A New Synthesis of Diphenyl *n*-Alkylphosphonates

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Diphenyl *n*-alkylphosphonates having large alkyl groups (C_8 or higher) can be prepared in one step in *ca.* 70% yield by heating triphenyl phosphite with the appropriate alcohol at 220–250° in the presence of a suitable halide catalyst, e.g., sodium iodide. Evidence has been obtained that the reaction proceeds through alkyldiphenyl phosphite intermediates, which are then rearranged to the isomeric phosphonates.

Diphenyl alkylphosphonates constitute a class of organophosphorus esters which are of value as chemical intermediates.[1] They have been prepared in a number of ways, among which are the pyrolysis or hydrolysis of adducts of alkyl halides and triaryl phosphites,[2] the reaction of alkylphosphonic dichlorides with phenol or sodium phenoxides,[3,4] and the reaction of alkyl tetrachlorophosphoranes with phenols.[4] For the preparation of α-hydroxyalkylphosphonate esters, the reaction of diphenylphosphorochloridite, $(C_6H_5O)_2PCl$, with carbonyl compounds has been used.[5] Recently, Rydon and Landauer have utilized the reaction between alkyl halide–triphenyl phosphite adducts and a wide variety of alcohols to transform the alcohol into the corresponding halide[6]:

$$(C_6H_5O)_3\overset{+}{P}R,\ X^- + R'OH \longrightarrow (C_6H_5O)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}R + R'X + C_6H_5OH \quad (1)$$

Diphenyl alkylphosphonates are also products of this reaction. This halide preparation may be carried out by simply heating together triphenyl phosphite, the alcohol, and a reactive alkyl halide.

Results.—This paper is concerned with a one-step synthesis of diphenyl alkylphosphonates by the halide-catalyzed reaction of the higher primary alcohols (C_8 and above) with triphenyl phosphite:

$$ROH + (C_6H_5O)_3P \xrightarrow[\text{Catalyst}]{\text{Halide}} R\overset{\overset{\displaystyle O}{\uparrow}}{P}(OC_6H_5)_2 + C_6H_5OH \quad (2)$$

The synthesis was best conducted by treating equimolar amounts of the alcohol and phosphite at 220–250° for approximately twenty hours in the presence of 2–10 mole% (relative to alcohol or phosphite) of catalyst. Extensive investigations of the preparation of diphenyl dodecylphosphonate by this reaction were made, the details of which are summarized in Table I. The yields under the optimum conditions (runs 10–14, 16, and 21) were consistently between 64 and 74%. The other homologs prepared are listed in Table II. This synthesis is markedly superior to the best

TABLE I

DIPHENYL DODECYLPHOSPHONATE SYNTHESES

Run No.	Catalyst	Moles of[a] $(C_6H_5O)_3P$	Mole % Catalyst	Temp., °C.	Time, Hr.	Yield, $RPO(OC_6H_5)_2$
			Bromides			
1	$C_{12}H_{25}Br$	0.167	...[b]	200	20	22
2	$C_{12}H_{25}Br$	0.10	...[b]	180	5	9
3	$C_{12}H_{25}Br$	0.10	100	200	20	61
4	$C_{12}H_{25}Br$	0.10	20	200	20	50
5	$C_{12}H_{25}Br$	1.00	5	240–250	12	54[c,e]
6	LiBr	0.10	2	220	20	17
7	CsBr	0.20	5	200	20	...[e]
			Iodides			
8	$C_{12}H_{25}I$	0.165	...[b]	180	5	30
9	$C_{12}H_{25}I$	0.352	10	200	20	55
10	$C_{12}H_{25}I$	0.10	10	220	20	65
11	$C_{12}H_{25}I$	0.10	5	200	40	68
12	$C_{12}H_{25}I$	1.00	5	250	18	71
13	$C_{12}H_{25}I$	0.50	5	235	20	68
14	$C_{12}H_{25}I$	1.27	10	250	16	74[c,f]
15	NaI	0.25	5	200	20	57
16	NaI	1.00	5	225	20	64
17	I_2	0.100	2	220	20	36
18	NaI	1.50	10	180–230	2	59[c,d,e,g]
19	$C_{12}H_{25}I$	1.50	10	180–208	4	...[c,d,h]
20	$C_{12}H_{25}I$	1.50	5	185–210	20	39[c,e]
21	NaI	2.08	10	220–225	19	71[c]
			Chlorides			
22	$C_{12}H_{25}Cl$	0.20	10	200	20	...[i]
23	LiCl	0.10	2	200	20	10

[a] In all reactions equimolar amounts of ROH and $(C_6H_5O)_3P$ were used. The indicated mole % of catalyst is relative to either reactant and not to the combined number of moles of alcohol and phosphite. [b] No alcohol; the phosphite and alkyl halide were heated together, then the reaction was worked up by hydrolysis, extraction, and distillation. [c] Phenol swept from reaction during heating period with nitrogen stream. In all other runs, the phenol was returned to the reaction by a reflux condenser. [d] Runs No. 18 and 19 combined and converted to phosphonate by heating with dodecyl iodide for 16 hr. at 225°. [e] Mixture of phosphonate and alkyl aryl phosphites formed. [f] Half of catalyst added during reaction. [g] Creased flask used. [h] Principally alkyl aryl phosphites formed (see Experimental). The distillate from the reaction amounted to 157 g., theory being 146 g. [i] Only alkyl aryl phosphites formed.

