ml. of benzene, and 930 mg. of *p*-phenoxyphenol (5 mmoles) was added in four portions as described above. Filtration and evaporation of the yellow solution gave IVh as a yellow oil, yield 1.85 g. (82%).

*Anal.* Calcd. for $C_{30}H_{38}O_3$ C, 80.68; H, 8.59; mol. wt., 446.60. Found: C, 80.50; H, 8.71; mol. wt., 436 (thermoelectric measurement in dioxane).

**4,4-Bis(pentachlorophenoxy)-2,6-di-*t*-butyl-2,5-cyclohexadiene-1-one (VII).**—Active manganese dioxide (26 g.) was added to a solution of 2.66 g. of pentachlorophenol (10 mmoles) and 1.43 g. of 4-bromo-2,6-di-*t*-butylphenol in 300 ml. of benzene. The suspension was shaken under $N_2$ for 30 min. The $MnO_2$ was removed by filtration through a fine sintered-glass funnel and washed with 200 ml. of benzene. Evaporation of the light yellow filtrate gave a light yellow, crystalline residue which was washed with 150 ml. of absolute ethanol; yield 3.05 g. (83%), m.p. 155°. The substance was recrystallized by dissolving in cold chloroform. Addition of absolute ethanol gave fine, colorless needles of VII, m.p. 166–167° dec.

*Anal.* Calcd. for $C_{26}H_{20}Cl_{10}O_3$: C, 42.49; H, 2.72; Cl, 48.25; mol. wt., 734.80. Found: C, 42.24; H, 2.82; Cl, 48.38; mol. wt., 698 (thermoelectric measurement in chloroform).

**Hydrolysis of VII.**—A suspension of VII (500 mg.) in 25 ml. of 96% ethanol was refluxed for 45 min. The clear, yellow solution formed was evaporated *in vacuo*, yielding a semisolid yellow residue. Treatment with 5 ml. of cold petroleum ether (b.p. 30–60°) and filtration gave 305 mg. (84%) of pentachlorophenol, m.p. 189–190°. Mixture melting point with authentic material gave no depression. Evaporation of the filtrate gave a yellow oil that formed yellow crystals of 2,6-di-*t*-butylbenzoquinone; yield 110 mg. (73%), m.p. 67–68° (lit.[14] m.p. 67–68°). The infrared spectrum was identical with that of authentic material.

**Oxidation of 4-bromo-2,6-di-*t*-butylphenol.**—A solution of 2.85 g. of 4-bromo-2,6-di-*t*-butylphenol (10 mmoles) in 175 ml. of benzene was shaken with 20 g. of active manganese dioxide for 35 min. The manganese dioxide was removed by filtration and washed with 50 ml. of benzene. Evaporation of the dark brown filtrate gave a solid, brown residue that was treated with 20 ml. of methanol, filtered, and dried at 105°. The yield of 3,3′,5,5′-tetra-*t*-butyldiphenoquinone was 1.9 g. (92%). The substance formed red-brown crystals upon heating; m.p. 245–246° (lit.[15] m.p. 245–247°). Mixture melting point with authentic material gave no depression.

**Oxidation of Pentachlorophenol.**—A solution of 2.66 g. of pentachlorophenol (10 mmoles) in 175 ml. of benzene was shaken with 20 g. of active manganese dioxide for 35 min. The yellow filtrate obtained after removal of the manganese dioxide was evaporated at room temperature *in vacuo*, yielding a solid yellow residue that was washed with 20 ml. of ethanol. Filtration gave 1.5 g. of yellow crystals having m.p. 165–167°. The substance was dissolved in a little benzene, cold methanol was added, and the mixture was kept at −20° a few minutes. Then most of the solvent was rapidly removed *in vacuo*, yielding 1.2 g. (45%) of 2,3,4,-5,6-pentachloro-4-pentachlorophenoxy-2,5-cyclohexadiene-1-one, m.p. 177–178° (lit.[7] m.p. 177–178°). Its infrared spectrum was completely identical with that of authentic material.

