Heteroatom Chemistry
Volume 17, Number 4, 2006

New Approaches to the Synthesis of Diphosphine Dioxides and Hypophosphoric Acid Esters

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Received 22 October 2005; revised 23 October 2005

ABSTRACT: *An anion >P–O⁻ has been applied as an efficient synthetic precursor of four coordination compounds of the $R_2P(O)$–$(O)PR_2$ type, namely diphosphine dioxides (R = alkyl, aryl) as well as hypophosphoric acid esters (R = alkoxy, aryloxy), in a one-pot reaction. Furthermore, there were elaborated some mechanistic aspects of the origin of the >P(O)–O–(O)P< anhydride, as a side-product of the reaction between the anion >P–O⁻ and >P(O)X (X = Cl, Br) electrophiles. Attention is focused on the synthesis of the >P(O)–(O)P< compounds.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:310–316, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20208

INTRODUCTION

Phosphorus chemistry is of key importance for the number of physiological processes. Adenosine triphosphate (ATP), flavin adenine dinucleotide (FAD), nicotinamide adenine dinucleotide (NAD), nucleoside polyphosphates and so on, all contain >P(O)–O–(O)P< fragment. An antitumor activity of hypophosphoric acid systems $(RO)_2P(O)$–$(O)P(OR)_2$ is of potential importance in cancer treatment because the synthesis of the deoxythymidine monophosphate (dTMP) is a critical process during the rapid cell proliferation [1]. Due to the fact that most normal mammalian cells grow slowly, which requires less amount of dTMP, the interruption of its synthesis can selectively kill cancer cells.

This explains the interest in diphosphine dioxides and hypophosphoric acid esters, compounds that contain a similar >P(O)–(O)P< skeleton. However, there are only few examples of structural analogue possess >P(O)–(O)P< fragment in the place of >P(O)–O–(O)P< system in the search for the potential inhibitors of the biologically important metabolic routes [2]. The inaccessibility of diphosphine dioxides and hypophosphoric acid esters is probably the most important reason for the lack of such compounds.

Generally, there are three methods for the synthesis of compounds that contain the >P(O)–(O)P< skeleton (Scheme 1). The first one is a reaction between electrophilic phosphorus acid halogens and ambident nucleophiles >P–O⁻ (path "A") [3]. The second is a reduction of phosphorus acid halogens (mainly chloride) by alkali metals in heterogeneous conditions (path "B") [4,5]. The third way is an oxygenation of the reaction products of >P–Cl electrophiles and >P(O)–H/base system (path "C") [6]. In all cases the mixtures formed are relatively complex. However surprisingly, such mixtures if tested, appeared to be very similar to each other, especially between the relative rate of the product formation and the product distribution profile [3,5,6].

Similarly, the reduction of phosphorus acid halogens by alkali metals in heterogeneous conditions

This paper is dedicated to Professor Michael Lappert.

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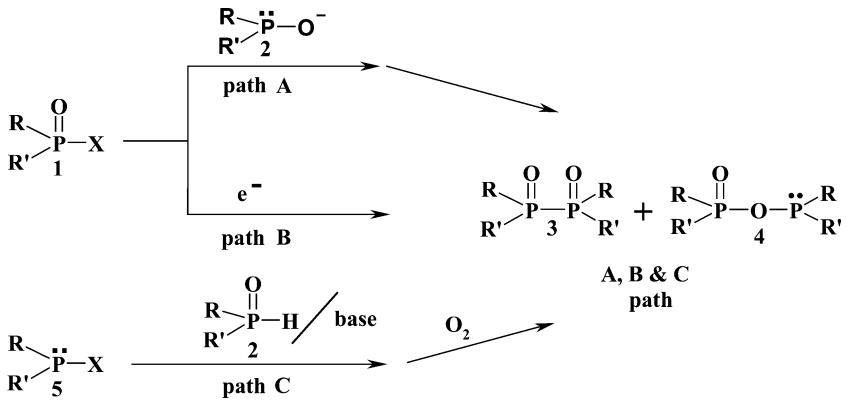


SCHEME 1 Synthesis of compounds of the type $R_2P(O)–(O)PR_2$ (**3**) by the reaction of electrophiles $R_2P(O)X$ (**1**, X = Cl, Br) with $R_2P–O^-$ (**2**) (path "A"), by the alkali metals reduction of **1** (path "B") or by the reaction of electrophiles R_2PCl (**5**) with $R_2P(O)–H$/base and oxygen (path "C").

often leads to a complex reaction mixture [7]. This is not surprising, because alkali metals can react both with the starting material (phosphorus acid halogens) and with the products (e.g., diphosphine dioxides or anhydride diphosphine dioxides), which are both electron acceptors [4].