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[1] K. D. Berlin and G. B. Butler, *Chem. Revs.*, **60**, 243 (1960).

[2] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley & Sons, Inc., New York, 1950, pp. 122, 328.

[3] Fr. Guichard, *Ber.*, **32**, 1572 (1899).

[4] A. Michaelis and A. Fleming, *Ber.*, **34**, 1291 (1901); M. I. Kabachnik, P. A. Rossiiskaya, and N. N. Novikova, *Izvest. Akad. Nauk. S.S.S.R., Odtel Khim. Nauk.* **1947**, 97; *Chem. Abstr.*, **42**, 4132 (1948); A. Michaelis, *Ann.*, **181**, 265 (1876).

[5] J. B. Conant, V. H. Wallingford, and S. S. Gandheker, *J. Am. Chem. Soc.*, **45**, 762 (1923).

[6] H. N. Rydon and S. R. Landauer, *J. Chem. Soc.*, 2224 (1953); *Chem. & Ind.* (London), 313 (1951); Brit. Pat. 695,468, Aug. 16, 1951; Brit. Pat. 698,699, Jan. 25, 1952.

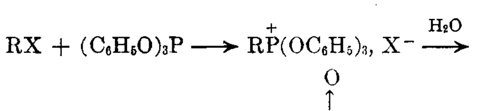
TABLE II

DIPHENYL ALKYLPHOSPHONATES

Compound	M.p. or n^{25}D	B.p./mm.	C Calcd.	C Found	H Calcd.	H Found	P Calcd.	P Found	Yield, %
$C_8H_{17}P(O)(OC_6H_5)_2$	1.5221	148°/0.006	69.4	69.9	7.70	7.6	8.96	8.8	47[d]
$C_{10}H_{21}P(O)(OC_6H_5)_2$	1.5202	178°/0.1	70.6	70.3	8.29	8.0	8.29	8.1	67[d]
$C_{12}H_{25}P(O)(OC_6H_5)_2$	1.5111	165°/0.01	71.6	71.4	8.70	8.75	7.71	7.81	...[b]
$C_{14}H_{29}P(O)(OC_6H_5)_2$	41.5–42°[a]	*ca.* 197°/0.02	72.6	72.6	9.10	9.07	7.20	7.40	74
$C_{16}H_{33}P(O)(OC_6H_5)_2$	49.5–51°[a]	*ca.* 215°/0.01	73.3	73.6	9.44	9.80	6.74	6.74	...[c]

[a] Recrystallized from n-pentane. [b] See Table I. [c] Partial loss prevented calculation of yield. [d] Run without distillation of phenol.

alternative route to such compounds, namely quaternization of triphenyl phosphite with an alkyl halide and hydrolysis of the resulting salt:



$$RX + (C_6H_5O)_3P \longrightarrow R\overset{+}{P}(OC_6H_5)_3,\ X^- \xrightarrow{H_2O} R\overset{\overset{O}{\uparrow}}{P}(OC_6H_5)_2 + C_6H_5OH \quad (3)$$

Although the older method is very useful with methyl or benzyl halides, it gives poor yields with the higher alkyl halides (runs 1, 2, and 8). The probable reason is that, at the temperatures required for quaternization, elimination reactions which form hydrohalic acids and lead to color and tar-producing side reactions occur. These are much less serious in the halide-catalyzed alcohol reaction.

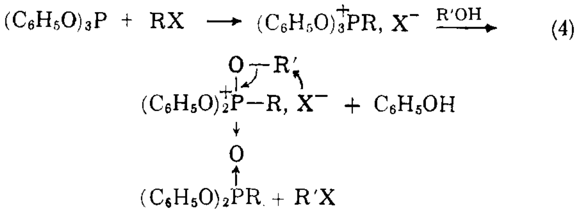
The present synthesis is most convenient for alcohols which boil appreciably higher than phenol (b.p. 182°). In such cases workup may be simplified by distilling phenol directly from the reaction as it is formed. In the case of octanol and decanol, phenol distillation could not be carried out because of the proximity of the boiling points of these alcohols to that of phenol. In principle, the reaction could be extended to lower alcohols by using pressure vessels.