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[14] E. Müller and K. Ley, *Chem. Ber.*, **88**, 601 (1955).

[15] H. Hart and F. A. Cassis, Jr., *J. Am. Chem. Soc.*, **73**, 3179 (1951).

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# Self-Condensation of Phthalide

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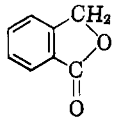
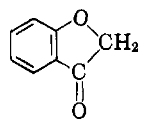
*Received May 1, 1964*

Phthalide (I) is known to react with aldehydes or esters in the presence of base to yield aldol condensation products or phthalidyl ketones.[1–3] It has now been observed that phthalide also can undergo a base-catalyzed self-condensation. The base-catalyzed self-condensation of the two isomers of phthalide, coumaranone (II) and isocoumaranone (III), had been reported earlier.[4,5]


I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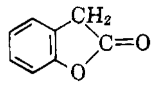
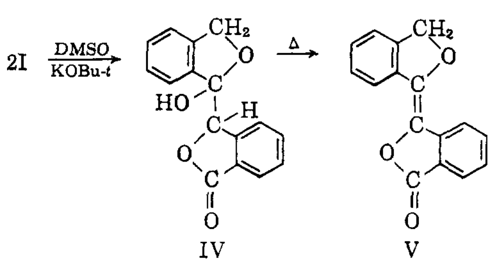
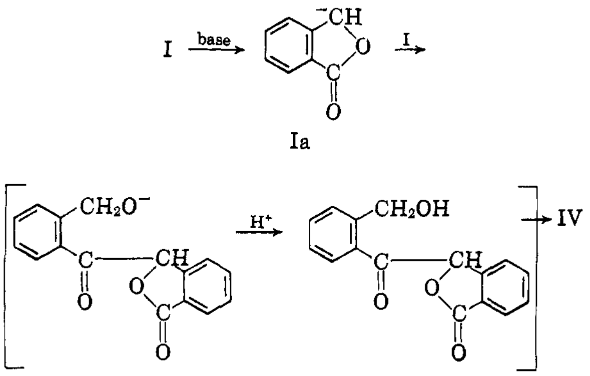

III

Treatment of phthalide in dimethyl sulfoxide with potassium *t*-butoxide at room temperature leads to a dimer (IV) that can be isolated in 75% yield. Upon being heating above its melting point, IV readily eliminates water to yield the stilbene V (phthalanylidenephthalide). This product is formed directly if the self-condensation of phthalide is carried out at 65°. On the basis of its ultraviolet spectroscopical comparison with the known biphthalide the *trans* structure can be assigned to V (Fig. 1).



The mechanism of the formation of IV probably involves the phthalidyl carbanion (Ia) that undergoes an ester condensation which is followed by intramolecular acetalization.



When the base-catalyzed reaction of phthalide was extended to 3-alkoxy-substituted phthalides (phthalaldehydic acid pseudo esters) in dimethyl sulfoxide or dimethylformamide, the only crystalline product was a colorless substance that analyzed for $C_{16}H_8O_4$ (formed in 15% yield). The color produced by $H_2SO_4$–$HNO_3$, the solubility properties, and the melting point (335°)[6] were all in agreement with biphthalide (VI). However, biphthalide has been reported to form yellow crystals.[7] It has been assigned the *trans* structure when its syn-

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[1] R. L. Horton and K. C. Murdock, *J. Org. Chem.*, **25**, 938 (1960).

[2] H. Zimmer and R. D. Barry, *ibid.*, **27**, 1602 (1962).

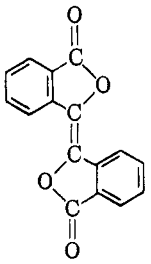
[3] W. Wislicenus, *Ber.*, **20**, 2061 (1887).