The >P–O$^-$ is an ambident nucleophile having a hard center on the oxygen, and a soft center on the phosphorus atom. Accordingly, many examples can be indicated where >P–O$^-$ reacts selectively: via the phosphorus [8] or the oxygen [9], respectively (Scheme 2).

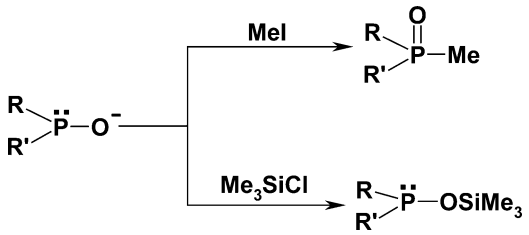
Quin and Anderson [6a] were the first who recognized duality in the chemical character of secondary phosphine oxides. Ambident phosphorus nucleophile like >P–O$^-$ (**2**) can react either through P or O nucleophilic center with electrophiles >P(O)X (**1**, X = Cl, Br), to produce both *P*-phosphorylated products, i.e., $R_2P(O)–(O)PR_2$ (**3**), and *O*-phosphorylated products, i.e., mixed anhydrides $R_2P(O)–O–PR_2$ (**4**) (Scheme 1; path "A"). The pattern of the yield distribution depends on the substituent located on the phosphorus atom, which controls this by steric and/or electronic factors.

Stec et al. [3a] studied the reaction of 2-chloro-5,5-dimethyl-(1,3,2)-dioxaphosphinane-2-oxide with $(EtO)_2P(O)H$, in the presence of Et_3N. Unexpectedly, they isolated only symmetric anhydride $OCH_2C(CH_3)_2CH_2OP(O)–O–(O)POCH_2C(CH_3)_2CH_2O$, namely 5,5,5′,5′-tetra-methyl-2,2′-oxy-bis-[1,3,2]dioxaphosphinane 2,2'-dioxide with 82% yield. They did not identify and/or isolate second possible symmetric anhydride $(EtO)_2P(O)–O–(O)P(OEt)_2$. This fact is very important for the explanation of the reactivity discussed. We supposed that in the first step mixed anhydride $R_2P(O)–O–P(OEt)_2$ is formed, as an *O*-phosphorylated product. Next, $(EtO)_2P(O)–H$, in the presence of Et_3N, produces $R_2P(O)O^-$, which in turn reacts with the $R_2P(O)Cl$ electrophile giving symmetric $R_2P(O)–O–(O)PR_2$ anhydride.

Stec and Zwierzak [3b] realized that the yields of hypophosphoric acid esters $(RO)_2P(O)–(O)P(OR')_2$ strongly depend on the excess of >P–O$^-$ nucleophiles.

The aim of the current study is the exploration of some synthetic routes giving the aforementioned compounds >P(O)–(O)P<. Thus, in a series of experiments a reaction between >P–O$^-$ nucleophiles and >P(O)X (X = Cl, Br) electrophiles were reinvestigated.

The analysis of the reaction mixture indicated that the formation of the target product, i.e. $R_2P(O)–(O)PR_2$, is always accompanied by the reduction giving [$R_2P(O)–PR_2$ and/or $R_2P–O–PR_2$], and the oxygenation resulting in [$R_2P(O)–O–(O)PR_2$]. Thus, the >P–O$^-$ nucleophile should be an efficient deoxygenating reagent. Moreover, it can be expected that the >P$^-$ anion should be a reactive reducing agent. In our previous paper [4], we presented the results of the reduction of mixed anhydrides >P(O)–O–P< to >P(O)–O$^-$ and >P$^-$ anions. The reduction ability of >P$^-$ anions implies the presence of >P–O$^-$ anion among the products formed. However, under such conditions we have not found a compound having a



SCHEME 2 >P–O$^-$ anion as an ambident nucleophile.

$>P–O^-$ group or its derivatives. This suggested that the products of reduction or oxygenation are formed by a different pathway. Therefore, further experiments were carried out in order to explain this mechanism.

