

194° dec. whose infrared spectrum was identical with that of the sample obtained by oxidizing XIV.

Reaction of Heptanal and Phosphine in the Presence of a Small Amount of HCl (Method B).—A solution of 24.6 g. (0.216 mole) of heptanal, 185 ml. of tetrahydrofuran and 2.08 g. (0.0216 mole) of 38.0% by weight HCl was treated with excess phosphine for 1 hour. The precipitated solid was collected giving 10.5 g. of tetrakis-(1-hydroxyheptyl)-phosphonium chloride, m.p. 123–124°. An additional 0.8 g., m.p. 122–123°, was recovered from the filtrate (total yield 99% based on HCl) along with 10.4 g. of unreacted heptanal, b.p. 40–42° (10 mm.).

Reaction of Phosphine and Heptanal in the Presence of Aluminum Chloride (Method B).—To a suspension of 13.3 g. (0.1 mole) of aluminum chloride in 150 ml. of dry chloroform was added 11.4 g. (0.1 mole) of heptanal with cooling to give a pale orange solution. Uptake of phosphine was vigorous and complete in 20 minutes. The solution was then hydrolyzed cautiously under nitrogen with 100 ml. of 2 *N* HCl. The chloroform layer was washed with 2 *N* HCl and water, separated, dried with sodium sulfate, and evaporated to give 13 g. of a colorless, pyrophoric liquid which had a foul odor. The infrared spectrum showed strong peaks at 3350 and 2290 cm^{-1} . Approximately

80% of this liquid distilled over a wide range at low pressures, but no plateau was observed. Heptanal was present in the distillate, although none was detected in the original liquid.

Reaction of Phosphine and Heptanal in the Presence of Aluminum Chloride (Method A).—A suspension of 35 g. (0.26 mole) of aluminum chloride in 400 ml. of dry chloroform was prepared and dry phosphine passed in until no more was absorbed. While maintaining a slow stream of phosphine, 30 g. (0.26 mole) of heptanal was added with external cooling to maintain a temperature of 20–25°. The mixture was hydrolyzed with 400 ml. of 3 *N* HCl and the chloroform layer was separated, washed with water, and dried with sodium sulfate. A yellow suspension was removed by filtration with the aid of Hyflo. The chloroform was evaporated to give a pyrophoric liquid which partially crystallized on exposure to air overnight. This was triturated with ether and filtered to give 12.4 g. (35%) of tris-(1-hydroxyheptyl)-phosphine oxide, m.p. 112–115°. Repeated recrystallization from ethyl acetate, then cyclohexane, gave the analytical sample, m.p. 113–114°. The infrared spectrum showed strong OH and P→O bands at 3150 and 1135 cm^{-1} , respectively.

Anal. Calcd. for $\text{C}_{21}\text{H}_{45}\text{O}_4\text{P}$: C, 64.25; H, 11.56. Found: C, 63.94; H, 11.76.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STATE UNIVERSITY OF NEW YORK, LONG ISLAND CENTER, OYSTER BAY, N. Y.]

New Reactions of Phosphite Esters: The Conversion of Phthalic Anhydride into Biphthalyl by Trialkyl Phosphites and into Phthalide-3-phosphonates by Dialkyl Phosphites¹

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Triethyl phosphite effects the conversion of phthalic anhydride into biphthalyl (III) in 70% yield. This new reaction is a convenient route to enediol-dilactones and hence to substituted benzoin. The conversion of tetrachlorophthalic anhydride into octachlorobiphthalyl (XIV) by triethyl phosphite is very rapid: $2\text{O}=\text{COC}=\text{O} + 2(\text{C}_2\text{H}_5\text{O})_3\text{P} \rightarrow \text{O}=\text{COC}=\text{COC}=\text{O} + 2(\text{C}_2\text{H}_5\text{O})_3\text{PO}$.

If phthalic anhydride (1 mole) is allowed to react with a trialkyl phosphite, $(\text{RO})_3\text{P}$ (excess), in the presence of a dialkyl phosphite, $(\text{R}'\text{O})_2\text{P}(\text{O})\text{H}$ (1 mole), practically no biphthalyl is formed; instead, a phthalide-3-phosphonate, $\text{O}=\text{COCHP}(\text{O})(\text{OR}')_2$, is produced in excellent yield. The same phthalidephosphonate can be made from *o*-phthalaldehydic acid and the dialkyl phosphite. It is suggested that the phosphorus atom of a phosphite ester attacks the oxygen of the anhydride carbonyl; the resulting intermediate generates a carbene and a *phosphate ester*. The carbene can either dimerize to biphthalyl or can be trapped by reaction with a dialkyl phosphite.

We have investigated the reaction of trialkyl phosphites with *p*-quinones,² *o*-quinones³ and α -diketones.³ Prompted by the formal analogy between quinones and cyclic unsaturated anhydrides we undertook an investigation of the reaction of trialkyl phosphites with phthalic anhydride and with substituted phthalic anhydrides. The results are reported in this paper.

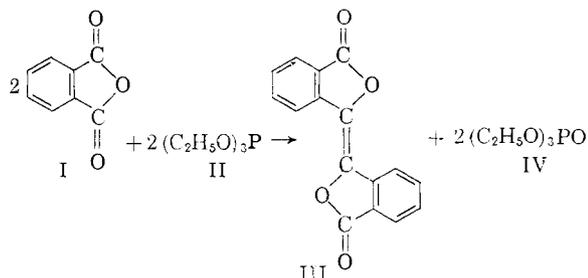
Results

It was found that triethyl phosphite (II) effected the conversion of phthalic anhydride (I) into biphthalyl (III) in satisfactory yield (70%). The reaction was carried out in an excess of the phosphite as solvent and the biphthalyl separated from the solution in nearly pure state. Table I summarizes the results of a typical experiment.