[4] K. Fries and W. Pfaffendorf, *ibid.*, **44**, 114 (1911); see also W. Baker and R. Banks, *J. Chem. Soc.*, 279 (1939).

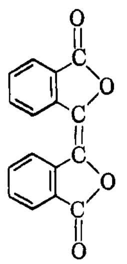
[5] J. N. Chatterjee, *J. Indian Chem. Soc.*, **33**, 175 (1956).

[6] See F. K. Beilstein, "Handbuch der organischen Chemie," 4th Ed., Vol. 19, p. 176; Suppl. I, p. 688; Suppl. II, p. 192.

[7] E. Ador, *Ann.*, **164**, 229 (1872); P. Karrer, *et al.*, *Helv. Chim. Acta*, **11**, 233 (1928); M. Pailer, H. Woerther, and A. Meller, *Monatsh.*, **92**, 1037 (1961).



VI



VII

thesis from *trans*-bifurandione was accomplished.[8] More recently a very convenient new synthesis of (yellow) biphthalide having a melting point of 352–354° was announced.[9] This product had been found to be identical with the biphthalide for which the *trans* structure had been proved.

We have prepared the yellow (*i.e.*, *trans*) biphthalide according to the reported[9] procedure and compared it with our colorless compound. The mixture melting point was between 335 and 345°, not conclusive evidence for the presence of two different compounds. However, the infrared spectrum of the yellow biphthalide was definitely different from that of the colorless biphthalide. While *trans*-biphthalide exhibits only one carbonyl peak at 1780 cm.$^{-1}$ (in KBr), the colorless biphthalide shows a split carbonyl absorption at 1720 and 1740 cm.$^{-1}$ (in KBr).

The ultraviolet spectra (Fig. 1) of the known *trans*-biphthalide and the colorless biphthalide are similar, but show significant differences. However, the differences in the ultraviolet spectra of the two biphthalides are equivalent to those between the spectra of *trans*-stilbene [$\lambda_{\max}$ 295 m$\mu$ ($\epsilon_{\max}$ 27,000 in ethanol)] and *cis*-stilbene [$\lambda_{\max}$ 280 m$\mu$ ($\epsilon_{\max}$ 13,500 in ethanol)].[10a,b] Therefore, one can assign the *cis* structure (VII) to the colorless biphthalide.

The generic relationship between the yellow and the colorless biphthalide was demonstrated by conversion of the *trans*-biphthalide into its colorless isomer by treatment with warm, concentrated sulfuric acid. Attempts to isomerize the *cis*-biphthalide into its *trans* isomer have not been successful.[11] This is in agreement with the findings on the isomerization of *trans*-bifurandione into *cis*-bifurandione, which itself could not be isomerized.[8]

Concerning the mechanism for the formation of biphthalide, the steps involving carbanion formation (1), displacement of the methoxy group (2), and elimination (3) involving a second carbanion intermediate VIII appear to represent a reasonable route. The stereochemistry of the carbanion VIII probably is responsible for the formation of the *cis* rather than the *trans* isomer.

The original older literature on biphthalide actually discloses that "completely colorless" biphthalide had been obtained earlier.[12] "Pure biphthalide" (*i.e.*, colorless) had been obtained by treatment of 3-ethoxyphthalide with potassium cyanide in 90% ethanol,[13] and in absolute ethanol.[14] It was later pointed out that this reaction yields a completely colorless biphthalide (yield 15%), while other procedures give "more or less yellow biphthalide which is very difficult to decolorize completely."[15] These findings apparently had been overlooked whenever the yellow form of biphthalide was reported later.

