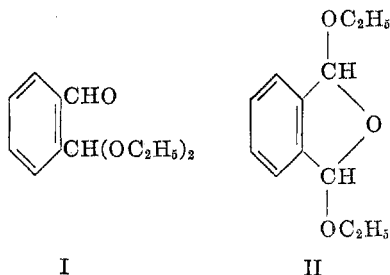
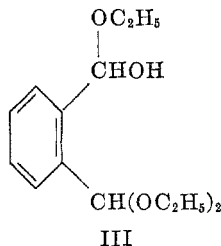


THE ETHYL ACETALS OF *ortho*-PHTHALALDEHYDEMALCOLM R. POWELL¹ AND DEAN R. REXFORD²*Received December 23, 1952*

o-Phthalaldehyde reacts rapidly at the reflux temperature with an equimolar amount of ethyl orthoformate in ethanol solution containing catalytic amounts of ammonium chloride to form *o*-diethoxymethylbenzaldehyde (I) as the principal product and the isomeric 1,3-diethoxy phthalan (II).



Ethanol is necessary to the formation of both products. In the formation of I, ethanol probably plays the part required by Post's mechanism (1). Since the distillation of the ethanol solution of I produces II, the phthalan (II) is probably formed by elimination of ethanol from the acetal-hemiacetal (III).



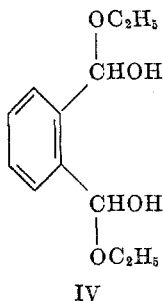
o-Phthalaldehyde can be converted directly to the cyclic acetal (II) by distillation of a solution of the aldehyde in ethanol-ammonium chloride. No mono acetal (I) is found in this distillate.

That the bis-hemi acetal (IV) is an intermediate in the reaction is strongly indicated by the rapid disappearance of the ultraviolet carbonyl absorption band on mixing *o*-phthalaldehyde with ethanol. The curve relating the extinction values in this region to time passes through a clear inflection which is interpreted to mean that two reactions, namely the formation of the mono- and di-hemiacetal, take place, the first of slower rate than the second. The absorption

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spectrum of the equilibrium mixture shows a band at 283 $m\mu$ which is also found in the absorption spectrum of II.



At the same time, intermolecular elimination of water from IV produces several polymers. The polymers appear to contain acetal linkages since they are rapidly hydrolyzed by boiling dilute hydrochloric acid to *o*-phthalaldehyde.

A compound of unknown structure of m.p. 117–117.5° was isolated in small amount from the ethanol-ammonium chloride-ethyl orthoformate reaction mixture.

Thiele and Guenther's mixture of compounds reported to result from the action of light on *o*-phthalaldehyde (2) was found to undergo rapid hydrolysis with boiling dilute hydrochloric acid to yield *o*-formylbenzoic acid.

EXPERIMENTAL

o-Diethoxymethylbenzaldehyde (I). A mixture of freshly crystallized *o*-phthalaldehyde (2), ethyl orthoformate, absolute ethanol, and powdered ammonium chloride in the molar ratio of 1:1.1:3:0.04 was refluxed 10 minutes and, after removal of the low-boiling components, was distilled under reduced pressure. Seventy five per cent of the distillate boiled at 88–90° (1 mm.). The forerun of this fraction was blue as was the residue (about 10% by weight of the reaction products). Redistillation yielded a colorless product of b.p. 86° (1 mm.), n_D^{20} 1.4979. The fraction gave positive aldehyde reactions with *Tollen's* and *Schiff's* reagents.

*Anal.*³ Calc'd for $C_{12}H_{16}O_3$ (208.264): C, 69.21; H, 7.74.

Found: C, 68.85, 68.75; H, 7.92, 7.77.

o-Diethoxymethylbenzaldehyde 2,4-dinitrophenylhydrazone. A portion of the above fraction was warmed with solid 2,4-dinitrophenylhydrazine and the product was recrystallized three times from 95% ethanol. The substance consisted of orange needles of m.p. 163–165° dec.⁴

*Anal.*³ Calc'd for $C_{18}H_{20}N_4O_6$ (397.444): C, 55.66; H, 5.19.

Found: C, 55.57, 55.35; H, 5.24, 5.08.

o-Phthalaldehyde bis-2,4-dinitrophenylhydrazone. The mono 2,4-dinitrophenylhydrazone above on treatment with a conc'd HCl-ethanol solution of 2,4-dinitrophenylhydrazine deposited at once the difficultly soluble dark orange bis-2,4-dinitrophenylhydrazone of m.p. 275° dec. identical with that prepared directly from *o*-phthalaldehyde.

*Anal.*⁵ Calc'd for $C_{20}H_{12}N_8O_8$ (492.360): N, 22.88. Found: N, 22.68.

