conditions of the phthalone condensation. Yellow substances that have low solubilities and melting points above 350° were obtained from 2-methylbenzimidazoles and 2-methylbenzothiazoles [29, 51-55]. 2-(2-Benzimidazolyl)indane-1,3-dione (X, X = NH) is an isomer of indigo. A product of condensation of 3-methylpyridazine that has a probable phthalone structure (XI) has been described [56]. 4-Phenyl-2-methylthiazole gives 2-(4-phenyl-2-triazolyl)indane-1,3-dione [57]. 2-Methylquinazolines also undergo the phthalone condensation to give yellow dyes XII [57-59]. The effect of linear annelation on the thermal stabilities of dyes of the phthalone type (for example, XIII) has been investigated in the case of 4-hydroxyquinazoline derivatives [60]. As yet, little study has been devoted to these compounds, but they are of undoubted theoretical and practical interest.



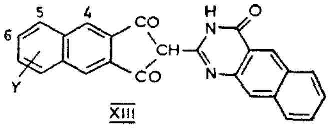
X



XI



XII



XIII

X X = NH, S ; XII R = H, CH_3, OH XIII Y = H; 5,6,7,8-Br; 5-NO_2

From the account above it is evident that the phthalone condensation is an extremely general reaction both for various acid anhydrides and for the most diverse heterocyclic bases. However, the only attempt to correlate the "mechanism and limits of the applicability of the phthalone condensation" was made at the start of the present century [17].

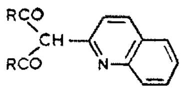
γ-Pyrophthalone and its N-alkyl-substituted derivatives are formed in the condensation of γ-picoline with phthalic acid esters: the nitrogen atom of the alkyl group of the corresponding ester is simultaneously alkylated [61, 62]. This reaction is also analogous to the phthalone condensation.

Other methods for the synthesis of phthalones and their analogs are based on the use of the reactivity of the active methylene group of indane-1,3-dione and other β-dicarbonyl compounds. There are as yet only a few such examples, but the number of accessible compounds of this type is increasing substantially. Pyridine and quinoline N-oxides in the presence of acylating reagents (acetic anhydride, benzoyl chloride, and 4-toluenesulfonyl chloride) react with compounds containing active methylene groups — cyanoacetic, nitroacetic, and malonic esters and indane-1,3-dione — during which the hydrogen atom of the active methylene group is replaced by a 2-quinolyl (2-pyridyl) residue [63]. Quinophthalone was obtained in this manner in 68% yield from indanedione and quinoline N-oxide in acetic anhydride at room temperature [64]. 8-Hydroxyquinoline and 5,7-dichloro-8-hydroxyquinoline N-oxides react under the same conditions to give 8'-acetoxyquinophthalones XIV, which are readily hydrolyzed to 8'-hydroxyquinophthalones (XV) [65]. Impure quinophthalone XVa was obtained in only negligible yield by condensation of 8-hydroxyquinaldine with phthalic anhydride [66]. Under similar conditions, quinoline N-oxide reacts with dimedone and dibenzoylmethane [64, 67] to give 2-quinolyl-substituted diketones (XVI).

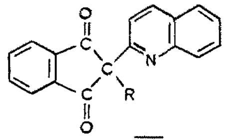
XIV

XV a, b

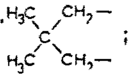
XV a X=H ; b X=Cl



XVI a, b

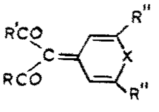


XVII

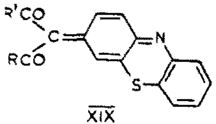
XVI a R—R =

$\mathrm{C(CH_3)_2(CH_2-)_2}$; b R=C_6H_5 XVII R=CH_3, Ar

Acetylacetone reacts with splitting out of an acetyl group to give 2-quinolylacetone [67]. Quinoline N-oxide also reacts with 2-monosubstituted indane-1,3-diones [64]. An alkoxycarbonyl group is split out from esters of 2-carboxyindane-1,3-dione to give quinophthalone, whereas the corresponding 2,2-disubstituted 2-quinolyl derivatives (XVII), which are difficult to obtain by another method (for example, see [29]), are formed from 2-aryl- and 2-methylindane-1,3-diones.

