Studies on the preparations of organophosphorus compounds from triphenylphosphine oxide

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July 2021

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Doctoral Program in Chemistry

Submitted to the Graduate School of

Pure and Applied Sciences

in Partial Fulfillment of the Requirements

for the Degree of Doctor of Philosophy in

Science

at the

University of Tsukuba

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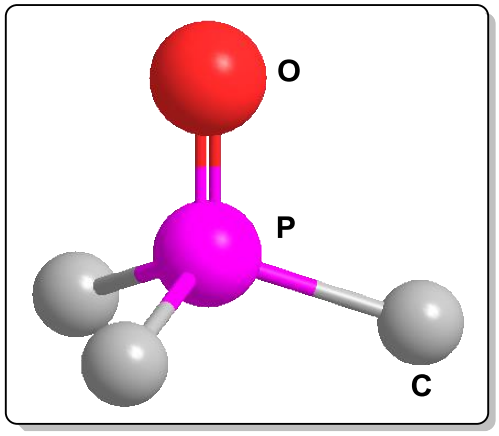
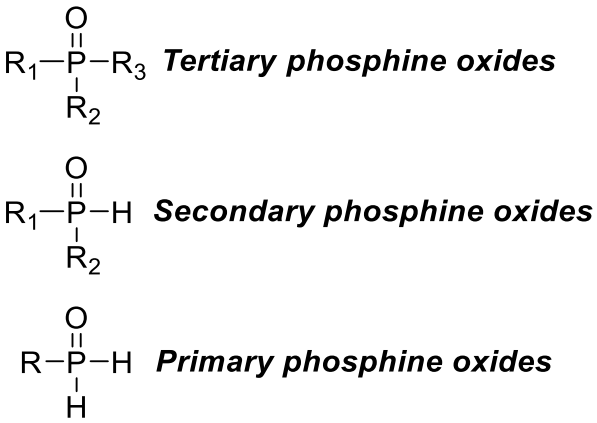
Chapter 1 General Introduction

1.1 Organophosphine Oxide Compounds

Organophosphine oxides are a class of pentavalent phosphorus compounds with the formula $R_3P(O)$ possessing one P=O bond and three P-R bonds wherein R is generally alkyl or aryl group, featuring tetrahedral structure with phosphorus atom at the center (Scheme 1.1).[1] Calculation and experimental studies have indicated that the P=O bond can be described as one highly polarized σ-bond plus strong back-bond of the oxygen π orbitals, and thus a highly ionic dative $R_3P^+–O^-$ is better than the traditional double bond to depict phosphine oxides.[1] Generally, there are three kinds of phosphine oxides (primary, secondary and tertiary phosphine oxides) shown in Scheme 1.1, among which tertiary phosphine oxides are the most studied and applied because of their strong chemical stability and diversity, whereas the primary and secondary phosphine oxides are usually used as starting materials for the preparation of other organophosphorus compounds.