(1) This work is being supported by the National Science Foundation (Grant NSF G 9917). Preliminary experiments were carried out (O.H.B.) at Columbia University under grants from the Public Health Service (Grants CY-3250 and RG-6136 A). Preliminary communication: F. Ramirez, H. Yamanaka and O. H. Basedow, *J. Org. Chem.*, **24**, 1838 (1959).

(2) (a) F. Ramirez, E. H. Chen and S. Dershowitz, *THIS JOURNAL*, **81**, 4338 (1959); (b) F. Ramirez and S. Dershowitz, *ibid.*, **81**, 587 (1959).

(3) F. Ramirez and N. B. Desai, *ibid.*, **82**, 2652 (1960).



It can be seen that most of the excess triethyl phosphite was isomerized to diethyl ethylphosphonate, $\text{C}_2\text{H}_5\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$, during the reaction. Pure triethyl phosphite was not changed under comparable conditions. The stoichiometric amount of triethyl phosphate (IV) was produced only when air was carefully excluded. Otherwise, a great deal of the excess triethyl phosphite was converted into triethyl phosphate, as can be seen from Table II. Molecular oxygen had no effect on pure triethyl phosphite under comparable conditions.

The reaction of other trialkyl phosphites with phthalic anhydride was examined and the results are given in Table III. Trimethyl phosphite was

TABLE I

REACTION OF PHTHALIC ANHYDRIDE (37 G., 0.25 MOLE) WITH TRIETHYL PHOSPHITE (83 G., 0.50 MOLE) IN A NITROGEN ATMOSPHERE, AFTER 48 HR. AT REFLUX TEMPERATURE

Substance	Grams	Substance	Grams
Biphtalyl (III)	24	Diethyl phthalate	2
Triethyl phosphate	37	Phthalic anhydride	3
Triethyl phosphite	3	Residue	8
Diethyl ethylphosphonate	34		

TABLE II

REACTION OF PHTHALIC ANHYDRIDE (15 G.) WITH TRIETHYL PHOSPHITE (33 G., 1:2 MOLE RATIO) AFTER 24 HOURS AT <REFLUX TEMPERATURE>

Substance	Grams (%)	
	Under N ₂	Under O ₂
Biphtalyl (III)	7 (52)	6 (43)
Triethyl phosphate	10 (95) ^a	19 (230) ^a
Triethyl phosphite	11	None
Phthalic anhydride	5 (31)	6 (36)
Diethyl ethylphosphonate	8	12

^a Based on phosphate expected from the biphtalyl isolated. Pure triethyl phosphite does not react with oxygen under comparable conditions.

a very poor reagent. This is attributed to a lower reaction temperature and to the relatively rapid disappearance of the phosphite which was converted into dimethyl methylphosphonate, CH₃-P(O)(OCH₃)₂. Tri-*n*-butyl phosphite was about as effective as the ethyl ester. Biphtalyl seems to be produced at a somewhat faster rate with triisopropyl phosphite; however, yields are lower and side-reactions are more noticeable (see Experimental). No reaction was observed with triphenyl phosphite.

TABLE III

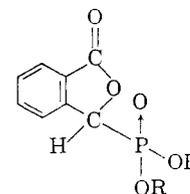
REACTION OF 1 MOLE OF PHTHALIC ANHYDRIDE WITH 2 MOLES OF TRIALKYL PHOSPHITE AT REFLUX TEMPERATURE, UNDER NITROGEN

Run	Trialkyl phosphite	Reacn. time,	
		hr.	Biphtalyl, %
1	Methyl	8	None
2	Methyl	24	5
3	Methyl ^a	24	None
4	Methyl ^b	24	8
5	Ethyl	8	25 ^c
6	Ethyl	24	50
7	Ethyl	37	65
8	Ethyl ^d	70	60
9	Ethyl ^b	40	66
10	<i>n</i> -Butyl ^e	8	20
11	<i>n</i> -Butyl ^e	20	52
12	Isopropyl ^f	8	55
13	Triphenyl ^g	48	None

^a Bromobenzene as solvent: 15 g. of anhydride, 25 g. of phosphite, 55 g. of bromobenzene. ^b Four moles of phosphite per mole of anhydride. ^c Crystals of biphtalyl were observed after 2.5 hours. ^d In *o*-dichlorobenzene as solvent: 15 g. of anhydride, 34 g. of phosphite, 60 g. of *o*-dichlorobenzene. ^e Temperature maintained at 200° (stirring). ^f Six moles of phosphite per mole of anhydride.

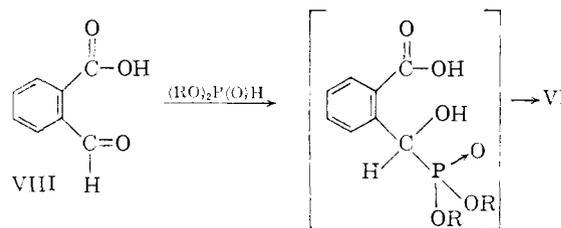
Among the products of the reaction of phthalic anhydride with triisopropyl phosphite we found small amounts of a colorless, crystalline substance which proved to be diisopropyl phthalide-3-phosphonate (V).