RESULTS AND DISCUSSION

To the best of our knowledge in the literature data, there is only one example [10] of the reaction of mixed anhydrides $(RO)_2P(O)–O–P(OR)_2$ with the $(RO)_2P–O^-$ nucleophile having the phosphorus atom surrounded by the same substituents. In the reaction mixture, a symmetrical pyrophosphite anhydride $(RO)_2P–O–P(OR)_2$ was identified as an *O*-phosphorylated product. The $(RO)_2P–O^-$ anion seems to favor a linear structure because of the orbital overlap of the oxygen and phosphorus atom.

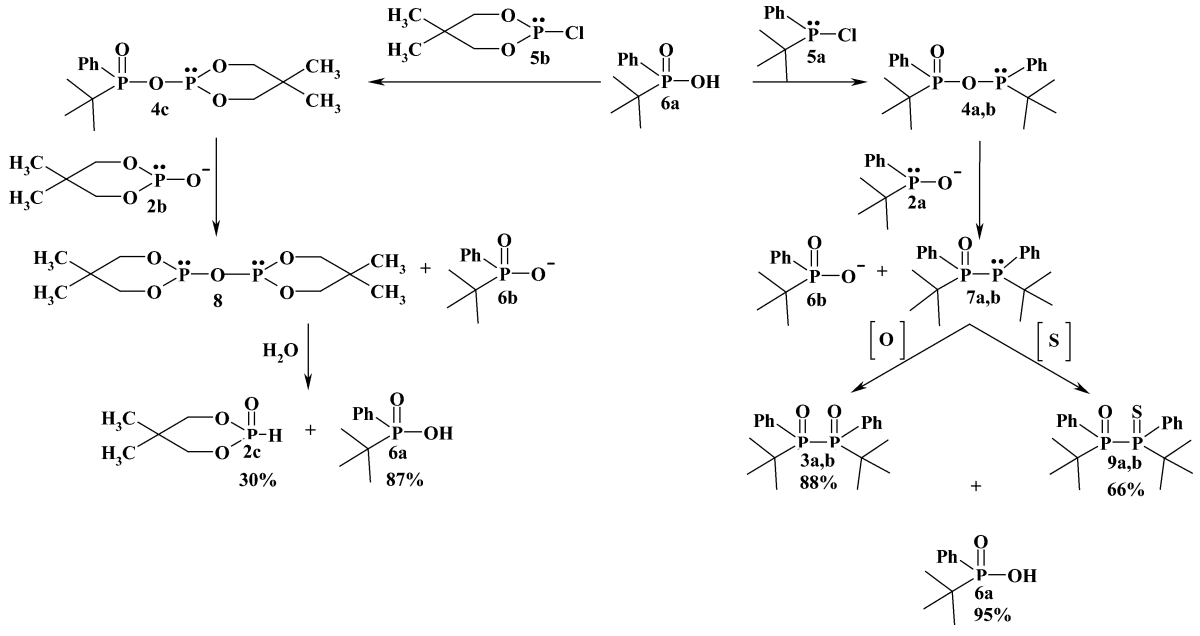
The behavior of reagents containing alkyl and/or aryl substituents on the phosphorus atom could be different. In order to explain the observed reactivity, we carried out a reaction between the mixed anhydrides Ph(*t*-Bu)P(O)–O–P(*t*-Bu)Ph (**4a,b**), or Ph(*t*-Bu)P(O)–O–$POCH_2C(CH_3)_2CH_2O$ (**4c**) and the nucleophiles $R_2P–O^-$ (**2**, R = alkyl and/or aryl or R = alkoxy) which possess the same or different substituents (Scheme 3).

Generally we observed that the reaction between a $>P–O^-$ nucleophile and mixed anhydrides $>P(O)–O–P<$ is very selective. Three coordinate phosphorus atoms are always attacked which gives *P*- or *O*-phosphorylated products, and a phosphinic acid anion $>P(O)–O^-$, as a leaving group. Depending on the nature of substituents, the diphosphine monoxides $R_2P(O)–PR_2$ (R = alkyl and/or aryl) or the pyrophosphites $R_2P–O–PR_2$ (R = alkoxy) were obtained. Hydrolysis, oxygenation, or sulfuration gave the final products in similar molar yields in both cases. Three coordinate phosphorus atom of diphosphine monoxides $R_2P(O)–PR_2$ was oxygenated (sulfurated) giving $>P(O)–(O)P<$ (**3**) [$>P(O)–(S)P<$ (**9**)] up to 90% (70%) yield, respectively.