Scheme 1.1 Phosphine oxides

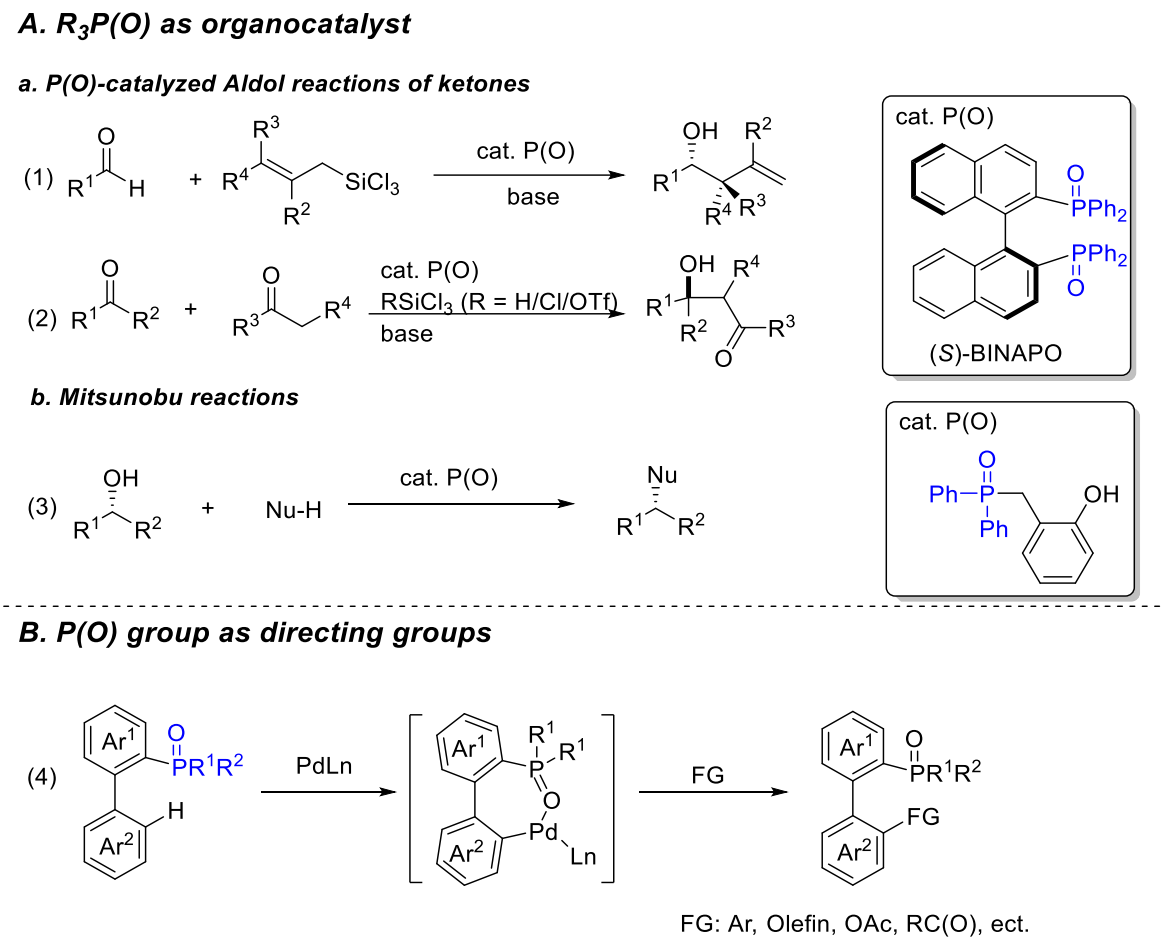




Tertiary phosphine oxides have seen extensive applications in tremendous fields, mainly in the synthetic industry,[2] medicine chemistry,[3] phosphorescent material,[4] flame retardants[5] as well as metal extraction.[6] For example, in the synthetic chemistry, (*S*)-bis-(diphenylphosphanyl)-binaphthyl dioxide ((*S*)-BINAPO) is used as efficient catalysts in the aldol reactions for the enantioselective addition of allyltrichlorosilane to aldehydes generating the corresponding homoallylic alcohols as well as the direct aldol reaction of two ketones (Scheme 1.2 A).[2a-2d] Very recently, Denton et al. smartly designed a novel phosphine oxide that can catalyze the classical Mitsunobu reactions with high efficiency and stereoselectivity (Scheme 1.2 A).[2e] Moreover, since the P=O

group features good coordination properties to transition metals, Yang and coworkers have developed a series of methodologies on P=O directed C-H bond functionalization by which a range of biphenyl compounds bearing a monophosphine oxide group are readily and efficiently modified with a series of functional groups such as aryl, olefin, AcO, RC(O), *via* a seven-membered cyclopalladium intermediate,[2f] demonstrating a unique landmark in the subject of C-H activation (Scheme 1.2 B).

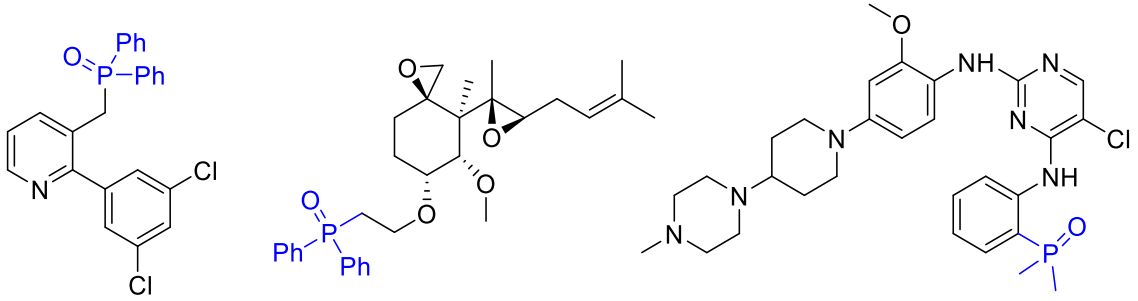
Scheme 1.2 Applications of phosphine oxides in organic synthesis.