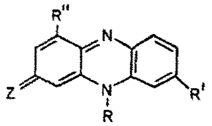
Homologs and structural analogs of γ-pyrophthalone (XVIII, for example) can be obtained by condensation of γ-pyrones and γ-thiopyrones (in the form of pyrylium salts) with the active methylene group of β-dicarbonyl compounds (indanedione, bindone, dimedone, barbituric acid, dibenzoylmethane, and dichlorocyclopentenedione) [68-72]. The absorption and luminescence spectra of the compounds obtained, which are also of practical interest as sensitizers of photographic emulsions, were investigated.



XVIII



XIX

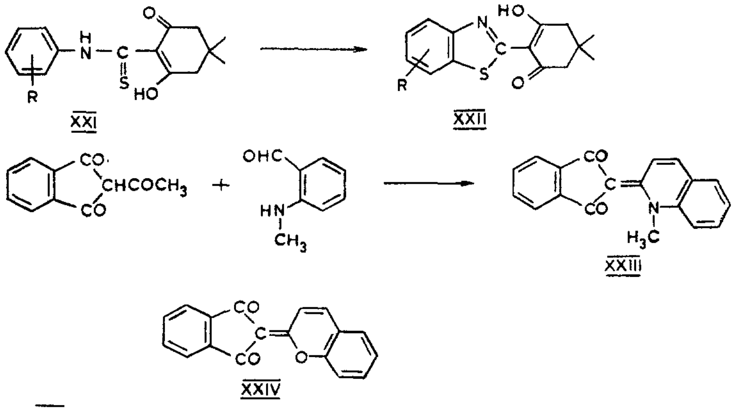


XX

XVIII R''=CH_3, C_6H_5 ; X=O, NCH_3, S ; XX R', R''=H, Cl, CN ; Z=$C(COOC_2H_5)_2$, $C(COC_6H_5)$, $C(CN)COOC_2H_5$

Acridine adds to the methylene group of indane-1,3-dione and dimedone, and the addition products undergo self-oxidation to give 9-acridinyl β-diketones [73]. The indane-1,3-dione derivative proved to be identical to the compounds synthesized from 9-methylacridine and phthalic anhydride [49]. Dyes of the XIX type are formed in the oxidation of phenothiazine with ferric chloride or iodine in the presence of β-dicarbonyl compounds (indanedione, dimedone, isopropylidene malonate, benzylidene malonate, and N,N-dimethylbarbituric acid) [74]. In the presence of alkoxides the quaternary salts of phenazine react with the anions of dicarbonyl compounds to give analogous dyes (XX) [75, 76].

A heterocyclic system can be created with the participation of the substituent of the methylene group of a dicarbonyl compound. Dimedone reacts with aryl isothiocyanates, and acylation product XXI undergoes cyclization under the influence of bromine to 2-(benzothiazolyl)dimedone (XXII) [77]. The formation of N-methylquinophthalone (XXIII) in the condensation of 2-acetylindane-1,3-dione with o-methylaminobenzaldehyde [78] serves as another example.



XXII R = H, CH_3, CH_3O

In the same study [78], an oxygen-containing analog of quinophthalone (XXIV) is mentioned.

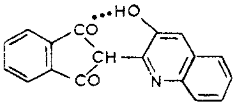
Absorption Spectra and Fine Structure of Phthalones

In contrast to the diketo derivatives of indane-1,3-dione, absorption in the double-bond region is not observed above 1700 cm^{-1} in the IR spectra of phthalones. The IR spectra of phthalones were considered in recent studies [28, 29]. Phthalones are characterized by an absorption band of variable (but not high) intensity at 1680 ± 10 cm^{-1} and very intense absorption at 1500-1640 cm^{-1}. Several bands that are frequently overlapped are observed in this region. The interpretation is difficult. Because of the inadequate solubility of phthalones, the IR spectra of solutions of them have received very little study, and this reduces their value in the discussion of the fine structure of phthalones.