V, R = *i*-C₃H₇
VI, R = H
VII, R = CH₃



The structure of this substance was deduced from: (1) elemental analysis and molecular weight determination, which conformed to formula C₁₄H₁₉O₅P; (2) the infrared spectrum which showed a lactone band at 5.60 μ, and a >P→O doublet at 7.83 and 7.93 μ but no OH band; (3) the results of drastic acid hydrolysis: two isopropyl groups were lost, but the phosphorus remained in the molecule in the form of a phthalide-3-phosphonic acid (VI) which still displayed a lactone band in the infrared; from this acid, dimethyl phthalide-3-phosphonate (VII) was obtained with diazomethane; (4) the oxidation of the phthalidephosphonic acid VI to phthalic acid by alkaline permanganate, which is reasonable if the α-hydroxyphosphonate formed by hydrolysis becomes oxidized to an α-oxophosphonate; the latter would readily lose the phosphorus.

Phthalide-3-phosphonic acid (VI) was independently prepared from the reaction of *o*-phthalaldehydic acid (VIII) with diethyl phosphite, (C₂H₅O)₂P(O)H, followed by acid hydrolysis of the resulting ester



It is evident that the formation of diisopropyl phthalide-3-phosphonate (V) from phthalic anhydride and triisopropyl phosphite involves a reduction step and requires a source of hydrogen atoms. Neither propylene⁴ nor acetone could be detected as by-products in this reaction and it seemed likely that the phthalidephosphonate resulted from small amounts of water or of dialkyl phosphite present in the reaction mixture. Consequently, the reaction of phthalic anhydride with dialkyl phosphites was investigated, with the following results:

When a mixture of phthalic anhydride (1 mole), diisopropyl phosphite (1 mole) and triisopropyl phosphite (3 moles) was refluxed, diisopropyl phthalide-3-phosphonate (V) was obtained in good yield. From one mole of anhydride, one mole of diethyl phosphite and three moles of triethyl phosphite, phthalide-3-phosphonic acid (VI) was isolated in 90% yield, after acid hydrolysis of the phosphonate ester. If phthalic anhydride is heated with triethyl phosphite in the presence of *diisopropyl* phosphite or of *dimethyl* phosphite, the products are diisopropyl phthalide-3-phosphonate (V) or

(4) Propylene was one of the products of the thermal decomposition of diisopropyl phthalidephosphonate (V). This decomposition occurred at relatively high temperature.

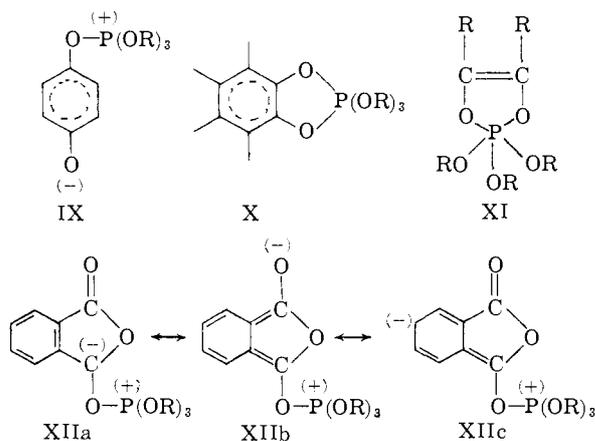
dimethyl phthalide-3-phosphonate (VII), respectively.

In the absence of trialkyl phosphite, the reaction of phthalic anhydride with dialkyl phosphites leads to violent decomposition. This was verified with the methyl, ethyl and isopropyl esters. However, in the particular case of diethyl phosphite, careful control of the reaction temperature (160–170°) permitted the isolation of some phthalide-3-phosphonic acid (VI) (after acid hydrolysis).

We conclude from these experiments that: (1) Some trialkyl phosphites react smoothly with phthalic anhydride to form an intermediate or intermediates which can dimerize to biphthalyl or which can be trapped by a rapid reaction with dialkyl phosphite; (2) the dialkyl phosphites themselves can act as reducing agents toward phthalic anhydride; however, in this role, they are much less effective than the trialkyl phosphites.

Discussion

We have previously shown that trialkyl phosphites tend to form new phosphorus-oxygen bonds in their reactions with the carbonyl functions of *p*-quinones,² *o*-quinones³ and α -diketones.³ In these processes, which occur readily at room temperature, a formal negative charge develops at the carbonyl-carbon and can be borne by the second carbonyl-oxygen (IX, X, XI). A similar situation (XII) is conceivable in the case of cyclic unsaturated anhydrides, although now under less favorable conditions

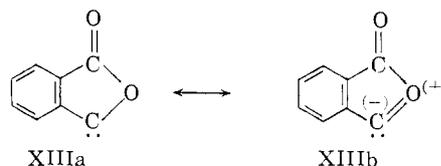


This hypothesis for the initial mode of attack of a trialkyl phosphite on a cyclic unsaturated anhydride⁵ suggests, in turn, two pathways for the formation of biphthalyl. (1) The direct formation of a carbene,⁶ XIII, with ejection of a trialkyl phosphite molecule. The carbene XIII, which should derive some stabilization from resonance structures such as XIIIb, would give biphthalyl (III) by dimerization.