The high polarity of phosphine oxides results to high solubility and metabolic stability,[3a] thus the phosphine oxide-base compounds can be applied in the medicinal chemistry. As exemplified in Scheme 1.3, some representative phosphine oxide drugs are present. For example, diphenyl(pyridin-3-ylmethyl)phosphine oxide derivative (also named as Kv1.5 inhibitor) has been considered as a potential drug for treatment of Atrial Fibrillation by inhibiting the Kv1.5 potassium ion channel.[3b] MetAP2 inhibitor bearing a diphenyl(ethyl)phopsphine oxide motif, had been used to treat obesity and the related diseases.[3c] A dimethylphosphine oxide-based drug named as Brigatinib, designed and synthesized by Huang and

coauthours,[3d] was the first drug approved by U.S. FDA in 2017 for the treatment of metastatic non-small-cell lung cancer (NSCLC) that accounts for 80%–90% of lung cancers that takes hundreds of thousands of people's lives annually.[3e]

Scheme 1.3 Applications of phosphine oxides in medicinal chemistry



Kv1.5 inhibitor for Atrial fibrillation

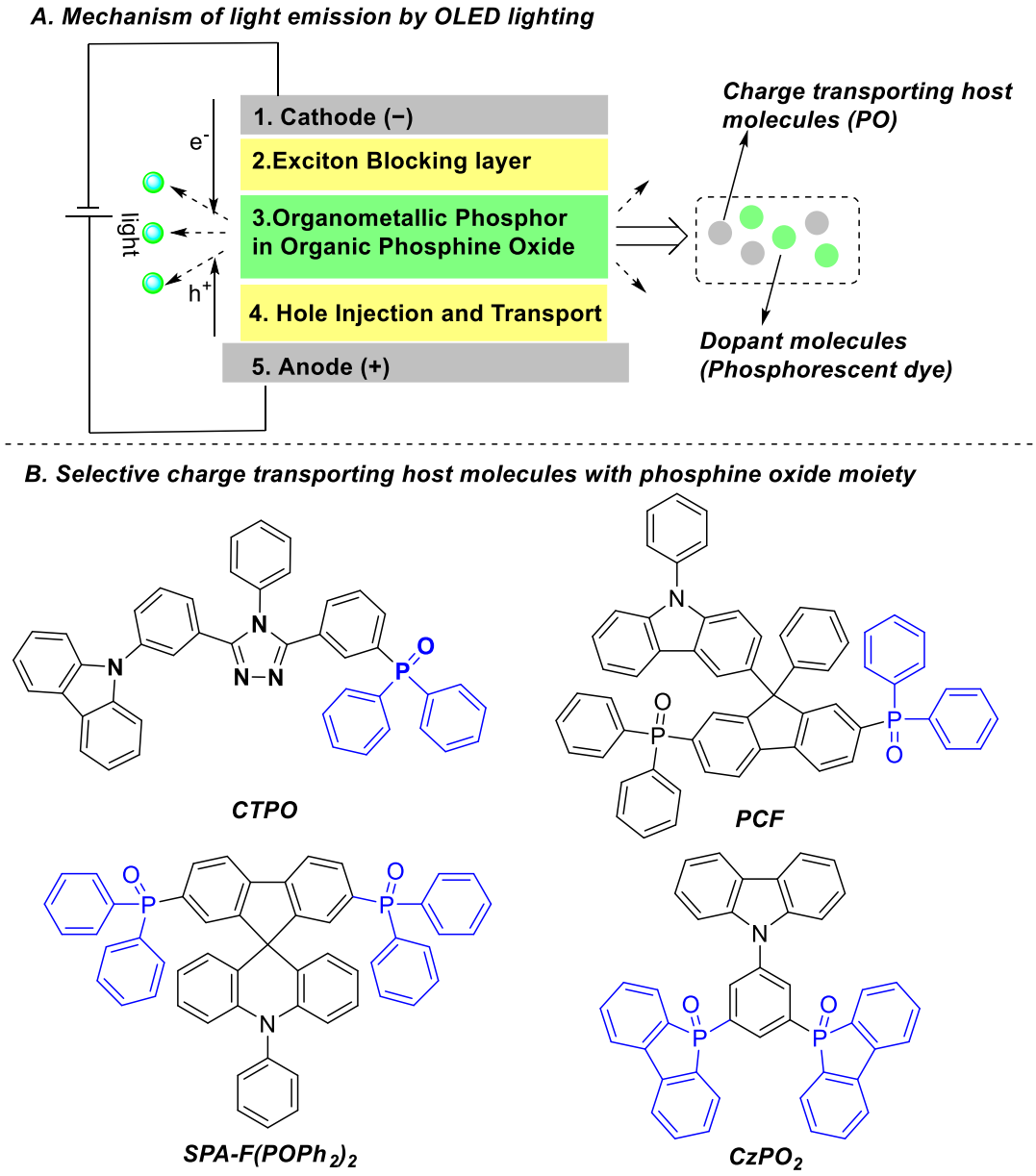
MetAP2 inhibitor for obesity diseases

Brigatinib for metastatic non-small-cell lung cancer

The phosphorescent organic light emitting diodes (PHOLEDs) have attracted extensive attentions because of their high internal quantum efficiency at low voltage than the traditional organic light emitting diodes (OLEDs).[4a] The mechanism of light emission of OLED device is that, the recombination energy of electrons (e^-) from the cathode (-) and holes (h^+) from the anode (+) excited the emissive layer (green layer), which then emits light when returning to the ground state (Scheme 1.4A).[4b, 4e, 4f] Due to the P=O group features high polarity and electron-withdrawing properties, so when employing phosphine oxides as the charge transporting host material (component of the emissive layer), they can facilitate both electron (e^-) and hole (h^+) injection and transport, thus greatly enhancing the quantum efficiency.[4a-4c] Another advantage is the specific tetrahedral geometrical structure of phosphine oxide motif does not extend the conjugation of the core after being introduced into the structures of light emitting materials, which well ensures the stability of electrochemical and photophysical properties of the original materials.