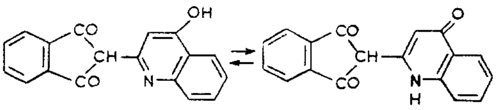
Inasmuch as there is a conjugated system in phthalones, the individual bands do not correspond to the vibrations of definite bonds but are a consequence of interaction and splitting of the vibrations of $C \cdots C$, $C \cdots O$, and $C \cdots N$ bonds with close orders. This is also characteristic for the usual anionic systems of indane-1,3-dione [79]. However, phthalones apparently cannot be relegated to simple anionic systems inasmuch as one of the carbonyl groups participates in the formation of a strong intramolecular hydrogen bond (IHB). The absorption at 1680 ± 10 cm^{-1} is therefore frequently assigned to the stretching vibrations of a free carbonyl group. The same band is also characteristic for imines of 2-acylindane-1,3-diones [80]. However, a similar band of lower intensity is also observed in the IR spectra of γ-pyrophthalone [81] and N-methylated phthalones (1677 cm^{-1} for N-methylquinophthalone [27]), where the effect of an IHB is excluded, and a betainelike structure with a symmetrical conjugated anion of the indanedione system is most likely. This compels one to suppose that the extremely low-intensity absorption of phthalones at 1680 cm^{-1} should be assigned to one of the vibrations of the $O \cdots C \cdots C \cdots C \cdots O$ system shifted to the high wavenumber region because of the electron-acceptor effect of the onium nitrogen atom and the possibility of direct conjugation, which may increase the order of the $C \cdots O$ bond.

The characteristic form of the absorption spectrum and the intensity ratio at 1570-1640 cm^{-1} are typical and may serve as a means to also recognize the phthalone structure in more complex compounds (for example, see [82]). Substantial changes in the IR spectrum under the influence of substituents in the phthaloyl ring (tetrachloro and carboxy derivatives of pyromellitic acid) and in 8'-hydroxyquinophthalones (XV) and their salts, where the spatial closeness of the 8'-hydroxy group or oxygen atom of the phenoxide anion could affect the phthalone system [65], are observed.

The characteristic frequency at 1680 ± 10 cm^{-1} in the spectra of 3'-hydroxyquinophthalones (XXV) is reduced by 30-40 cm^{-1}, and this is ascribed to the effect of a second IHB of the =O···HO type [27]. The same reduction is also observed for 4'-hydroxyquinophthalones (XXVI), where the formation of an IHB is impossible. One cannot exclude the possibility that the structure of XXVI differs from that of the usual phthalone system (the formation of a 4-quinolone structure has been discussed in, for example, [83]). When the 4'-hydroxy group is replaced by a methoxy or acetoxy group, the possibility of this tautomeric form is excluded, and the typical absorption of a quinophthalone (1680 cm^{-1}) is observed. However, one should note that the same effect may be observed as a result of strong intermolecular hydrogen bonds (HB) or the electron-donor effect of the 4'-hydroxy group, which is in direct conjugation with the nitrogen atom.



XXV



XXVI

An increase in the size of the ring of the dicarbonyl system to a six-membered ring in quinonaphthalones (IV) [27] and in 2-(2-quinolyl)dimedone [64] and to a seven-membered ring in diphenones (V) [39] or an acyclic diketone structure [(2-quinolyl)dibenzoylmethane] [64] leads to a decrease of 30-40 cm^{-1} in the higher wavenumber. This is in agreement with the shifts of the absorption maxima in the IR spectra in the anionic systems of the β-diketones referred to above (dimedone, perinaphthindanedione, and dibenzoylmethane) as compared with the anionic system of indane-1,3-dione [we did not observe the band at 1690 cm^{-1} presented in [67] for 2-(2-quinolyl)dimedone in either the crystalline state or in solutions].

Stretching vibrations of O—H or N—H bonds are not found in the IR spectra of phthalones, and this apparently indicates the existence of a strong IHB.

The IR spectra of phthalones consequently provide evidence that there is a conjugated system with an IHB, but it is scarcely possible to unambiguously decide which of the structures (A, B, C, or D) predominate.

The integral intensities of the absorption at 1600-1700 cm^{-1} give a certain amount of information [79]. The intensities of the two absorption maxima (1650-1685 and 1620-1640 cm^{-1}), which are related to the vibrations of the carbonyl groups in a conjugated system (ν_{sym} and ν_{asym}), are compared. One of them (1650-1685 cm^{-1}) is therefore of lower intensity (1.2-1.8 A practical units), whereas the second (1620-1640 cm^{-1}) has considerable intensity (3.5-5.6 A practical units). This provides evidence that the low-intensity band at 1650-1685 cm^{-1} can in no way be ascribed to the absorption of an individual carbonyl group. The increase in the intensity of this band above 2 A practical units may attest to considerable nonequivalence of the two carbonyl groups.

The PMR spectra of phthalones have received little study in view of their low solubility [27, 28, 67, 81]. Even less is known regarding the PMR spectra of indane-1,3-diones. An analysis of the chemical shifts of the protons of the phthaloyl ring as a function of the structure of the phthalone is therefore premature. The proton of the IHB is strongly deshielded and gives a signal at 14-19 ppm, the position of which does not change as the polarity of the solvent changes.