The halide catalyst may be either the alkyl halide corresponding to the alcohol used, certain inorganic halides, or free halogens. Iodides were the most effective of the halogens; sodium iodide was a particularly convenient and effective catalyst. Alkyl bromides were used, but larger amounts were required than were necessary with iodides. Alkyl chlorides were ineffective. Only transesterification reactions of the phosphite and the alcohol occurred in attempts to use dodecyl chloride as the catalyst. Lithium chloride catalyzed the reaction, but gave very low yields (Run No. 23, Table I).

The major side reaction products observed were alkyl phenyl and dialkyl ethers in which the alkyl group corresponded to that of the alcohol used. Ether formation may have occurred by reaction of alkyl halide with phenol or with alcohol. It was established that heating dodecyl alcohol, phenol, and dodecyl iodide together produced both didodecyl and dodecyl phenyl ethers.[7]

For such a high temperature reaction surprisingly little color is developed. However, in a number of runs, an orange precipitate formed rather suddenly during the last few hours of heating. This was found to be red phosphorus. It might have come from hydrolysis of triphenyl phosphite by small amounts of water, followed by disproportionation of the resultant phosphonate. Diphenyl phosphonate $[(C_6H_5O)_2P(O)H]$ forms the same color at these temperatures,[8] while triphenyl phosphite does not.

Reaction Sequence.—It is of interest to consider the relationship between this phosphonate synthesis and Rydon and Landauer's preparation of alkyl halides.[6] The latter reaction can best be rationalized as follows:



$$(C_6H_5O)_3P + RX \longrightarrow (C_6H_5O)_3\overset{+}{P}R,\ X^- \xrightarrow{R'OH} \quad (4)$$

$$(C_6H_5O)_2\overset{\overset{O-R'}{|}}{\overset{+}{P}}-R,\ X^- + C_6H_5OH \downarrow (C_6H_5O)_2\overset{\overset{O}{\uparrow}}{P}R + R'X$$

This type of mechanism requires that phenol and phosphonate be formed simultaneously.[9] This is *not* the case in the present phosphonate synthesis; the phenol is formed much more rapidly than is the phosphonate. Furthermore, mixed phosphites, probably $ROP(OC_6H_5)_2$, are intermediates in the process. These statements are supported by the fact that carrying out the reaction appreciably below 220° (Run No. 19), produced essentially the same amount of phenol distillate as at higher temperatures (Runs 10, 14) but the product at that point contained very little phosphonate, as evidenced by the low intensity of certain infrared bands characteristic of the phosphonate ester. This infrared spectrum, which showed bands characteristic of both aryl and alkyl substituents, as well

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(7) These ethers could possibly have been formed by alkylation of phenol or fatty alcohol with the alkoxyphosphonium ion which is the probable intermediate in the formation of the phosphonate. Their direct formation in the absence of phosphite simply demonstrates that it is not necessary to invoke this more complicated explanation.

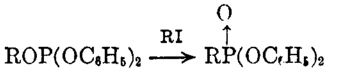
(8) A. E. Arbuzov and M. G. Imaev (*Izv. Akad. Nauk S.S.S.R., Otd. Khim. Nauk*, **1959**, 171) report that red phosphorus and phenol are always formed during redistillation of diphenyl phosphonate, b.p. 150°/1 mm. Similar observations have been made a number of times in these laboratories.

(9) The only assumption that is necessary is the very reasonable one that the phosphonium ion intermediate does not accumulate in the reaction.

as the reactivity of the product towards mercuric chloride, a mild oxidizing test reagent, leaves little doubt that a major product of the low-temperature reaction is alkyldiphenyl phosphite. Also consistent with the idea that phosphites are intermediates is the fact that a mixture of phosphites and diphenyl alkylphosphonate is obtained if an insufficient amount of catalyst or insufficiently active catalysts are used, or if the conditions of time and temperature are not sufficiently vigorous (Runs 5, 7, 18, 20, 22, Table I). It was demonstrated that in such cases further heating with alkyl iodide catalyst under the optimum conditions of the phosphonate synthesis completely rearranges any phosphites to phosphonates. The fact that vigorous conditions are required also serves to differentiate this phosphonate synthesis from the reaction studied by Rydon and Landauer, which frequently proceeds near room temperature or upon mild warming.