[4a] For example, Cui et al designed a bipolar host material 9-(3-(5-(4-(diphenylphosphoryl)phenyl)-4-phenyl-4H-1,2,4-triazol-3-yl)phenyl)- 9H-carbazole (**CTPO**) bearing carbazole, triazole and phosphine oxide moieties (Scheme 1.4B) that exhibits high thermal stability, suitable HOMO and LUMO levels, high triplet energy and excellent bipolar charge transport abilities.[4g] Besides, 2,7-bis(diphenylphosphine oxide)-9-(9-phenylcarbazol-3-yl)-9-phenylfluorene (**PCF**),[4b] spirophenylacridine-2,7-(diphenylphosphineoxide)-fluorene (**SPA-F(POPh$_2$)$_2$**)[4h] and star-shaped molecule 9-

(3,5-bis(diphenylphosphoryl)phenyl)-9H-carbazole (**C_ZPO_2**)[4i] etc. had been developed as the representative charge transporting host materials.

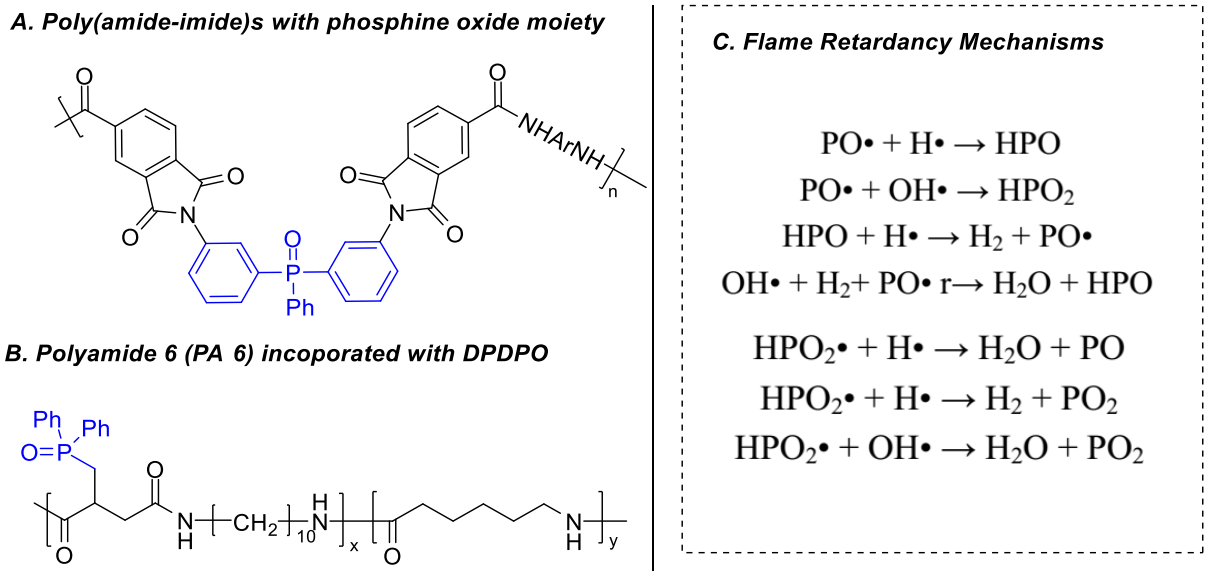
Scheme 1.4 Phosphine oxides applied in OLEDs



Flame retardants are consumed in millions of tons each year and the consumption will be growing substantially in the future with the development of electronics, construction and transportation. Among them, organophosphorus flame retardants (OPFRs) are a class of promising and efficient flame retardants that share 14% of global flame retardant consumption, and tend to be the main substitution of the traditional halogenated flame retardants for fulfilling the environmental protection and sustainable development.[5a-b] Generally, organic phosphate esters are the most widely employed flame retardants.[5c-d] On the other hand, recent decades of years

have seen the rapid development of the flame-retardant polymers with phosphine oxide moieties, since the phosphine oxide groups have hydrolytically stable P-C bonds and oxidatively stable P=O bonds.[5e] The flame retardant mechanism is that PO radicals can play important roles in the gas phase where hydrogen and hydroxy radicals are rendered by the radical recombination with PO radicals, thus slowing down the oxidation of hydrocarbons in the gas phase (Scheme 1.5C).[5e] Researchers found that, the relevant polymer materials containing phosphorus usually exhibit better flame-retardant properties and high thermal oxidative stability. There are selective examples depicted in Scheme 1.5, incorporation of phosphine oxide moieties into different polymeric backbones such as poly(amide-imide)s and polyamides, can significantly improve the flameretardant properties.[5f-g]