The electronic spectra (Table 1) of phthalones have as yet received little detailed study. The available data constitute evidence that intense absorption is observed at 400 nm, and this is responsible for the yellow color of these compounds. This maximum is shifted bathochromically on passing from pyrophthalones to quinophthalones and is sensitive to the polarity of the solvent. This is most clearly seen for solutions of pyrophthalones in ethanol and carbon tetrachloride (Fig. 1). Particularly strong shifts are observed for the crystalline state: for example, a polycrystalline film of pyrophthalone has an absorption maximum at 350 nm and a weakly expressed inflection at 400-460 nm [84]. The solvatochromism that is characteristic for inner salts of indane-1,3-dione, which attests to a more polar state as compared with the excited state, is observed. Great similarity in the electronic spectra of phthalones and their N-methyl-substituted derivatives is observed [86, 87], and this pro-

TABLE 1. Long-Wave Absorption in the Electron Spectra and Solvatochromic Shifts

Compound	λ_{max}, nm		$\Delta\nu_{max}$ cm^{-1}
	CCl_4	ethanol	
Pyrophthalone	407		1270
	425	387	2300
Quinophthalone	420	410	600
	445	431	700
Quinonaphthalone	415	396	1100
	438	411	1150
Quinodiphenone	422	411	600
	443	431	700
Quinolyldimedone	402	388	900
	425	402	1400
Quinolyldibenzoylmethane	419	402	1000
Pyrodiphenone	336	383	−3700
N-Methylpyrophthalone	407	370	3460
N-Methylquinophthalone	444		560
	465	433	1600
2-Acetylindane-1,3-dione anil	342	336	600

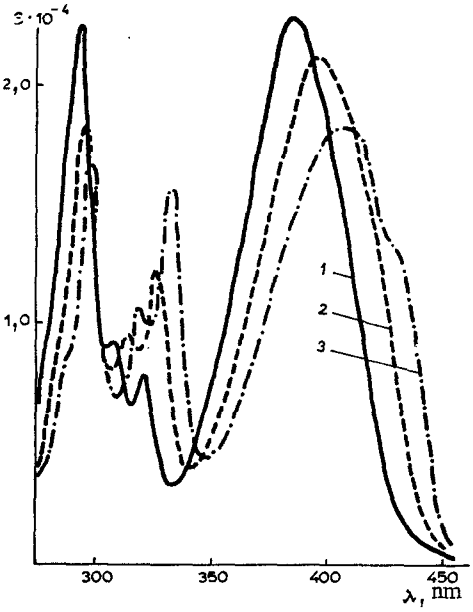


Fig. 1. UV spectra of pyrophthalone: 1) in ethanol; 2) in dioxane; 3) in carbon tetrachloride

vides a basis for assignment of betainelike structure A to phthalones. The structure of the β-diketone residue has little effect on the long-wave absorption. However, it should be noted that differences in the solvatochromic shift of pyrophthalones and quinophthalones are observed. These shifts are considerably less for quinophthalones, and this may constitute evidence for the lower polarity of the ground state, i.e., for a large contribution of structure B or D. A large solvatochromic shift is also observed for N-methylquinophthalone, in which a more polar structure is predicted.

Calculations by the Hückel MO LCAO method for the π-electron system of pyrophthalone [87] have made it possible to assign the long-wave absorption to definite electron transitions. The best agreement with experiment was obtained when pyrophthalone with structure A was considered (without allowance for the effect of the IHB). The long-wave absorption is formed as a result of two electron transitions — a low-intensity transition characteristic for anions of indane-1,3-dione, and an intense band associated with intramolecular transfer of an electron to the onium heterocyclic residue.

Proceeding from these concepts regarding the intense long-wave transition, one may indicate methods for the synthesis of phthalones with more bathochromically shifted absorption. First, one may increase the donor properties of the β-diketone residue, and, second, one may increase the electron affinity of the heterocyclic residue. This has already been confirmed by the available data (compare the derivatives of cyclohexanedione and indanedione, pyrophthalones and quinophthalones; phthalones from 3,6-dithia-3,4,5,6-tetrahydrophthalic acid are red [32]). Derivatives of β-dicarbonyl compounds with phenothiazine and phenazine residues [74, 75] are characterized by intense long-wave absorption at 600-700 nm.