(2) Another path from the dipolar intermediate XII to biphthalyl (III) would be a nucleophilic

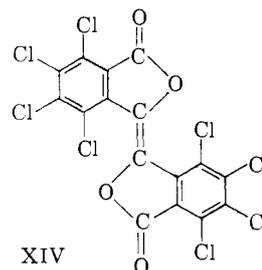
(5) A. J. Speziale and R. C. Freeman, *THIS JOURNAL*, **82**, 903 (1960). An attack of the phosphorus atom of a trialkyl phosphite on the oxygen atom of *N,N*-disubstituted trichloroacetamides was suggested. Other pertinent literature is reviewed in this article.

(6) (a) W. v. E. Doering and A. K. Hoffmann, *THIS JOURNAL*, **76**, 6162 (1954); (b) P. S. Skell and A. Y. Garner, *ibid.*, **78**, 5430 (1956); (c) J. Hine and A. M. Dowell, Jr., *ibid.*, **76**, 2688 (1954).

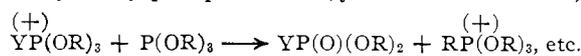


attack of XII on a second molecule of anhydride; this could then form an epoxide and a trialkyl phosphite. It is known⁷ that some simple epoxides are converted to olefins by trialkyl phosphites.

If the formation of the dipolar adduct XII is an important step in the reaction of phthalic anhydride with trialkyl phosphites, tetrachlorophthalic anhydride should exhibit a greater reactivity (*cf.* resonance structure XIIc). Indeed, a considerable amount of octachlorobiphthalyl (XIV) was produced when a solution of tetrachlorophthalic anhydride and triethyl phosphite was refluxed for five minutes.



The dipolar adduct XII is a form of quaternized phosphite ester and as such it could trigger the isomerization of the trialkyl phosphites to the dialkyl alkylphosphonates (*cf.* Tables I and II).

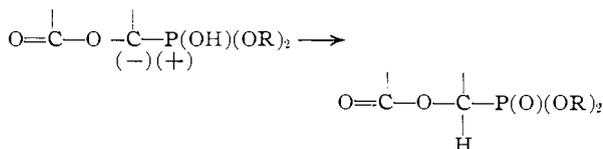


The dipolar intermediate XII or perhaps the carbene XIII itself, might be the oxygen-sensitive species required to explain the effect of oxygen on the course of the reaction (*cf.* Table II). Pure trialkyl phosphites are not oxidized by molecular oxygen under comparable conditions. It may be relevant to recall that the adducts formed from trialkyl phosphites and α -diketones³ (formula XI) react with molecular oxygen to give the α -diketone, the corresponding anhydride, $\text{R}'\text{CO}\cdot\text{O}\cdot\text{COR}'$, and the trialkyl phosphate.⁸ The oxidation phenomena observed in the anhydride reactions may be related to those observed in the α -diketone case.

The hypothesis that a carbene XIII is generated during the reaction of trialkyl phosphites with phthalic anhydride is *sufficient* to explain the formation of the phthalidephosphonates (V, VII), when the dialkyl phosphites are also present. The carbene would be trapped by a rapid and irreversible reaction with the dialkyl phosphite, either by direct insertion at the H-P bond of the tautomer H-P(O)(OR)_2 or by an electrophilic attack on the phosphorus atom of the tautomer P(OH)(OR)_2 to give

(7) (a) C. B. Scott, *J. Org. Chem.*, **22**, 1118 (1957); (b) N. P. Neureiter and F. G. Bordwell, *THIS JOURNAL*, **81**, 578 (1959).

(8) F. Ramirez, R. B. Mitra and N. B. Desai, *ibid.*, **82**, 2651 (1960).

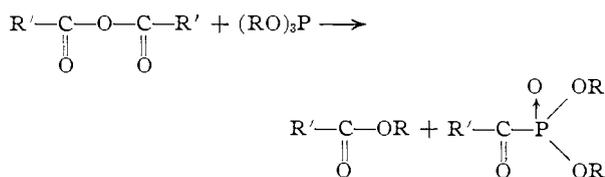


We were unsuccessful in other attempts to trap the carbene, for instance by carrying out the reaction in the presence of olefins such as α -methylstyrene or of secondary amines.

It was not found possible to prepare tetrachlorophthalide-3-phosphonate from the reaction of tetrachlorophthalic anhydride with diethyl phosphite in excess of triethyl phosphite; the only crystalline material isolated was octachlorobiphtalyl.

By analogy with trialkyl phosphites, dialkyl phosphites might be able to reduce phthalic anhydride (in the absence of trialkyl phosphite).

In the past,⁹ reactions of simple anhydrides with trialkyl phosphites have been pictured as involving nucleophilic attacks by phosphorus on the carbonyl-carbon. The outcome would be the formation of carboxylic esters and acylphosphonates. We had earlier¹ considered this type of reaction as the precursor of the carbene intermediate but have found no basis to support it, in the case of cyclic unsaturated anhydrides.



We are extending the scope of the reaction of phosphite esters with suitably constituted anhydrides and are applying the working hypotheses presented in this paper to other carbonyl systems which may show promise in synthesis.

Experimental¹⁰

The trialkyl phosphites were purified by treatment with sodium ribbon followed by fractional distillation. Except when noted, all reactions were carried out under nitrogen.