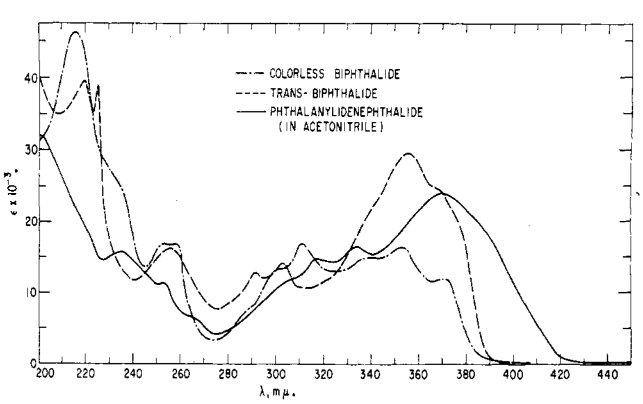
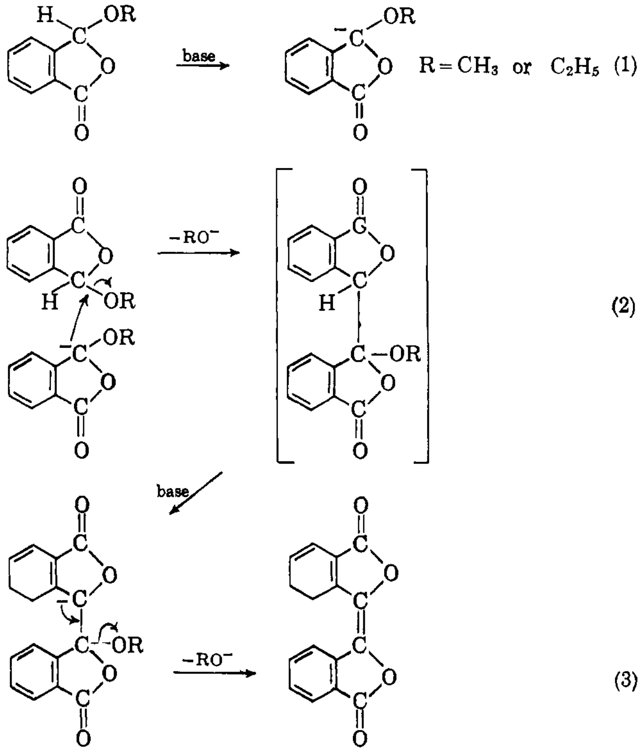


Figure 1.



VIII

## Experimental

Dimethyl sulfoxide was dried over calcium hydride and distilled at about 1 mm. Potassium *t*-butoxide was a commercial product. All condensation experiments were carried out by agitating the reaction mixture with a stream of nitrogen. Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Analyses were carried out by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

**Self-Condensation of Phthalide (IV).**—Potassium *t*-butoxide (2.8 g., 23 mmoles) was added to a solution of 2.68 g. of phthalide (20 mmoles) in 100 ml. of dimethyl sulfoxide. The reaction mixture was kept at room temperature by means of an ice bath, and stirred by a stream of nitrogen. After 1 hr., 50 ml. of ice-

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[8] J. C. Sauer, R. D. Cramer, V. A. Engelhardt, T. A. Ford, H. E. Holmquist, and B. W. Howk, *J. Am. Chem. Soc.*, **81**, 3677 (1959).

[9] F. Ramirez, H. Yamanaka, and O. H. Basedow, *ibid.*, **83**, 173 (1961).

[10] (a) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold, Publishers, Ltd., London, 1955, pp. 233, 234; (b) H. Suzuki, *Bull. Chem. Soc. Japan*, **33**, 379 (1960).

[11] Treatment of colorless biphthalide with warm, concentrated sulfuric acid led to quantitative recovery of the starting material.

[12] J. Wislicenus, *Ber.*, **17**, II, 2178 (1884).

[13] C. Graebe and P. Juillard, *Ann.*, **242**, 219 (1887).

[14] G. Goldschmidt and L. Egger, *Monatsh.*, **12**, 49 (1891).