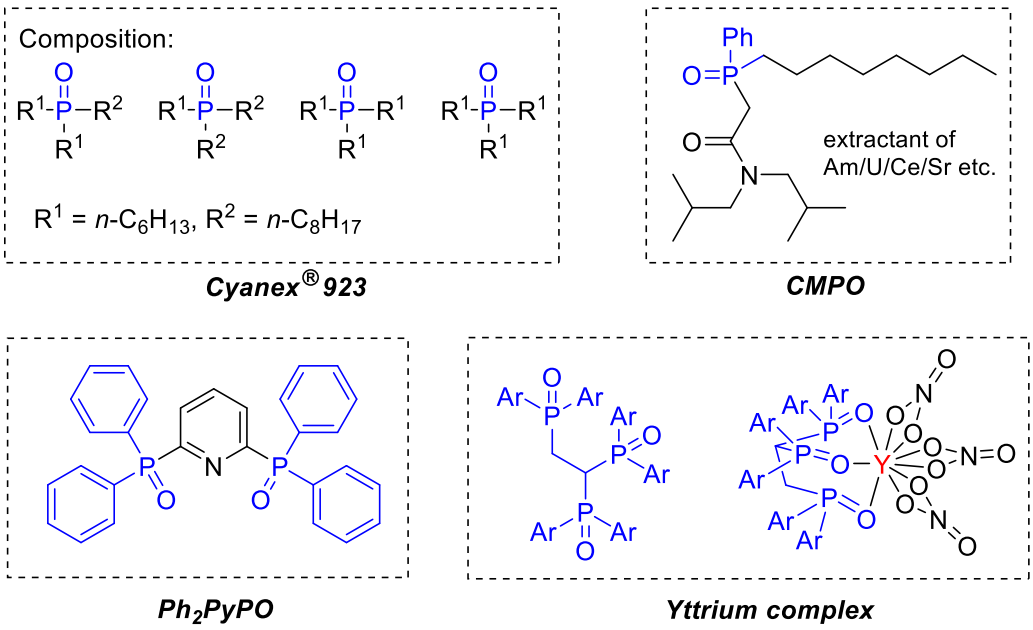
Scheme 1.5 Phosphine Oxide-Containing Polymers as Fire Retardant Materials



With the increasing demand for rare earth elements as well as environmental protection associated with heavy-metals (such as lead, mercury, chromium, cadmium, etc.), separation of the mineral metals and selective extraction of the toxic heavy metals are significant in the modern industry and society.[6] Because P=O groups feature good coordination properties to metals, the phosphine oxides are used as metal extractants (Scheme 1.6). The commercial CYANEX® 923 that is composed of several different kinds of trialkylphosphine oxides, can be used as metal or solvent extractants. [6a-6b] In addition, the well-known extractant, octyl(phenyl)-*N*,*N*-diisobutylcarbamoylmethylphosphine oxide (**CMPO**), has been widely employed to extract radioactive metal

ions such as radioactive americium (Am), uranium (U) and other metals like cerium (Ce), strontium (Sr) with high efficienvy.[6c-g] Borisova reported a phosphine oxide-based extractant pyridine-2,6-diylbis(diphenylphosphine oxide) (**Ph_2PyPO**) that can extract and separate americium (Am) which is a high-level radioactive waste in the nuclear power industry.[6h] In 2012, Morris and coworkers designed and synthesized a series of tripodal phosphine oxide extraction agents toward the rare-earth metal yttrium (Y) that has wide applications in many fields such as garnets synthesis, material enhancer, medical and superconductors etc.[6i]