Reaction of Phthalic Anhydride I with Triethyl Phosphite (II).—A mixture of anhydride (37 g.) and ester (83 g., 1:2 mole ratio) was kept 48 hours at reflux temperature, *under nitrogen*. The colorless solution soon became yellow and then deep red as the sparingly soluble yellow biphtalyl separated out. The mixture was cooled and the biphtalyl (III) was collected and washed with hot benzene; yield 23.5 g. (70%), m.p. 347–350°. One recrystallization from xylene raised the m.p. to 352–354°. The previously reported¹¹ m.p. is considerably lower.

Anal. Calcd. for $\text{C}_{16}\text{H}_{18}\text{O}_4$: C, 72.7; H, 3.0. Found: C, 72.9; H, 3.3.

This material did not depress the melting point of a sample of biphtalyl kindly provided by Dr. J. C. Sauer of E. I. du Pont de Nemours and Co., and prepared in 3% yield from unsymmetrical phthaloyl chloride.¹²

The mother liquid from which biphtalyl (III) had been

(9) G. Kamai and V. A. Kukhtin, *Akad. Nauk, S.S.S.R., Trudy 1-Oi Konferents*, 91–97; *C. A.*, **52**, 241 (1958).

(10) Analyses by Micro-Tech Laboratories, Skokie, Ill., and Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.

(11) Beilstein, "Handbuch der organischen Chemie," 4th Ed., Vol. 19, p. 176 (I 688), (II 192), J. Springer, Berlin, 1918.

(12) P. Karrer, W. Wehrli, E. Biederman and M. dalla Vedova, *Helv. Chim. Acta*, **11**, 233 (1928).

removed was separated into two fractions by a preliminary distillation at *ca.* 2 mm. Fraction 1 was 80 g. of colorless oil collected at 50–110° (2 mm.); fraction 2 was 12 g. of residue.

Redistillation of fraction 1 gave 76 g. of oil, b.p. 50–70° (2 mm.) (fraction 1A) and 3 g. of residue (fraction 1B).

Careful fractional distillation of fraction 1A using a spinning-band column at 4 mm. afforded: 2.5 g. of unreacted triethyl phosphite; 34 g. of diethyl ethylphosphonate, $\text{C}_2\text{H}_5\text{P}(\text{O})(\text{OC}_2\text{H}_5)_2$; and 37 g. of triethyl phosphate. These substances were characterized by comparison of their infrared spectra and of their refractive indexes with those of authentic samples.

The original residue (fraction 2) was subjected to short-path distillation at 0.1 mm., giving 4 g. of distillate (fraction 2A) and 8 g. of residue (fraction 2B). The former (fraction 2A) was combined with fraction 1B obtained above and the mixture was dissolved in benzene. On cooling, 2.3 g. of unreacted phthalic anhydride separated. The mother liquid was evaporated and then submitted to short-path distillation (0.5 mm.) affording 1.5 g. of additional triethyl phosphate. The residue from this distillation was hydrolyzed (1 hour at 80° with 10% aqueous sodium carbonate); the ether-soluble neutral fraction gave 2.1 g. of diethyl phthalate (after distillation) and the water-soluble fraction gave only phthalic acid (0.4 g. after acidification).

Two grams of fraction 2B (residue obtained above) was mixed with 30 ml. of triethyl phosphite and the mixture kept 16 hr. at reflux temperature. No biphtalyl was formed indicating that a possible precursor of the latter was not lost in the 8 g. of unidentified residue.

It was independently established that triethyl phosphate can convert phthalic anhydride into diethyl phthalate at elevated temperature. Triethyl phosphate has no effect on triethyl phosphite even under drastic conditions; no isomerization to phosphonate was observed.

The Effect of Molecular Oxygen on the Course of the Reaction of Phthalic Anhydride with Triethyl Phosphite.

Two comparable reactions were carried with 15 g. (0.10 mole) of phthalic anhydride and 33.2 g. (0.20 mole) of triethyl phosphite at reflux temperature for 24 hours. In one case air was replaced by nitrogen and in the other by dry oxygen. The work up was similar to that detailed above. The results are summarized in Table II. Pure triethyl phosphite does not react appreciably with molecular oxygen. After 24 hr. at reflux temperature in oxygen atmosphere, 18.3 g. of triethyl phosphite was recovered unchanged from an initial charge of 20 g.

The Reaction of Phthalic Anhydride with Various Trialkyl Phosphites.—Table III summarizes the results of several runs in which the reaction time was varied using different trialkyl phosphites. In all cases the reactions were carried out in a nitrogen atmosphere. The biphtalyl which separated was filtered off and washed repeatedly with hot benzene in which it is sparingly soluble; it had m.p. 350–352°.

Reaction of Phthalic Anhydride with Triisopropyl Phosphite. Isolation of Diisopropyl Phthalide-3-phosphonate (V).—A mixture of phthalic anhydride (15 g.) and triisopropyl phosphite (90 g., 1:6 mole ratio) was kept 8 hr. at reflux temperature. On cooling, 7.5 g. (55%) of biphtalyl (III) separated (m.p. 352–354° after hot benzene washings).

The mother liquid was freed from material which boiled below 130° at 10 mm. (1 g., 6% of phthalic anhydride recovered). The residue was allowed to crystallize in the ice-box and was then treated with small amounts of ether and filtered. Colorless crystals of diisopropyl phthalide-3-phosphonate (V) (4 g., 14% yield, m.p. 90–95°) were obtained. The analytical sample had m.p. 98–99° (benzene-cyclohexane).