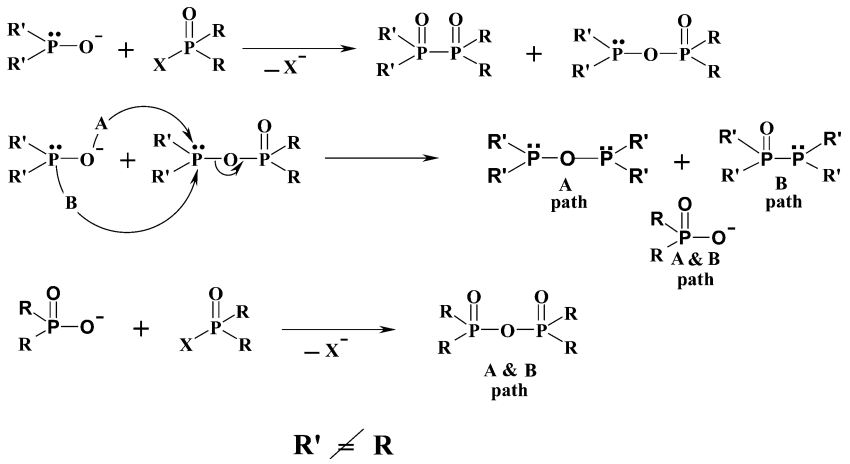
In the next step $>P(O)–O^-$ acid anions reacted easily with phosphorus electrophiles $>P(O)Cl$ to produce phosphorus acid anhydrides $>P(O)–O–(O)P<$ (as "oxygenated" products) (Scheme 4).

In the reaction between $>P–O^-$ nucleophile and $>P(O)X$ (X = Cl, Br) electrophiles, two nucleophiles coexisted in the reaction mixture: $>P–O^-$ and $>P(O)–O^-$. The $>P–O^-$ anion as a α-nucleophile should react faster with $>P(O)Cl$ than the $>P(O)–O^-$ nucleophile. Thus the increase of $>P–O^-$ concentration should increase the amount of $R_2P(O)–(O)PR_2$.

According to the R.G. Pearson's hard and soft acids and bases principle [11], leaving group should affect the ratio of *P*- vs. *O*-phosphorylated product. Thus, nucleophilic substitution proceeds faster when the nucleophile and the leaving group are either both hard or soft. As a consequence, to obtain a higher yield of the compound $R_2P(O)–(O)PR'_2$, it is necessary to modify the softness of the phosphorus atom substituents. This can be achieved by the modification of the halogen atom bound to the phosphorus in $>P(O)X$, from Cl through Br to I, respectively.



SCHEME 3 Reaction of $R_2P–O^-$ (**2**) anions with mixed anhydrides $R_2P(O)–O–PR_2$ (**4**).

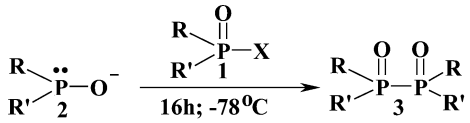


SCHEME 4 Mechanism proposed for the explanation of the origin of $R_2P(O)–O–(O)PR_2$ anhydride in the reaction mixture between >P–O$^-$ nucleophiles and >P(O)X electrophiles (X = Cl, Br).

However, we observed that the replacement of halogen does not result in the change of the yield of compound **3**, as expected, which is shown by the result presented in Scheme 5.

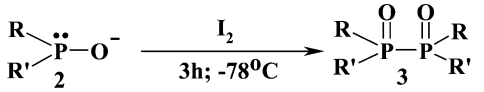
A reaction of >P–O$^-$ (**2**) with iodine seems to be an interesting idea, which guarantees a temporary excess of nucleophile. Moreover iodine, as opposite to bromine, does not react with diphosphine dioxides and hypophosphoric acid esters in a quantitative manner (Scheme 6).

Quite surprisingly, the reaction of >P–O$^-$ (**2**) and iodine in THT or THF/NH_3 yielded efficiently compounds **3**, i.e. diphosphine dioxides, as well as hypophosphoric acid esters. This facile and convenient synthesis enabled to obtain compounds **3**, i.e. diphosphine dioxides in 98% and hypophosphoric acid esters in 48% yield. The reaction of I_2 and



Entry	R	R'	X	Yield of 3 (%)
1	Ph	*t*-Bu	Cl	67
2	Ph	*t*-Bu	Br	65
3	Ph	Ph	Cl	70
4	$OCH_2C(CH_3)_2CH_2O$		Cl	28
5	$OCH_2C(CH_3)_2CH_2O$		Br	29

SCHEME 5 Synthesis of compounds of the type $R_2P(O)–(O)PR_2$ (**3**).