The problem of the actual structure of an individual compound of the phthalone type requires special study in each concrete case. The best methods for this are measurement of the integral intensities of the absorption in the IR spectra and a study of the solvatochromic shifts in the electronic spectra [85]. As revealed above by the studies mentioned, the problem of the fine structure of phthalones reduces to two limiting states A and B, or, more accurately, to the redistribution of the electron density and to localization of the

TABLE 2. Acid-Base Properties of Phthalones

Compound	pK_a		Method*
	I	II	
Pyrophthalone	−1,75	10,2	A 87
	—	13,6	B 48
N-Methylpyrophthalone	−0,5	—	A 87
2-(3-Isoquinolyl)indane-1,3-dione	—	12,2	B 48
Quinophthalone	—	14,9	B 48
γ-Pyrophthalone	2,6	8,7	C 81
2-(3-Pyridyl)indane-1,3-dione	2,3	6,7	C 81

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*Method A involves spectrophotometric measurements of aqueous solutions, method B involves titration in 75% aqueous dioxane ($pK_\alpha = \alpha N_2 + b$), and method C involves titration of the hydrochlorides in dioxane-water (2:1), $pH_{1/2}$.

centers of gravity of the negative and positive charges in these compounds, which are of the inner-salt type. Only quantum-mechanical methods can give an accurate answer for each individual type.

Chemical Properties of Phthalones

Acid-Base Transformations. Phthalones have very weak basic properties because of the decrease in the electron density on the oxygen and carbon atoms in the indanedione grouping under the influence of the electron-acceptor effect of a pyridinium substituent. Phthalones are also very weak acids, and this may also be ascribed to the strong electron-donor effect of the indanedione anion and the formation of an IHB. The electronic spectra of aqueous solutions of pyrophthalone (XXVII) and N-methylpyrophthalone (XXVIII) have been recorded over a wide pH range, and the tautomeric equilibria and protolysis constants have been determined [87] (Table 2). Dipolar ion XXVII which is stabilized by an IHB, exists over a broad pH range of solutions from 5 M HCl to pH 10. Pyrophthalone is protonated exclusively at the oxygen atom to give enol XXVII-E ($pK_E = -1.75$), whereas N-methylpyrophthalone forms a mixture of products of C and O protonation ($pK_E = -0.5$). The differences may be explained by coplanarity and retention of the IHB in enol XXVII-E, which in this case increases the acidity of this particle. Splitting out of a proton from the pyrophthalone is observed only in alkaline media ($pK_A = 10.2$), and this is in agreement with the results of titration in aqueous dioxane solutions [48]. A pK_A value of 10.65 was determined for pyrophthalone in [88], whereas $pK_A = 9.25$ for 5-nitropyrophthalone. This makes it possible to assert that the O—H rather than the N—H bond undergoes photolysis. It is characteristic that the acidity of 2-(3-isoquinolyl)indane-1,3-dione does not differ from the acidity of pyrophthalone, whereas quinophthalone is a weaker acid. The interval between the two photolysis constants is reduced for the isomers of pyrophthalone [γ-pyrophthalone and 2-(3-pyridyl)-indane-1,3-dione] [48].

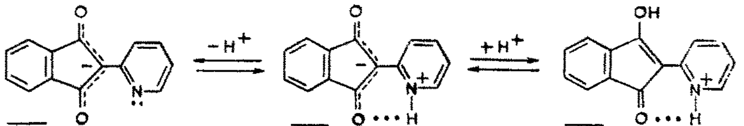
Reaction with Electrophilic Reagents. Dilute nitric acid oxidizes phthalones to phthalic acid [6, 86]. Attempts to effect nitration with nitrogen oxides did not give nitro compounds [8, 9, 42, 89, 90]. Like other indanediones, phthalones are nitrated by concentrated nitric acid or by a mixture of nitric and acetic acid [91-97] to give 2-nitro derivatives XXIX. Nitro derivatives of phthalones rapidly decompose in the presence of traces of nitric acid, but are completely stable after recrystallization. Esters of ω-nitroacetophenone-o-carboxylic acids (XXX) are formed on prolonged refluxing of nitro compounds XXIX in alcohol or by the action of alkoxide. At room temperature 2-nitro derivatives of phthalones are rapidly cleaved by alkali solutions to phthalic acid and α-nitromethyl derivatives of the heterocycles (XXXI) [98, 99].