Scheme 1.6 Applications of Phosphine Oxides as Extractants



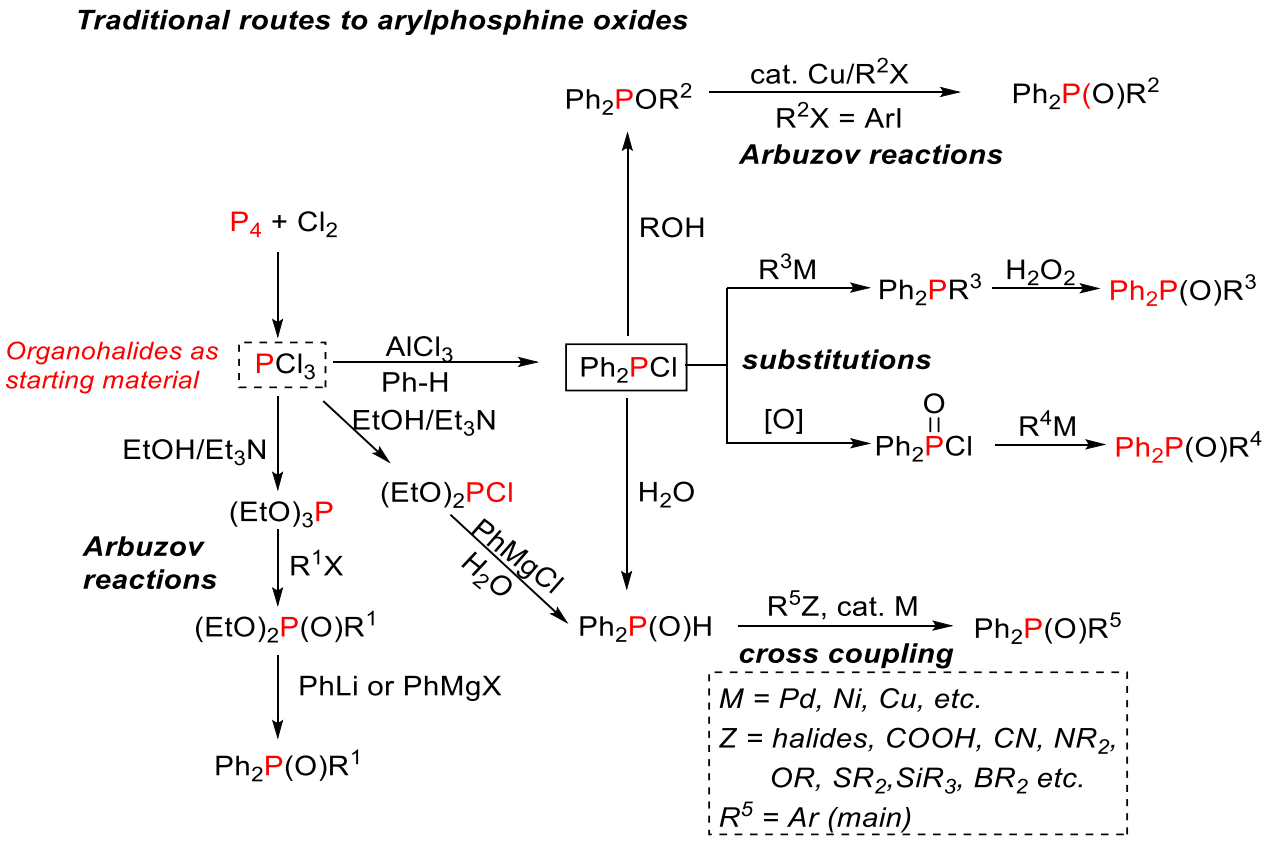
1.2 Traditional Methods for the Synthesis of Phosphine Oxides

Considering the wide applications of phosphine oxides in the modern chemistry, tremendous methods for their preparation have been thrivingly developed in the past several decades of years. The most frequently used is the substitution reactions of diphenyl chloride Ph_2PCl with organometallic reagents RM (organolithium reagents RLi or Grignard reagents RMgX) followed with oxidation by air or H_2O_2,[7a] similarly, direct treatment of diphenylphosphinyl chloride $Ph_2P(O)Cl$ with organometallic reagents RM is another basic classical route to phosphine oxides.[7b] However, these methods suffered from the harsh conditions, limited substrate scope and employment of toxic reagents. Equally importantly, construction of P-C bonds also depends on the Michaelis-Arbuzov reaction of a trivalent triethyl phosphite ($P(OEt)_3$) with an alkyl halide RX forming a pentavalent phosphonate $RP(O)(OEt)_2$ and subsequent substitution reaction with Grignard reagents PhMgX that finally

result to diphenyl(alkyl)phosphine oxide $Ph_2P(O)R$.[7b,7c] Or briefly, in 2014, Taillefer and coworkers developed a copper-catalyzed Michaelis-Arbuzov reaction of ethyl diphenyl phosphinite (Ph_2POEt) with aryl iodides (ArI) in the presence of 4 equivalents of Cs_2CO_3 to form phosphine oxides.[7d]