Entry	R	R'	Yield of 3 (%)
6	Ph	*t*-Bu	67
7	Ph	*t*-Bu	65
8	Ph	Ph	70
9	$OCH_2C(CH_3)_2CH_2O$		28

SCHEME 6 Reaction $R_2P–O^-$ (**2**) with I_2.

>P–O$^-$ (**2**) anion generated in situ proceeds efficiently both in THF and liquid ammonia. Moreover, it appeared that the reactivity of I_2 in liquid ammonia was limited by the rate dissolution of solid I_2 at −78°C. We identified also a minute amount of Ph(*t*-Bu)P(O)I (**1d**) in the reaction mixture. Obtained results, especially from liquid ammonia, suggest that the reaction proceeds via radical mechanism rather than a pure nucleophilic substitution. In order to prove conclusively their structures, we obtained these compounds using a different procedure. The >P–O$^-$ (**2**) anion generated in electron reduction procedure [4] was treated with Me_3SiCl, and such a formed >P–O–$SiMe_3$ ester was reacted with I_2 to produce quantitatively phosphorus acid iodide.

CONCLUSION

A new strategy for the synthesis of P–P bond in the compound containing >P(O)–(O)P< skeleton is presented. The method can be applied efficiently both

for the derivatives substituted with the alkyl and/or aryl groups. The alkoxy group as a phosphorus substituent decreases the efficiency because the iodine anion can also react with such substituents. The method presented is a convenient and easy way to control general synthesis procedure yielding diphosphine dioxides and hypophosphoric acid esters. The surprising results suggest that the reaction proceeds via radical mechanism rather than a pure nucleophilic substitution.

According to Quin and Anderson [6a] we suggest that >P–O$^-$ anion reacts with >P(O)X (X = Cl, Br) electrophiles to produce >P(O)–(O)P<, as well >P(O)–O–P< mixed anhydride, which is a key intermediate in the origin of >P(O)–O–(O)P< side-product. The >P–O$^-$ anion selectively reacts with mixed anhydrides >P(O)–O–P< to produce acid anion >P(O)–O$^-$, which reacts further with >P(O)X giving >P(O)–O–(O)P< anhydride.

EXPERIMENTAL

All reactions were carried out under argon atmosphere in anhydrous solvents (benzene, diethyl ether, and THF dried over benzophenone ketyl, MeOH dried over Mg, $CHCl_3$ dried over P_2O_5, hexane dried over potassium). Chromatography was carried out on silica gel 60 (0.15–0.3 mm) Machery Nagel. NMR measurements were performed on Varian Gemini 500 MHz or 200 MHz (all J values are given in Hz, the chemical shifts are expressed as δ values (ppm)); MS were acquired on a MASPEC II system [II32/99D9] in EI mode and if necessary liquid SIMS technique was applied. Compounds **4a,b** as a *meso* and *rac* isomers [12] were synthesized according to procedures described in the literature.

Synthesis of t-Butylphenylphosphinic-5,5-dimetyl-(1,3,2)-dioxaphosphinan Anhydride **4c**

Compound **4c** was prepared similarly to **4a,b** [12]; ^{31}P NMR (THF/C_6D_6) $\delta_{PIII} = 108.59$, $\delta_{PV} = 43.29$, $^2J_{P-P} = 26.29$ Hz.

Reaction of Potassium Salt of t-Butylphenylphosphine Oxide **2a** *(potassium Salt of 5,5-Dimethyl-(1,3,2)-dioxaphosphinane-2-oxide* **2b***) with t-Butylphenylphosphine t-Butylphenylphosphinic Anhydride (***4a,b** *or* **4c***), respectively*