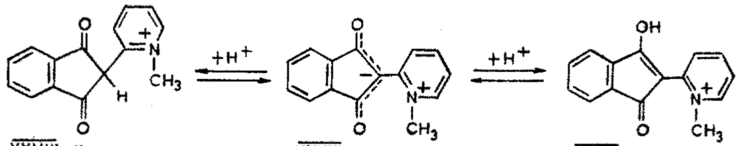
Colorless 2-bromo derivatives [10, 29] are formed by bromination of phthalones, and 2-chloro derivatives XXXII [100] are formed by the action of sulfuryl chloride. The halogen atoms in 2-halo derivative of phthalones are polarized positively and display oxidizing capacity. Debromination to the starting phthalones occurs on reaction with amines, alcohols, and alkali solutions. In aqueous alkali, 2-chlorophthalones are converted to 3-(3-pyridyl)-

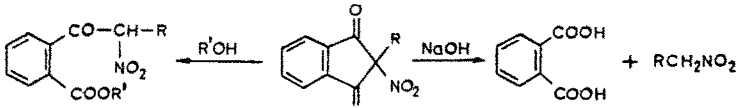
or 3-(2-quinolyl)-4-hydroxyisocoumarins (XXXIII) [101], to which the 2-hydroxyphthalone structure (XXXIV) [44] was initially erroneously assigned. 3-(2-pyridyl)-4-hydroxyisocoumarin is also evidently formed in the oxidation of pyrophthalone with m-chloroperbenzoic acid [102] (structure XXXIV is presented in [102]).

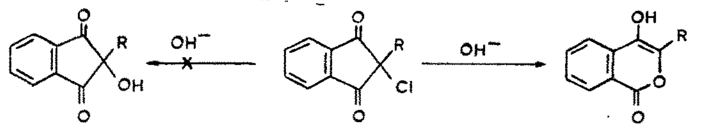
The action of dimethyl sulfate on the sodium salt of pyrophthalone or the potassium salt of quinophthalone gives exclusively N-methyl-substituted products [86]. N-Methylpyrophthalone is also formed as the only producer of methylation with diazomethane. N-methyl-α-pyridone and N-methyl-α-quinolone were isolated from the products of oxidation of N-methylphthalones [86] (picolinic or quinaldinic acid, respectively, are formed in the oxidation of phthalones). The products of alkylation at the oxygen atom (enol ethers) are as yet unknown. Prolonged refluxing of pyrophthalone with benzyl chloride in nitrobenzene gave 2-benzyl-2-(2-pyridyl)indane-1,3-dione (XXXVI), which is possibly formed as a result of rearrangement of N-alkylation product XXXV [103]. Alkylation with phenacyl bromide under the same conditions gives 3-phenyl-1,2-phthaloylindolizine (XXXVII). Quinophthalone reacts similarly [103].

Catalytic Hydrogenation. The catalytic hydrogenation of pyrophthalone over platinum oxide gives, depending on the conditions, 2-(2-piperidyl)indane-1,3-diol (XXXVIII) or complely hydrogenated diol XXXIX; attempts to achieve Clemens reduction or reduction with sodium borohydride were unsuccessful [29]. Dihydrostilbazole-o-carboxylic acid (XL), which is converted to 1-indanone derivative XLI on refluxing in absolute ethanol [104], is formed on treatment with zinc dust in aqueous alkali.