³ Analysis by Carl Tiedecke, 705 George St., Teaneck, N. J.

⁴ All melting points are micro-corrected.

⁵ Analysis by Joseph F. Alicino, P.O. Box 267, Metuchen, N. J.

1,3-Diethoxyphthalan (II). *o*-Diethoxymethylbenzaldehyde (25 g.) of b.p. 88–90° (1 mm.) was transferred with absolute ethanol to a 9-plate distillation assembly and subjected to a 45-hour fractional distillation. The b.p. ranged from 120–129° (25 mm.) and, except for the first 3 g. which contained some free *o*-phthalaldehyde, the n_D^{25} was constant between 1.500 and 1.498.

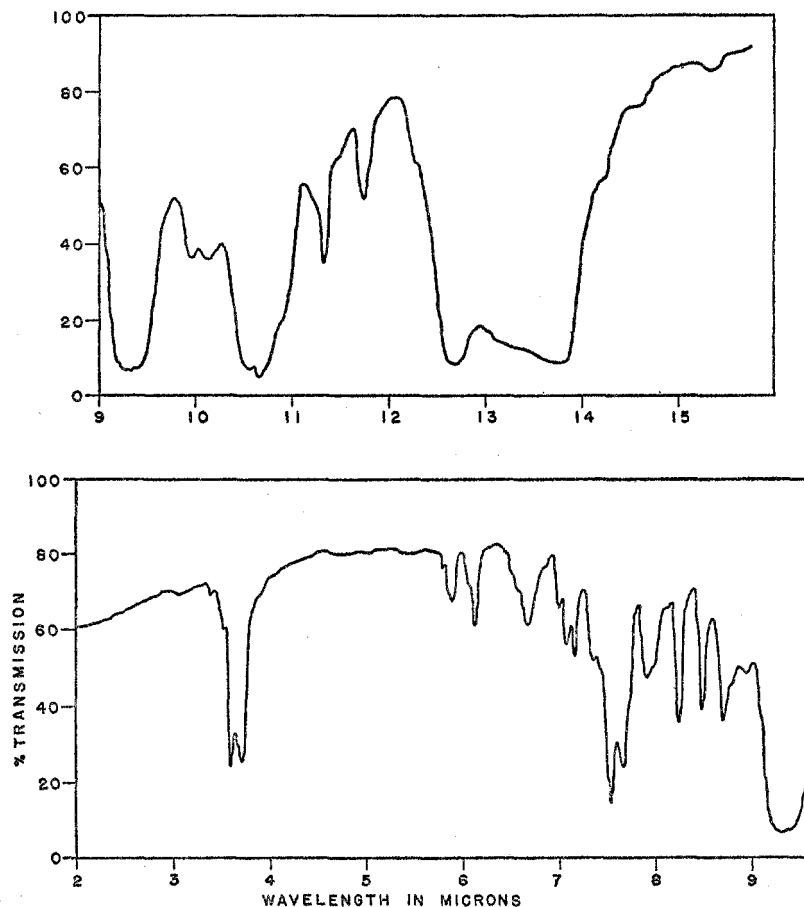


FIG. 1. INFRARED ABSORPTION OF 1,3-DIETHOXYPHTHALAN (II) 10%, IN CCl_4 .

The middle fractions deposited colorless crystals from petroleum ether at -30° . The product was recrystallized seven times from the same solvent when it melted at 54° .

*Anal.*⁵ Calc'd for $\text{C}_{12}\text{H}_{16}\text{O}_8$ (208.264): C, 69.21; H, 7.74.

Found: C, 69.53; H, 7.89.

Mol. Wt. Det'n. Found (cryoscopic): Camphor, 223, 200; Benzene, 201.

The substance gave no reaction with *Tollen's* reagent and deposited no 2,4-dinitrophenylhydrazone in the absence of acid in the reaction mixture. The infrared absorption spectrum of the substance in CCl_4 is shown in Fig. 1.

The curve shows the presence of what is probably an ether band at 9.3μ and has no carbonyl band. The curve is comparable with those of tetrahydrofuran and tetrahydropyran (3).

o-Phthalaldehyde separated from chilled 6 *N* HCl in which the substance had been refluxed 0.5 hours.

Dilute $\text{KMnO}_4\text{-Na}_2\text{CO}_3$ oxidized the substance rapidly at the temperature of the steam-bath to phthalic acid.

Addition of conc'd H_2SO_4 to the colorless CCl_4 solution of the substance causes a yellow color which was discharged by water. The formation of an oxonium salt is postulated.