[15] C. Graebe and A. Landriset, *Ber.*, **24**, 2296 (1891).

water was added to the dark red solution. Acidification with 50 ml. of 0.5 *N* HCl gave a fine crystalline, colorless precipitate, m.p. 155°, yield 2 g. (75%). Recrystallization from warm chloroform raised the melting point to 163–165°. The substance turned yellow upon melting.

*Anal.* Calcd. for $C_{16}H_{12}O_4$ (268.26): C, 71.63; H, 4.51. Found: C, 71.41; H, 4.37.

**3-Phthalanylidenephthalide** (V).—Phthalide (2.68 g., 20 mmoles) in 10 ml. of dimethyl sulfoxide was added to a solution of 2.16 g. of sodium methoxide (40 mmoles) in 35 ml. of dimethyl sulfoxide at 60–65°. The solution turned orange, and after a few minutes brown-red. The reaction mixture was kept at 65° for 25 min. Then about half of the solvent was removed by distillation at about 1 mm. and 65° bath temperature. Addition of 25 ml. of ice-water and 20 ml. of concentrated hydrochloric acid gave a cloudy solution that was twice extracted with 50 ml. of chloroform. The organic layer was separated and the solvent was removed by distillation. To remove traces of water and dimethyl sulfoxide, the oily residue was subjected to vacuum distillation at 1 mm. and 70° bath temperature. Treatment of the yellow, oily residue with methanol gave yellow crystals that exhibit a greenish fluorescence, m.p. 225–227°, yield 1.06 g. (42%). The substance can be recrystallized from hot chloroform. It was only slightly soluble in methanol.

*Anal.* Calcd. for $C_{16}H_{10}O_3$ (250.24): C, 76.79; H, 4.03. Found: C, 76.90; H, 4.18; mol. wt., 287 (thermoelectric measurement in dioxane).

**V from IV.**—IV, 250 mg., was placed in a test tube and heated for 15 min. at 185°. The colorless substance turned yellow with evolution of gas. The solid yellow residue was washed with a mixture of chloroform and methanol, yielding 210 mg. of V (90%), m.p. 225–227°; mixture melting point with V obtained by direct self-condensation of phthalide showed no depression.

***cis*-Biphthalide** (VII).—Potassium *t*-butoxide (2.4 g., 21 mmoles) was added to a solution of 3.3 g. of phthalaldehydic acid pseudo methyl ester (3-methoxyphthalide, 20 mmoles) in 50 ml. of dimethylformamide. The deep red solution was kept under nitrogen for 20 min. Addition of 50 ml. of ice-water and slow addition of 100 ml. of 0.5 *N* HCl gave a colorless precipitate (needles) in 400-mg. yield (15%). The substance can be recrystallized from boiling acetic acid; m.p. 334–335°. It exhibited a bright, blue fluorescence. (*trans*-Biphthalide fluoresces yellow.)

*Anal.* Calcd. for $C_{16}H_8O_4$(264.22): C, 72.73; H, 3.05. Found: C, 72.84; H, 3.08; mol. wt. 286 (osmometric in benzene).

Extraction of the aqueous filtrate with chloroform yielded 250 mg. of yellow needles besides an unidentifiable resin. The infrared spectrum of the yellow crystalline material indicated a mixture of *cis*- and *trans*-biphthalide.

**Conversion of *trans*-Biphthalide into *cis*-Biphthalide.**—*trans*-Biphthalide (264 mg., 1 mmole) was dissolved in 30 ml. of concentrated sulfuric acid at 110° and kept at this temperature under nitrogen for 1 hr. Addition of about 80 g. of ice gave an almost colorless precipitate. It was recrystallized from hot acetic acid, giving 240 mg. of very faintly yellow needles, m.p. 320°. According to ultraviolet and infrared spectra the product was *cis*-biphthalide contaminated with about 20% *trans*-biphthalide.