XXVII-A XXVII XXVII-E

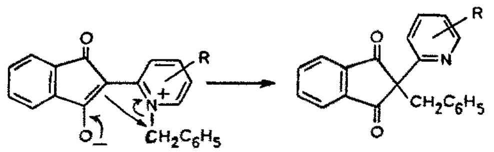

XXVIII-K XXVIII XXVIII-E

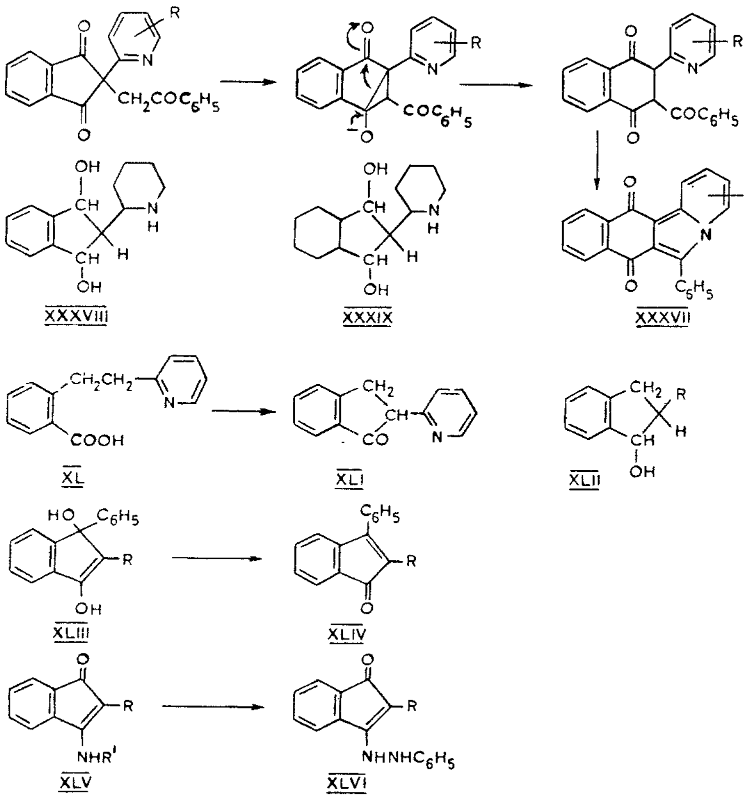

XXX XXIX XXXI


XXXIV XXXII XXXIII

XXIX, XXX, XXXI

R = 2-pyridyl ; 2-quinolyl ; 2-benzimidazolyl ; 2-benzothiazolyl


XXX$^-$ XXXVI



XXXVIII XXXIX XXXVII

XL XLI XLII

XLIII XLIV

XLV XLVI

XXXVI R = H, 5',6' = benzo" XLII R = 2-pyridyl, 2-quinolyl, 2-benzimidazolyl

Pyrophthalone, 6'-phenylpyrophthalone, and γ-pyrophthalone were reduced with zinc dust in acetic acid. A 2-pyridylindanol structure (XLII) was assumed for the reduction products [42], but a mixture of various compounds is evidently formed under these conditions.

Action of Organometallic Compounds on Phthalones. Phthalones react with phenyllithium to give carbinols XLIV, which are readily dehydrated to 3-aryl-1-indenones (XLIV) [29]. These compounds have low toxicity and have been proposed for the treatment of inflammatory processes [105].

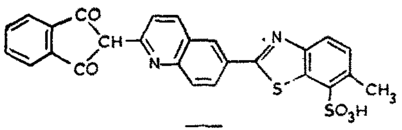
Reaction of Phthalones with Ammonia and Primary Amines. Conjugation of a heterocyclic substituent with a dicarbonyl system suppresses the reactivity of the carbonyl groups. Monoimines are obtained under severe conditions with ammonia and primary amines [8]. Phenylhydrazine does not react with phthalones, whereas the reaction of phthalone imines XLV gives dark-red phenylhydrazones XLVI, which are cleaved to p-phenylenediamine and the starting phthalone on reaction with concentrated hydrochloric acid [16, 21, 42].

Dyes of the Quinophthalone Group

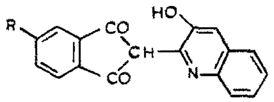
Interest in dyes of the quinophthalone group has increased markedly in the last 10-15 years in connection with their application for dyeing synthetic materials. An extensive review [106] encompassing the history and modern trends in this field was recently published.

Anionic dyes of quinophthalone, usually the salts of the mono- or disulfonic acids, and in some cases the salts of carboxylic acids, impart a yellow color to wool and natural silk, but they do not have adequate photostability. The products of sulfonation of 5,6-benzoquinophthalone and phthaloyl-ring-chlorinated 7,8-benzoquinophthalone are good substantive dyes for cellulose. Dye XLVII, which contains a benzimidazole residue in the quinoline ring, is distinguished by its high substantive character, without the use of mordants, with respect to cellulose-containing materials [107]. Sulfonated bisquinophthalones based on 6,6-diquinaldines also give alkali- and acid-resistant dyes for cotton and silk [107-110]. Quinophthalonesulfonic acids are harmless and are used for dyeing food produts.