In the freshly prepared potassium naphthalenide in 25 mL of THF at −78°C, *t*-butylphenylphosphinic acid chloride (**1a**) (2-chloro-5,5-dimethyl-(1,3,2)-dioxaphosphinane-2-oxide **1b**) (5 mmol) in THF (5 mL) was added, respectively. The reaction mixture was stirred until the disappearance of the blue color. Thus, the generated **2a** (**2b**) (5 mmol) at −78°C was added to the solution of **4a,b** (**4c**) (5 mmol) in THF (20 mL), respectively. After 3 h at −78°C, a sample of the reaction mixture was taken, C_6D_6 was added, and the ^{31}P NMR spectrum was recorded. The ^{31}P NMR (THF/C_6D_6) spectrum of the reaction mixture showed two resonance lines attributable to the potassium salt of *t*-butylphenylphosphinic acid anion (**6b**) ($\delta_{31P} = 31.95$) and diphosphine monoxides (**6b** ($\delta_{31P} = 35.82$) and 5,5,5′,5′-tetramethyl-2,2′-oxybis[1,3,2]dioxaphosphinane (**8**) ($\delta_{31P} = 110.36$)), respectively. The ^{31}P NMR spectra shows two groups of signals of 1,2-di-*t*-butyl-1,2-diphenyldiphosphane monoxides (**7a,b**) [13], for the *rac* and the *meso* isomers (in a 1:4 ratio) (**7a** .$\delta_{PIII} = -12.61$, $\delta_{PV} = 50.57$, $J_{P-P} = 277.16$ Hz, and **7b** $\delta_{PIII} = -4.66$, $\delta_{PV} = 56.04$, $J_{P-P} = 285.47$ Hz). Sulfur in benzene (run 1), dry air (run 2), or toluene and a water solution of $KHSO_4$ (run 3) were added to the reaction mixture, respectively. After 16 h, toluene/$KHSO_4$ water solution was added, (runs 1 and 2). The organic phase was separated and dried ($MgSO_4$). Then, the solvent was evaporated and the residue was purified by crystallization and chromatography.

Run 1: Sulfur Addition. t-Butylphenylphosphinic acid **6a**: 0.940 g (4.7 mmol, 95%), mp = 155–156°C; ^{1}H NMR ($CDCl_3$) $\delta = 0.93$ (d, $^3J_{P-H} = 15$ Hz, *t*-Bu, 9H), 6.93–7.57 (m, aromatic, 5H), 11.0 (s, OH, 1H), ^{31}P NMR ($CDCl_3$) $\delta = 52.00$.

1,2-di-t-Butyl-1,2-diphenyldiphosphane P^1*-Oxide P*^{2}*-Sulfide* **9a,b**: **9a** ($CHCl_3$) 1.189 g (3.1 mmol, 60%), mp = 174–176°C, ^{1}H NMR ($CDCl_3$) $\delta = 0.94$ (d, $^3J_{P(O)H} = 18$ Hz, *t*-Bu, 9H) 1.09 (d, $^3J_{P(S)H} = 16$ Hz, *t*-Bu, 9H), 7.27–8.74 (m, aromatic, 10H), ^{31}P NMR ($CDCl_3$) $\delta_{P(S)} = 43.40$, $\delta_{P(O)} = 41.11$, $J_{P-P} = 52.40$ Hz, MS : (SIMS) M^+ 378, HRMS: *m/z* Calcd for $C_{20}H_{28}OP_2S$ (M^+): 378.13350. Found 378.13454. **9b**: ($CHCl_3$) 0.105 g (0.3 mmol, 6%), mp = 136–137°C, ^{1}H NMR ($CDCl_3$) $\delta = 1.47$ (dd, $^4J_{P(S)H} = 1$ Hz, $^3J_{P(O)H} = 16$ Hz, *t*-Bu, 9H) 1.39 (dd, $^4J_{P(O)H} = 1$ Hz, $^3J_{P(S)H} = 15$ Hz, *t*-Bu, 9H), 7.07–7.66 (m, aromatic, 10H), ^{31}P NMR ($CDCl_3$) $\delta_{P(S)} = 54.96$, $\delta_{P(O)} = 53.37$, $J_{P-P} = 52.40$ Hz, MS : (SIMS) M^+ 378.

Run 2: Dry Air. **6a** *0.931g (4.7 mmol, 94%). 1,2-di-t-Butyl-1,2-diphenyldiphosphane 1,2-Dioxide* **3a,b** *(mixture of meso and rac)* [4,14]. **3a**: ($CHCl_3$: MeOH = 50 : 1) 1.593 g (4.4 mmol, 88%), mp_{meso} = 205°C, ^{1}H NMR ($CDCl_3$) $\delta_{meso} = 0.98$ (d, $^3J_{P-H} = 16$ Hz, *t*-Bu, 18H), 7.40–8.45 (m, aromatic, 10H), ^{31}P NMR ($CDCl_3$) $\delta_{meso} = 39.8$, MS : (SIMS) M^+ 362. **3b**: $mp_{rac} = 192$–193°C, ^{1}H NMR ($CDCl_3$) $\delta_{rac} = 1.38$ (d, $^3J_{P-H} = 17$Hz, *t*-Bu, 18H), 7.00-7.80

(m, aromatic, 10H), ^{31}P NMR ($CDCl_3$) $\delta_{rac} = 50.7$, MS : (SIMS) M^+ 362.