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_5\text{P}$: C, 56.4; H, 6.4; P, 10.4; mol. wt., 298. Found: C, 55.9; H, 6.5; P, 10.4; mol. wt., 258 ($\text{C}_{14}\text{H}_{18}\text{O}_5\text{P}$ requires C, 53.5; H, 6.1).

The infrared spectrum of the phthalidephosphonate III was examined in carbon tetrachloride and carbon disulfide solutions and in a mineral oil mull: there was no OH band; there were bands at 5.60 μ (strong, sharp, lactone moved to 5.65 in mull), 6.25(w), 6.8(m), 7.20(m), 7.25(in), 7.83 and 7.93 (strong, $\geq\text{P}\rightarrow\text{O}$ moving to 7.85 and 7.98 and reversing intensity in the mull), 9.1(w), 9.5(m), 9.7(m) and 9.9(in), 10.03 (very strong, moving to 10.10 in mull; appears to be typical of P–O–C (isopropyl)).

Further Evidence for the Structure of Diisopropyl Phthalidephosphonate (V). (a) **Acid Hydrolysis.**—The substance V, m.p. 98–99°, obtained from the reaction of phthalic anhydride with triisopropyl phosphite, was treated with hydrochloric acid (1 g. in 10 ml. of 10% aq. hydrochloric acid, at reflux temperature for 7 hr.). The clear solution was allowed to stand overnight at room temperature and then concentrated *in vacuo*. The resulting crystalline material was recrystallized from water affording 0.8 g. of the phthalidephosphonic acid (VI), m.p. 253–254° with decomposition; band at 5.68 μ (lactone) in mineral oil mull.

Anal. Calcd. for $C_8H_7O_6P \cdot H_2O$: C, 41.4; H, 3.9. Found: C, 41.8; H, 4.1.

A solution of the phosphonic acid VI in concd. hydrochloric acid was allowed to reflux for 4 days. The substance was recovered unchanged.

(b) **Reaction of the Phthalidephosphonic Acid (VI) with Diazomethane.**—An ether solution of diazomethane was added to an ethanol solution of the acid VI (0.5 g.) of m.p. 253–254° dec. After the usual work up, 0.4 g. of dimethyl phthalide-3-phosphonate (VII) of m.p. 96–97° (benzene-cyclohexane) was obtained. The infrared spectrum showed the typical 5.60 μ lactone band, the 7.8 μ doublet of the $>P \rightarrow O$ and the very strong 9.6 μ band of P–O–C (methyl).

Anal. Calcd. for $C_{10}H_{11}O_5P$: C, 49.6; H, 4.6; P, 12.8. Found: C, 49.9; H, 4.6; P, 12.7.

(c) **Oxidation of Phthalidephosphonic Acid (VI).**—A solution of the phosphonic acid VI, m.p. 253–254° dec., 0.3 g., in 10 ml. of water containing 0.1 g. of potassium hydroxide was treated with potassium permanganate (0.3 g. added in small portions at ca. 90°). After 3 hr. at room temperature, 3 ml. of ethanol was added, and the mixture was filtered. The filtrate was concentrated *in vacuo* to ca. 3 ml., cooled and acidified (10% hydrochloric acid). The crystals which separated were identified as phthalic acid (0.15 g., after recrystallization from water); m.p. 207–208° alone and mixed with authentic phthalic acid. No phthalic acid was produced by alkaline treatment in the absence of oxidizing agent.

(d) When a solution of the phthalidephosphonate (V) (3 g.) in *o*-dichlorobenzene (3 g., 1:2 mole-ratio) was brought to reflux, decomposition ensued after ca. 5 minutes. Propylene was produced and was identified as 1,2-dibromopropane (3.0 g.). The residue from the decomposition afforded 1.7 g. of phthalidephosphonic acid (VI), m.p. 248–250° after one recrystallization from water.

Reaction of *o*-Phthalaldehydic Acid VIII with Diethyl Phosphite.—A mixture of *o*-phthalaldehydic acid (3 g.) and diethyl phosphite (12 g.) was refluxed for 3 hr. (under nitrogen). No decomposition was noted and the reaction mixture remained practically colorless. The mixture was distilled *in vacuo* and the residue was refluxed with 20 ml. of concd. hydrochloric acid for 8 hr. Approximately 15 ml. of water was removed *in vacuo* and the remaining solution was allowed to crystallize in the cold: 4.1 g. (88%) of phthalide-3-phosphonic acid (V), m.p. 240–245°, was obtained (m.p. 250–253° after one recrystallization from water).

Reaction of Phthalic Anhydride with Triisopropyl Phosphite in the Presence of Water.—The mixture of anhydride I (7.5 g.) and ester (42 g., 1:4 mole-ratio) was kept at reflux temperature under nitrogen for 0.5 hr. At this point, water was slowly introduced (one drop at about 1-hour intervals for a total of 1 ml. of water in 6 hours). The mixture was allowed to cool to room temperature, the small amount of biphtalyl (III) which had separated (0.3 g., m.p. 348–350°) was collected, and the mother liquid was allowed to stand overnight in the ice-box. The diisopropyl phthalidephosphonate (V) (4.3 g., m.p. 98–99°) was filtered and the mother liquid was distilled. The residue left after the removal of low-boiling material (100° at 3 mm.) afforded on cooling a second crop (2.9 g.) of phosphonate; total yield of phosphonate: 7.2 g., 70%.