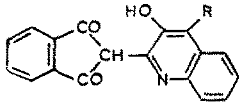
All derivatives of 3'-hydroxyquinophthalone are distinguished by their high photostability. Cationic dyes (which are used to dye polyacrylonitrile and polyester fibers) have been obtained from 5-amino-, 5-carboxy-, and 5-hydroxy-3'-hydroxyquinophthalones (XLVIII) and also from 3'-hydroxyquinophthalone by means of the Mannich reaction and subsequent quaternization (XLIXa) [111-115] or from 4'-bromo-3'-hydroxyquinophthalone by reaction with nucleophilic reagents (for example, XLIXb) [116]. The syntheses of dispersed dyes and pigments, particularly light-fast dyes based on 3'-hydroxyquinophthalone (XLIXc,d) [117, 118], seemed to be the most promising method. Of the total amount of dispersed dyes (primarily azo- and anthraquinone dyes) being produced, ∿ 3% are quinophthalone dyes (in 1968) [106]. Dyes based on quinophthalone derivatives are finding increasing application for bulk dyeing of polymers (polypropylene, polyvinyl chloride (PVC), rubbers, and polyesters). Yellow and red-orange pigments, for example, L, are obtained as a result of condensation of substituted 2-methylbenzimidazoles with anhydrides of o-dicarboxylic acids [119].



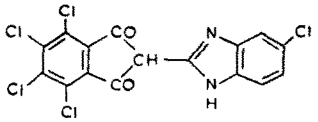
XLVII



XLVIII a-c

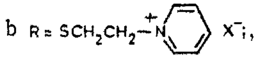


XLIX a-d



L

XLIX a $\mathrm{R = CH_2\overset{+}{N}R'_3X^-}$;,



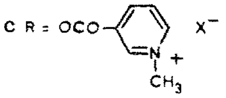
b $\mathrm{R = SCH_2CH_2-\overset{+}{N}}$ $\mathrm{X^-}$;,

c $\mathrm{R = CONR'_2}$;

d $\mathrm{R = SCH_2CH_2NR'_2}$

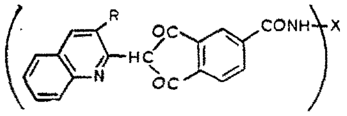
XLVIII a $\mathrm{R = NH(CH_2)_3\overset{+}{N}(CH_3)_3\ X^-}$;

b $\mathrm{R = CONH(CH_2)_3\overset{+}{N}H(CH_3)_2\ X^-}$;

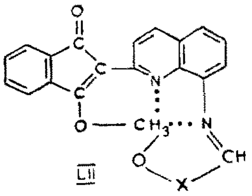


c $\mathrm{R = OCO}$ $\mathrm{X^-}$

Difunctional quinophthalone derivatives are obtained from dianhydrides of pyromellitic and naphthalene-1,4,5,8-tetracarboxylic acids [27, 28]. Stable dyes LI are also formed from 5-carboxyquinophthalone and aromatic diamines [120]. In this respect, quinophthalone derivatives based on tetracarboxydiphenyl oxide dianhydride [82] and 4-hydroxyquinophthalones [30] may be of interest. The latter have good migration resistance and photostability in PVC [106]. New heat-resistant and light-fast pigments have been obtained from 8-aminoquinophthalone. The corresponding phthalimide derivatives are formed with halo derivatives of phthalic anhydrides [121], whereas Schiff bases, which give complexes with metals (LII), are formed with salicylaldehyde [122].



LI



LII X = phenylene, naphthalene

It has been shown [60] in the case of quinazolone-4-phthalones that annelation of the phthaloyl and heterocyclic portions of the phthalone molecule (for example, XIII) increases the thermal stability, the migration resistance, and the photostability and also deepens the colors of these dyes.

Electrophysical Properties of Phthalones

Pyrophthalone derivatives have been proposed as photosemiconductors for the preparation of electrophotographic materials [123]. A study of the electrophysical properties of pyrophthalones in thin-film systems [84] showed that pyrophthalone, tetrachloropyrophthalone, and γ-pyrophthalone have considerable photosensitivity, and the quantum efficiency (β) is 10^{-3}-10^{-1} electron/photon at 300-500 nm.

Physiological Effect of Phthalones and Their Derivatives

γ-Pyrophthalone, N-alkyl-γ-pyrophthalones (particularly the ethyl and isopropyl derivatives), and α-pyrophthalone display considerable anticoagulant activity and low toxicity. Antiphlogistic and analgesic action has been found for these compounds [61, 62]. 3-Arylindenones XLIV have been proposed for the treatment of inflammatory processes [105]. Further study of the physiological action of phthalones and their derivatives may give valuable results for the chemistry of medicinals.

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