As the rapid development of transition-metal catalyzed reactions, 1981, Hirao first reported the cross coupling of a diakyl phosphite $(RO)_2P(O)H$ with aryl halide ArX to form a phosphonate $(RO)_2P(O)Ar$, providing a landmark of forming P-C bonds.[7e] After that, catalyzed by transition metals (Pd, Ni, Cu etc.), diakyl phosphites $(RO)_2P(O)H$ as well as secondary phosphine oxides $R_2P(O)H$ had been used to couple with a series of prefunctionalized arenes such as aryl halides (ArX),[7f] arylphenol derivatives (aryl mesylates, tosylates or pivalates, etc),[7g-i] aryl sulfides (ArSR),[7j] aryl boronic acids $(ArB(OH)_2)$,[7k] arylhydrazines $(ArNHNH_2)$,[7l] aryldiazoium salts (ArN_2X),[7m] activated aryl carboxylates (ArCOOH)[7n] and amides $(ArCONR_2)$,[7o] aryl nitriles (ArCN),[7p] and aryl silanes $(ArSiR_3)$,[7q] via the C-X, C-O, C-S, C-B, C-N, C-C, C-Si bond cleavage, efficiently delivering the corresponding phosphine oxides. Recently, C-H activation strategies had been applied to the P-C bond formations.[7r-s]

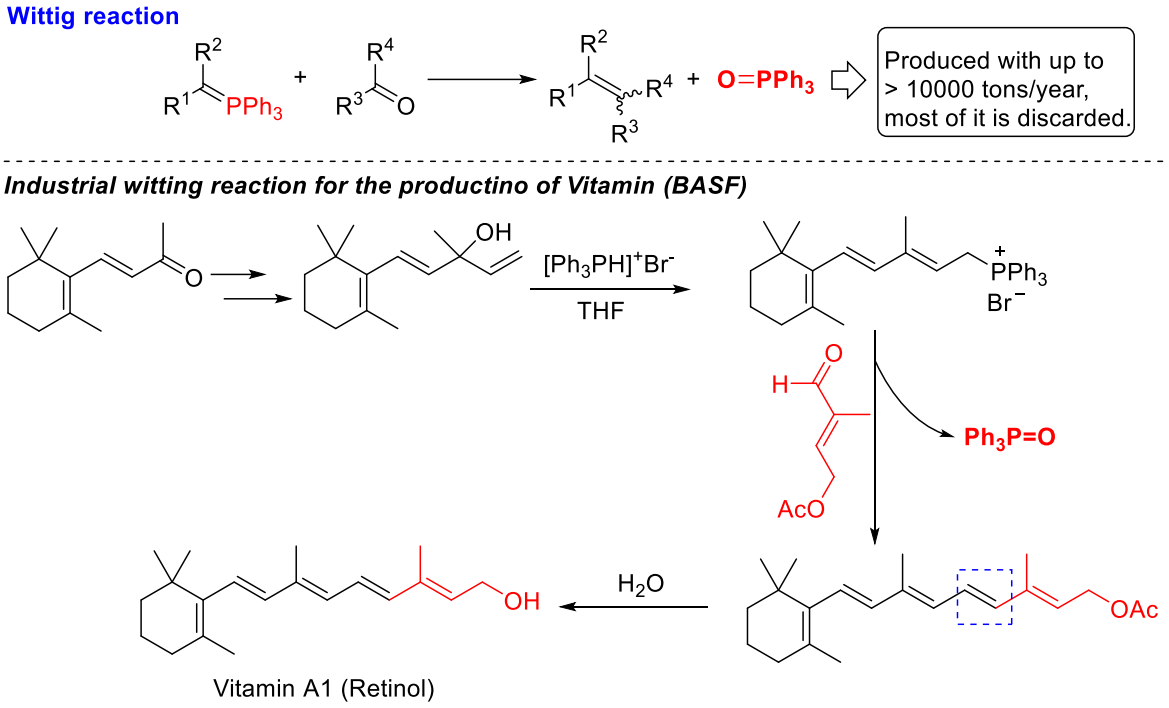
Scheme 1.7 Summary of the known methods toward phosphine oxides