From the mother liquid, 3 g. of diisopropyl phthalate was collected at ca. 110° (0.2 mm.).

Reaction of Phthalic Anhydride with Triisopropyl Phosphite in the Presence of Diisopropyl Phosphite.—A mixture of anhydride (7.5 g.), triisopropyl phosphite (30 g., 3 mole equivalents) and diisopropyl phosphite (9 g., one mole equivalent) was kept 5 hr. at reflux temperature. The resulting viscous yellow oil was filtered. Only 0.3 g. of biphtalyl could be isolated. The filtrate was distilled *in vacuo* and the residue was treated with aqueous hydro-

chloric acid as before to effect hydrolysis of phthalidephosphonate. The yield of phthalidephosphonic acid VI was 8.7 g. (73%).

Attempted Reaction of Phthalic Anhydride with Diisopropyl Phosphite, (*iso*- C_3H_7O) $_2P(O)H$.—When a mixture of anhydride (7.5 g.) and diisopropyl phosphite (32 g., 1:4 mole ratio) was heated, decomposition began at ca. 140°. At higher temperatures (140–180°) vigorous decomposition ensued. A black gum resulted. No phthalide phosphonate could be isolated, but 4.0 g. of phthalic anhydride was recovered.

Using xylene (5 ml. for 7.5 g. for anhydride and 10 g. of phosphite) and keeping the temperature at ca. 165°, the decomposition was reduced, but after 6 hr. only phthalic anhydride (6.2 g.) could be recovered.

Reaction of Phthalic Anhydride with Triethyl Phosphite in the Presence of Diethyl Phosphite.—The mixture containing 0.1 mole (15 g.) of anhydride, 0.3 mole (50 g.) of triethyl phosphite and 0.1 mole (14 g.) of diethyl phosphite was kept 8 hr. at reflux temperature. The dark orange solution (no biphtalyl was present) was evaporated to one third of its volume (*in vacuo*) and allowed to stand overnight, at which time no crystals had separated. Final distillation left a residue which was subjected to acid hydrolysis and afforded 20 g. (ca. 90%) of crude phthalide-3-phosphonic acid VI.

Reaction of Phthalic Anhydride with Diethyl Phosphite.—The anhydride (6.0 g.) and the diethyl phosphite (14 g.) were kept 7 hr. at ca. 180°. Water was then added to the dark brown viscous oil. No biphtalyl was detected. After the usual acid hydrolysis 3.1 g. (34%) of phthalidephosphonic acid VI was isolated.

Reaction of Phthalic Anhydride with Triethyl Phosphite in the Presence of Diisopropyl Phosphite.—The anhydride (7.4 g.) and triethyl phosphite (1:2 mole ratio) were heated to reflux and the diisopropyl phosphite (9 g., 1 mole equivalent) was then introduced dropwise. After 8 hr. the mixture was cooled. Some biphtalyl (1.0 g.) was formed. The filtrate was worked up as described and afforded 7.6 g. (ca. 50% yield) of diisopropyl phthalide-3-phosphonate (V), m.p. 90–95°.

Reaction of Tetrachlorophthalic Anhydride with Triethyl Phosphite. (a) Without Solvent.—A mixture of anhydride (5.7 g., 0.02 mole) and phosphite (34 g.) was kept at reflux temperature for 5 minutes. The mixture was cooled and filtered; the orange-yellow octachlorobiphtalyl (XIV) was washed with hot benzene; yield 2.2 g. (40%), m.p. 365–370°. The analytical sample had m.p. 375–377° (from *o*-dichlorobenzene); band at 5.60 μ (mineral oil mull).

Anal. Calcd. for $C_{16}O_4Cl_8$: C, 35.5. Found: C, 35.3.

The excess triethyl phosphite was recovered unchanged; no isomerization to diethyl ethylphosphonate was observed.

(b) **In Benzene Solution.**—The solution consisting of 5.7 g. of tetrachlorophthalic anhydride, 17 g. of triethyl phosphite and 50 ml. of boiling benzene was kept at reflux temperature for 24 hr. The octachlorobiphtalyl (2.9 g., m.p. 370–374°, 50% yield) was filtered off.

(c) **In 1,3,5-Trimethylbenzene Solution.**—A solution containing 0.02 mole (5.72 g.) of tetrachlorophthalic anhydride, 17 g. of triethyl phosphite and 24 g. of 1,3,5-trimethylbenzene afforded 2.2 g. (40%) of octachlorobiphtalyl (XIV) after 15 minutes at reflux temperature. Under identical conditions no appreciable amount of biphtalyl (III) was obtained from phthalic anhydride (3 g.) even after 3 hr. After 72 hr., 1.0 g. of biphtalyl was isolated and 1.1 g. of phthalic anhydride was recovered.

(d) Octachlorobiphtalyl (XIV) reacts further with triethyl phosphite. For instance, a suspension of octachlorobiphtalyl (2.8 g.), triethyl phosphite (8.5 g.) and 1,3,5-*sym*-trimethylbenzene (12 g.) was kept 10 hr. at reflux temperature (ca. 150–155°); only 0.2 g. of octachlorobiphtalyl was recovered. Likewise, practically all the octachlorobiphtalyl disappeared in about 2 hr. when a mixture of XIV (2.0 g.), triethyl phosphite (8.5 g.) and triethyl phosphate (8.5 g.) was heated (ca. 180–190°). These conditions obtain in the original reaction of tetrachlorophthalic anhydride with triethyl phosphite. The times given in a, b and c above gave, roughly, optimum yields.