The available information suggests that the most likely reaction sequence for the formation of the phosphonates involves a transesterification reaction followed by a Michaelis-Arbuzov rearrangement:

$$ROH + (C_6H_5O)_3P \longrightarrow ROP(OC_6H_5)_2 + C_6H_5OH \quad (5)$$



$$ROP(OC_6H_5)_2 \xrightarrow{RI} R\overset{\overset{O}{\uparrow}}{P}(OC_6H_5)_2 \quad (6)$$

The transesterification reaction is reported in the literature,[10] and the Michaelis-Arbuzov rearrangement is a well-established reaction of trivalent phosphorus species with an alkoxy substituent.[11] It is probable that the alkyl halide is the actual catalyst for the rearrangement reaction, even though the halogen is initially present as inorganic halide. In such cases, the forerun to the distillation of the phosphonates gives a positive qualitative test for alkyl halide. Inorganic halides would be expected to convert alcohols to alkyl halides under the conditions of this reaction.[6]

Experimental[12]

In a typical experiment, the reactants were combined in a three-neck flask of appropriate size equipped with thermometer, nitrogen inlet, stirrer, and vacuum jacketed distillation head. The head was connected to a condenser, the lower parts of which were wrapped with heating tape to prevent crystallization of phenol. Water from an approximately 50° reservoir was circulated through the condenser. The flask was heated at the desired temperature by a cone-type radiant heater (of *ca.* 500 watts) controlled by a Therm-O-Watch electronic controller (the sensor for which clips onto the thermometer), while 2–3 cu. ft./hr. nitrogen was swept over the reaction. Phenol commenced distilling from the reaction as the reaction temperature was reached. The contents of the flask remained colorless during all or a large portion of the reaction, but in certain cases an orange-red precipitate of red phosphorus formed rather suddenly during the last few hours of the reaction. In one such case the red phosphorus was filtered, washed with solvent, and identified by comparison of x-ray powder patterns, combustion analysis, and its thermal behavior (sublimes $> 350°$ at 0.02 mm.).

The weight of distillate swept out of the reaction was usually 10–20% greater than that required for the theoretical amount of phenol, due to the fact that some alcohol and phosphites were also collected. After vacuum distillation of the main reaction mixture through simple large bore apparatus, preferably at < 0.05 mm., it was taken up in ether, washed with 2 *N* sodium hydroxide, dried, and redistilled to yield the product.

A number of minor variations of the above procedure were tried. For example, in using decanol and octanol the phenol was simply refluxed, because sweeping it from the reaction would have resulted in excessive loss of the C_8 or C_{10} alcohols. When this was done, the system was maintained under a slight positive nitrogen pressure. This procedure can be used also with the higher alcohols. Another variation which was tried, without significant improvement in yield, was to add half of the dodecyl iodide catalyst initially and the remainder dropwise over the first several hours of the reaction (Table I, Run No. 14).

When alkyl halides reacted with triphenyl phosphite in the absence of alcohols (runs 1, 2, and 8), darkening of the reaction occurred, particularly in the case of the iodide, and tarry distillation residues were formed. If the alkyl bromide reactions were heated to 220°, copious evolution of hydrogen bromide occurred.

When the product contained alkyldiphenyl phosphites, they could be detected by either or both of two methods: addition of a few drops of sample to fresh saturated alcoholic mercuric chloride, or by comparison of infrared spectra. The phosphonates are inert to the mercuric chloride reagent in alcohol solvent, whereas the phosphites give a copious precipitate within a few minutes. In the infrared spectra, the phosphites have an intense band near 11.7 μ, where the phosphonates are nearly transparent, while the phosphoryl band of the phosphonate, at 7.92 μ, is of course absent in the phosphites. The phosphonates are also characterized by a band at 10.8 μ which is of significantly greater intensity than the phenyl ether bands at 8.2–8.4 μ. The crude product (before distillation) from Run No. 19 had strong bands at 3.4 and 11.7 μ, no OH absorption, a weak band at 7.9 μ, and a band at 10.8 μ which was about half the intensity of the 8.4 μ band, and appreciably smaller than the 11.8 μ band.

From the forerun of Run No. 4, Table I, a crystalline solid (crystallized from ether, m.p. 32.5–34°) was isolated which was shown to be didodecyl ether by comparison of melting points and infrared spectra with those of authentic material.[13] In the forerun to Run No. 11, and in other reactions as well, a band was seen at 8.0 μ corresponding to phenyl dodecyl ether, but none at 9.0 μ for didodecyl ether. Refluxing dodecanol, dodecyl iodide, and phenol (equimolar amounts) at *ca.* 160° for 20 hr. yielded a mixture of didodecyl and phenyl dodecyl ethers, predominantly the former, in about 25% total yield.

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(10) Reference 2, p. 191; J. Rosin and O. G. Birsten, U.S. Patent, 2,970,166, Feb. 7, 1961.

(11) Reference 2, p. 121.

(12) Boiling points and melting points are uncorrected. Redistilled triphenyl phosphite and refractionated alcohols of >99% purity by gas chromatographic analysis were used, except in certain of the larger scale runs in which commercial 95% dodecanol was used.

(13) E. C. Butterworth and O. H. Hey, *J. Chem. Soc.*, 388 (1940).