Run 3: Reaction of **2b** *with* **4c**. **6a** *0.861g (4.3 mmol, 87%). 5,5-Dimethyl-(1,3,2)-dioxaphosphinane 2-oxide* **2c**: 0.225 g (1.5 mmol, 30%), ^{1}H NMR ($CDCl_3$) $\delta = 0.96$ (s, CH_3, 3H), 1.28 (s, CH_3, 3H), 3.00–4.00 (m, CH_2, CH_2, 4 H), 6.43 (d, $J_{P-H} = 660$ Hz, PH, 1H), ^{31}P NMR ($CDCl_3$) $\delta = 3.5$.

Synthesis of t-Butylphenylphosphinic Acid Bromide **1c**

To the suspension of **6a** (7 g, 35 mmol) in benzene (50 mL) PBr_5 (15.22 g, 35 mmol) was added. Reagents were heated under reflux for 6 h (until HBr disappeared). Then toluene/K_2CO_3 water solution was added. The organic phase was separated and dried ($MgSO_4$). The solvent was evaporated, and the crude product was purified by distillation. **1c** (Kügelrohr, 136°C/0.5 mmHg), 8.590 g (32.9 mmol, 94%), ^{1}H NMR ($CDCl_3$) $\delta = 1.03$ (d, $^3J_{P-H} = 16$ Hz, *t*-Bu, 9H), 7.10–7.77 (m, aromatic, 5H), ^{31}P NMR ($CDCl_3$) $\delta = 73.51$.

*Direct Reaction between $R_2P{-}O^-$ (**2**) and $R_2P(O)X$ (**1**, X = Cl, Br) Electrophiles*

Into the freshly prepared potassium naphthalenide (10 mmol) in 25 mL of THF at −78°C, an appropriate $R_2P(O)Cl$ (5 mmol) in THF (5 mL) was added. The reaction mixture was stirred until the disappearance of the blue color. The suitable $R_2P(O)X$ electrophile (X = Cl or Br) (5 mmol) was added in the 1:1 stoichiometry. After 16 h a sample of the reaction mixture was taken, C_6D_6 was added, and the ^{31}P NMR spectrum was recorded. Then, to the reaction mixture at −78°C toluene $KHSO_4$ water solution was added. The organic phase was separated and dried ($MgSO_4$). The solvent was evaporated, and the crude product was purified by crystallization and chromatography:

Entry 1. **3a,b** ($CHCl_3$: MeOH = 50:1), 1.213 (3.4 mmol, 67%)

Entry 2. **3a,b** ($CHCl_3$: MeOH = 50:1), 1.178 g (3.2 mmol, 65%)

Entry 3. Tetraphenyldiphosphane *P,P′*-dioxide **3c** [6]: 1.408 g (3.5 mmol, 70%), mp = 168–169°C; ^{1}H NMR ($CDCl_3$/DMSO) $\delta = 6.90$–6.99 (m, aromatic, 6H) 7.81–7.85 (m, aromatic, 4H), ^{31}P NMR ($CDCl_3$/DMSO) $\delta = 24.92$.

Entry 4. 5,5,5′,5′-tetramethyl-bis-(1,3,2)-dioxaphosphinane 2,2′-dioxide **3d** [3]: (diethyl ether), 0.418 g (1.4 mmol, 28%), mp = 248–249°C; ^{1}H NMR ($CDCl_3$) $\delta = 0.90$ (s, CH_3, 6H), 1.36 (s, CH_3, 6H), 3.97 (dd, $J_{H-H} = 10.57$ Hz, $J_{P-H} = 22.21$ Hz, CH, 4H), 4.68 (d, $J_{H-H} = 10.57$ Hz, CH, 4H), ^{31}P NMR ($CDCl_3$) $\delta = -0.68$.

Entry 5. **3d** (diethyl ether), 0.438 g (1.4 mmol, 29%).