# Dianhydrophenylosazone Acetates from Isomaltose and Gentiobiose

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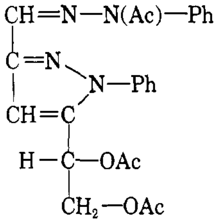
*Received April 3, 1964*

Boiling acetic anhydride converts[2,3] monosaccharide phenylosazones into dianhydrophenylosazone acetates which have a pyrazole ring structure. The structure I was established for the product from any D-hexose precursor by transhydrazonation experiments and, after *O*-deacetylation, by oxidation to give known pyrazole derivatives. Similarly, the dianhydrophenylosazone acetates from the 6-deoxy-L-hexoses and the pentoses were assigned the structures II and III, respectively.

This work describes the unambiguous characterization of I, II, and III by n.m.r. spectroscopy and also reports the conversion of the disaccharides isomaltose and gentiobiose into the corresponding dianhydrophenylosazone acetates (IV and V, respectively).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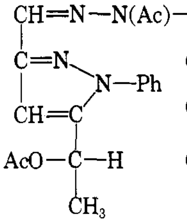
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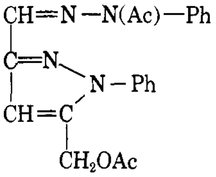
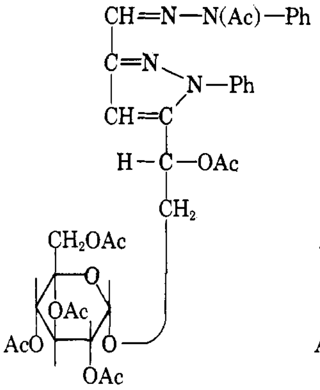
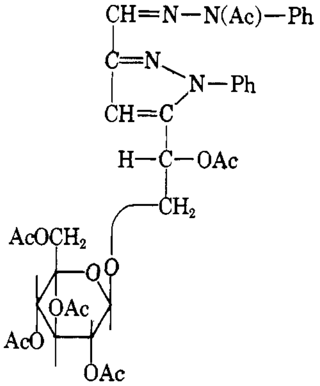

III


IV


V

The n.m.r. spectra of the compounds I, II, and III (Fig. 1–3) permit detailed structural analysis. Aromatic resonances in the $\tau$ 2.5–2.7 region may be assigned to the phenyl group protons and the proton of the pyrazole ring. The singlet of unit-proton intensity at $\tau$ 3.08, 2.98, and 3.05 in the three spectra respectively may be assigned to the strongly deshielded methine hydrogen of the hydrazone function. A singlet of three-proton intensity appears at $\tau$ 7.42, 7.40, and 7.44 in each spectrum, respectively, and may be assigned to the methyl protons of the *N*-acetyl group. The other singlet at $\tau$ 8.01, 8.10, and 7.89, respectively, may be assigned to the methyl protons of the *O*-acetyl groups; for II and III this peak has intensity of three protons, while for I the peak is of six-proton intensity. The spectrum of III shows a two-proton singlet, $\tau$ 4.90, attributable to the methylene group from C-5 of the pentose precursor. The methyl group of II, corresponding to C-6 of the 6-deoxy-L-hexose precursor, appears as a three-proton doublet, $\tau$ 8.45, being split by the adjacent proton, with a spin–spin coupling constant, $J = 6.5$ c.p.s. The latter proton, from C-5 of the 6-deoxy-L-hexose, appears as the expected quartet, $\tau$ 4.08, of unit-proton intensity, spin–spin coupling constant, $J = 6.5$ c.p.s. The D-hexose derivative I showed the methylene group from C-6 of the hexose as a two-proton doublet,

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[1] Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt, U. A. R.

[2] H. El Khadem and M. M. Mohammed-Ali, *J. Chem. Soc.*, 4929 (1963).

[3] H. El Khadem, Z. M. El-Shafei, and M. M. Mohammed-Ali, *J. Org. Chem.*, **29**, 1565 (1964).