REACTIONS OF *o*-PHTHALALDEHYDE WITH ETHANOL

(a) Freshly crystallized *o*-phthalaldehyde (0.5 g.) was dissolved in absolute ethanol (0.87 ml., 4 equivalents). Addition of a trace of ammonium chloride to the refluxing solution caused the color to change suddenly to that of permanganate. After evaporation of excess solvent, the residue was dissolved in petroleum ether and chromatographed on 20 g. of alumina (Fisher Scientific Co.). After developing with benzene and ether, the column showed four bands; from top to bottom, black, red, black, and pink. Ethanol eluted a deep purple oil which underwent rapid hydrolysis in hot 6 *N* HCl to *o*-phthalaldehyde.

(b) A similar ethanol reaction mixture was distilled. The pale yellow product of b.p. 145–147° (17 mm.) and n_D^{20} 1.5055, which did not react with 2,4-dinitrophenylhydrazine, deposited crystals at –30°, which on recrystallization from cold petroleum ether were identical with 1,3-diethoxyphthalan. The residue of the distillation was blue.

(c) A 1-ml. aliquot of a 10 ml. solution of 2.8 mg. of *o*-phthalaldehyde in CHCl_3 was diluted to 10 ml. with absolute ethanol containing a trace of ammonium chloride. The absorption at 282 μ was followed with time after the addition of ethanol. The value of $\log \epsilon$ which at two minutes after mixing was 2.20, fell to 1.60 in 18 minutes and levelled off at 1.55 in 70 minutes. The curve relating $\log \epsilon$ to time passes through an inflection point at about 6 minutes and $\log \epsilon$ 2.15. The spectrum of the equilibrium mixture shows a general absorption from 300 μ with $\log \epsilon$ 1.20, to 230 μ with $\log \epsilon$ 2.30. Weak bands are apparent at 253, 258, and 283 μ .

o-Phthalaldehyde in CHCl_3 shows maxima at 259 μ ($\log \epsilon$ 3.86) and 299 μ ($\log \epsilon$ 3.43); 1,3-diethoxyphthalan in the same solvent shows maxima at 253 μ ($\log \epsilon$ 3.13) and 283 μ ($\log \epsilon$ 2.39).

Compound of m.p. 117–117.5°. The chilled latter fractions from the distillation under 1,3-diethoxyphthalan deposited a compound which on repeated crystallization from benzene-ethanol and sublimation (100°, 12 mm.) melted at 117–117.5°.

Anal.⁵ Found: C, 59.63; H, 4.73.

A micro-molecular weight determination (camphor) indicated a molecular weight of about 160. Lack of material prevented the further investigation of the substance.

1,3-Diethoxyphthalan was recovered by chromatography from the mother liquors.

o-Formylbenzoic acid from Thiele and Guenther's mixture (2). A nearly white sample of decomposed *o*-phthalaldehyde which had been stored for some days unprotected from light, was repeatedly washed with hot petroleum ether. The residue was taken up in hot 6 *N* HCl.

The colorless crystals of *o*-formylbenzoic acid of m.p. 94–96° (dec.) which deposited on cooling were collected and recrystallized from dil. HCl when they melted at 97° (dec.) (4). The oxime (5) melted at 118–120° (dec.) and, on heating was converted to phthalimide. The phenylhydrazone consisting of yellow needles (6) melted at 106–107°.

Acknowledgement. A fraction whose ultimate analysis corresponded to *o*-diethoxymethylbenzaldehyde was first prepared in this laboratory with the assistance of Charles A. Thomas III.

SUMMARY

o-Phthalaldehyde has been shown to react with ethyl orthoformate in ethanol in the presence of ammonium chloride to yield *o*-diethoxymethylbenzaldehyde

and 3,5-diethoxyphthalan, the ratio of the two products apparently depending on the effective concentration of ethanol.

The reactions between *o*-phthalaldehyde and ethanol in the presence of ammonium chloride were studied. 1,3-Diethoxyphthalan and acetal polymers have been shown to be products of the reactions.

It has been established that the petroleum ether-insoluble product resulting from the action of light on *o*-phthalaldehyde is related to *o*-formylbenzoic acid.

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REFERENCES

- (1) POST, *The Chemistry of Aliphatic Orthoesters*, Reinhold Publishing Corp., 1943, p. 46.
- (2) THIELE AND GUENTHER, *Ann.*, **347**, 108 (1906).
- (3) SHREYE, HEETHER, KNIGHT, AND SWERN, *Anal. Chem.*, **23**, 281 (1951).
- (4) EHRLICH, *Monatsh.*, **10**, 576 (1889).
- (5) RACINE, *Ann.*, **239**, 85 (1887).
- (6) MITTER AND SEN, *J. Chem. Soc.*, **115**, 1146 (1919).