*Reaction of $R_2P{-}O^-$ (**2**) with I_2 in THF*

In the freshly prepared potassium naphthalenide (10 mmol) in THF (25 mL) at −78°C, $R_2P(O)Cl$ (5 mmol) in THF (5 mL) was added. The reaction mixture was stirred until the disappearance of the blue color. Then, the solid I_2 (5 mmol) was added. After 3 h to the reaction mixture at −78°C, toluene/$KHSO_4$ water solution was added. The organic phase was separated and dried ($MgSO_4$). Solvent was evaporated, and the crude product was purified by crystallization and chromatography:

Entry 6. *t*-Butylphenylphosphinic acid iodide (**1d**) [15] ($CHCl_3$), 0.015 g (0.05 mmol, 1%) ^{1}H NMR ($CDCl_3$): $\delta = 1{,}26$ (d, $^3J_{P-H} = 20$ Hz, *t*-Bu, 9H), 7,47–7,66 (m, 3H), 7.82–7.96 (m, 2H); ^{31}P NMR ($CDCl_3$) $\delta = 62.64$; MS : (EI) $[M\text{-}I]^+$ 181; **3a,b** ($CHCl_3$: MeOH = 50:1), 0.878 g (2.4 mmol, 97%).

Entry 7. **3c** 1.408 g (3.5 mmol, 70%).

Entry 8. **3d** (diethyl ether), 0.358 g (1.2 mmol, 48%).

Reaction of **2a** *with I_2 in NH_3/THF*

Potassium (0.78 g, 10 mmol) was dissolved in the mixture prepared from liquid ammonia (50 mL) and THF (50 mL). The reaction mixture was stirred up to the complete dissolution of metal, than cooled to −78°C and **1a** (2.16 g, 10 mmol) in THF (5 mL) was added and stirred at −78°C for additional 30 min. Then, the solid I_2 (2.54 g, 10 mmol) was added. The reaction mixture was stirred until the complete dissolution of I_2. After 45 min NH_4Cl (1.5 g) was added and the ammonia was evaporated at 10 mm of Hg. The residue was poured into the mixture of toluene and $KHSO_4$ solution. The water layer was extracted with toluene, and the combined organic phase was dried over $MgSO_4$. The solvent was evaporated, and the crude product was purified by crystallization and chromatography:

Entry 9. **1d** ($CHCl_3$), 0.009 g (0.03 mmol, 0.6%); **3a,b** ($CHCl_3$: MeOH = 50 : 1), 1.776 g (4.9 mmol, 98%).

TABLE 1 Synthesis of $R_2P(O)I$ (**1d–g**)

1	R	R′	^{31}P NMR (THF/C_6D_6) of 1 δ (ppm)
d	Ph	*t*-Bu	60.64[15]
e	Ph	Ph	27.08[16]
f	$OCH(CH_3)_2$	$OCH(CH_3)_2$	−45.20[17]
g	$OCH_2C(CH_3)_2CH_2O$		−45.65

Synthesis of $R_2P(O)I$ [$R_2P(O)Br$]

$R_2P(O)Cl$ (5 mmol) in THF (5 mL) was added into the freshly prepared potassium naphthalenide (10 mmol) in THF (25 mL) at −78°C. The reaction mixture was stirred until the disappearance of the blue color. Then, chlorotrimethylsilane (1.2 mL, 10 mmol) was added. After 3 h, the reaction mixture changed color from yellowish to milk white, and I_2 (Br_2) (10 mmol) was added at −78°C, respectively. The cooling bath was removed, and after 16 h the reaction mixture was filtered through a short pad of silica gel. A sample of the reaction mixture was taken, C_6D_6 was added, and the ^{31}P NMR spectrum was recorded for $R_2P(O)I$ (Table 1). To the reaction mixture at −78°C, toluene/$KHSO_4$ water solution was added. The organic phase was separated and dried ($MgSO_4$). The solvent was evaporated, and the crude product purified by crystallization, distillation and chromatography for $R_2P(O)Br$.

*Synthesis of $R_2P(O)Br$ (**1c** and **1h**)*

Entry 14. 2-bromo-5,5-dimethyl-(1,3,2)-dioxaphosphinane-2-oxide (**1h**) [3] 0.878 g (7.7 mmol, 77%), mp = 91–92°C; ^1H NMR ($CDCl_3$) $\delta = 0.82$ (s, CH_3, 3H), 1.19 (s, CH_3, 3H), 3.87 (dd, $J_{H-H} = 10.25$ Hz, $J_{P-H} = 29.75$ Hz, CH, 2H), 4.13 (dd, $J_{H-H} = 10.25$ Hz, $J_{P-H} = 2.75$ Hz, CH, 2H), ^{31}P NMR ($CDCl_3$) $\delta = -14.30$.

Entry 15. **1c** (Kügelrohr, 136°C/0.5 mmHg), 1.227 g (9.4 mmol, 94%).

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