Reaction of Tetrachlorophthalic Anhydride with Triisopropyl Phosphite.—A mixture of anhydride (5.7 g.)

and phosphite (30 g.) gave 2.2 g. of octachlorobiphtalyl (XIV) (40%, m.p. 375° after hot benzene washings) after 5 minutes at reflux temperature.

Reaction of Tetrachlorophthalic Anhydride with Triethyl Phosphite in the Presence of Diethyl Phosphite.—The anhydride (5.72 g.), triethyl phosphite (20 g.) and diethyl phosphite (5.5 g.) (1:6:2 mole ratio) were heated to reflux and kept there for 5 minutes. On cooling, 1.65 g. (30%)

of octachlorobiphtalyl (XIV), m.p. 375–377°, separated.

In the absence of diethyl phosphite, the yield of octachlorobiphtalyl was 40%.

Attempted Reaction of Phthalic Anhydride with Triphenyl Phosphite, (C₆H₅O)₃P.—A mixture of anhydride and ester was kept 48 hours at about 200°. From the brown mixture 87% of unreacted phthalic anhydride could be recovered. No biphtalyl was detected.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY, NEW YORK 58, N. Y.]

Sydnones. III. Preparation and Interconversion of Mercured Derivatives of N-(3-Pyridyl)-sydnone^{1–3a}

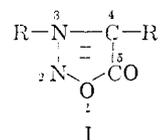
BY JACK M. TIEN AND I. MOYER HUNSBERGER^{3b}

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Mercuration of N-(3-pyridyl)-sydnone (II) has produced either the sydnone-mercuric chloride "adduct" (V), C-chloromercuri-N-(3-pyridyl)-sydnone (VI) or C,C'-mercuri-bis-[N-(3-pyridyl)-sydnone] (VII), depending on the reaction conditions. The adduct V has been converted to VI and to VII. Transformation of VI to VII was accomplished in pyridine solution at room temperature, while VII was converted to VI with excess mercuric chloride. All reactions proceeded in high yield. Sydnones undergo electrophilic substitution virtually as easily as thiophene. Objections to the tropone-like formulation (XI) of sydnones are presented. Preparation of N-(3-pyridyl)-glycine hydrochloride via a Strecker-type reaction between 3-aminopyridine and glycolonitrile is more convenient than the earlier process and permits the preparation of large quantities of sydnone II.

Introduction

Considerable effort has been expended on the preparation of a large variety of sydnones (I) and on attempts to elucidate the unusual bond structure of the sydnone ring.⁴ The quasi-aromatic nature of this ring was recognized as early as 1946,⁵ and N-phenylsydnone (I, R = C₆H₅, R' = H) was reported to undergo halogenation^{5b,6a–c} and nitration^{6d} under very mild conditions. Recent work in Japan,⁷ in the Soviet Union⁸ and in Eng-



land⁹ has concentrated on exploring the chemical reactions of sydnones and has provided additional evidence for the aromatic nature of the sydnone ring. Thus, sydnones unsubstituted in the 4-position (I, R' = H) have been sulfonated with dioxane-sulfur trioxide,^{8a} acetylated in the presence of boron trifluoride etherate^{8b} and deuterated with deuterium sulfate.^{9b}

The successful mercuration of N-phenylsydnone^{7b,8a} suggested to us that the sydnone ring undergoes electrophilic substitution as easily as thiophene. Accordingly, we have found that sydnones can be formylated at the 4-position by reaction with N-methylformanilide and phosphorus oxychloride.¹⁰ The present work on the mercuration of N-(3-pyridyl)-sydnone (II) was initiated in order to extend the analogy between sydnones and thiophene and to investigate the effect mercuration would have on the unusual phototropism exhibited by II.^{2,11} The known phototropism of certain compounds containing mercury¹² and the antiseptic and fungicidal activity of 3-pyridyl-mercuric chloride¹³ provided added incentive for this study.

Nakahara and Ohta^{7b} obtained C-chloromercuri-N-phenylsydnone (III) by mercuration of N-

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(2) Paper II, J. M. Tien and I. M. Hunsberger, *THIS JOURNAL*, **77**, 6604 (1955).

(3) (a) Supported, in part, by a research grant (CY-2962) from the National Cancer Institute of the Public Health Service and by the U. S. Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under Contract No. AF18 (603)-127. Reproduction in whole or in part is permitted for any purpose of the United States Government. (b) To whom all inquiries should be sent: Department of Chemistry, University of Massachusetts, Amherst, Mass.

(4) For a recent review on sydnones and other "mesoionic" compounds see W. Baker and W. D. Ollis, *Quart. Revs. (London)*, **11**, 15 (1957). Also consult: H. U. Daeniker and J. Druex, *Helv. Chim. Acta*, **40**, 918 (1957); P. Zuman, *Z. physik. Chem. (Leipzig)*, Sonderheft July, 243 (1958); W. Pütter and G. Wolfrum (to Farbenfabriken Bayer Akt. Ges.), German Patent 1,069,633 (Nov. 26, 1959); Farbenfabriken Bayer Akt.-Ges., British Patent 823,001 (Nov. 4, 1959); W. H. Edgerton (to Smith, Kline and French), U. S. Patent 2,916,495 (Dec. 8, 1959).

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