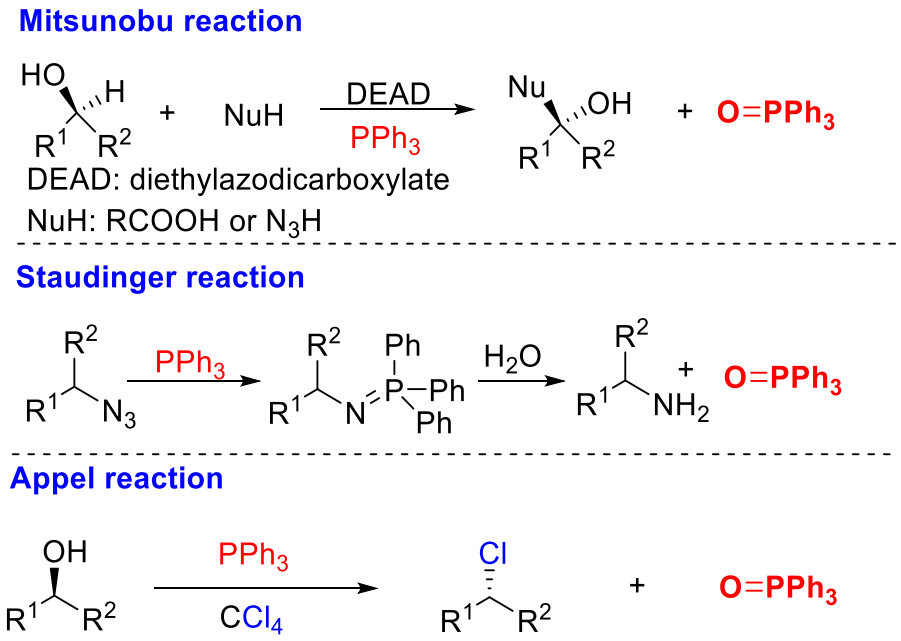
1.3 Triphenylphosphine Oxide: An Industry Waste and the Relevant Solutions

Owing to the extensive application of triphenylphosphine (Ph_3P) in synthetic industry such as Wittig, Mitsunobu, Staudinger, and Appel reactions, triphenylphosphine oxides ($Ph_3P(O)$) is generated as a main byproduct with tens of thousands of tons every year (Scheme 1.8 and 1.9).[8a-d]

Scheme 1.8 Triphenylphosphine oxide is produced as byproduct from wittig reactions.



Scheme 1.9 Other reactions generating triphenylphosphine oxide in the synthetic chemistry.

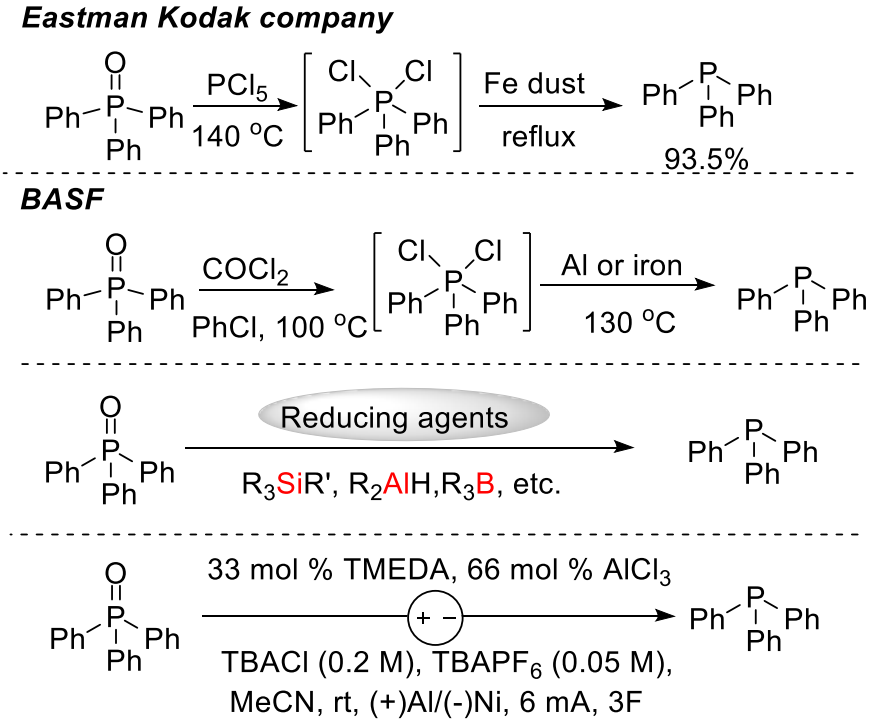


Majority of $Ph_3P(O)$ is generated by the wittig reactions for the producing Vitamin in the industry (BASF

process),[8e,] with over tens of thousands of $Ph_3P(O)$ each year, what's worse, most of it has been discarded as a useless waste because of its high bond strength of the P=O bond (about 500 KJ/mol)[9] and difficult utilization in industry.

For the perspective of recycling of phosphorus resources and sustainable development, tremendous efforts have been devoted to deal with the waste issue of $Ph_3P(O)$. Until now, the most common solutions concentrated on the reduction of $Ph_3P(O)$ to its original form Ph_3P by using all sorts of reducing reagents, and the most frequently used reduction strategy in the industry is the treatment of phosphine oxide with PCl_5 or phosgene $COCl_2$ forming the pentavalent Ph_3PCl_2 and subsequent addition of active metals like aluminum or iron that gives Ph_3P efficiently.[10a-b] Later, a series of other reductants such as silanes, aluminum hydrides, borane, oxalyl chloride and other agents (Scheme 1.10) had been developed in the laboratory that had been highlighted in

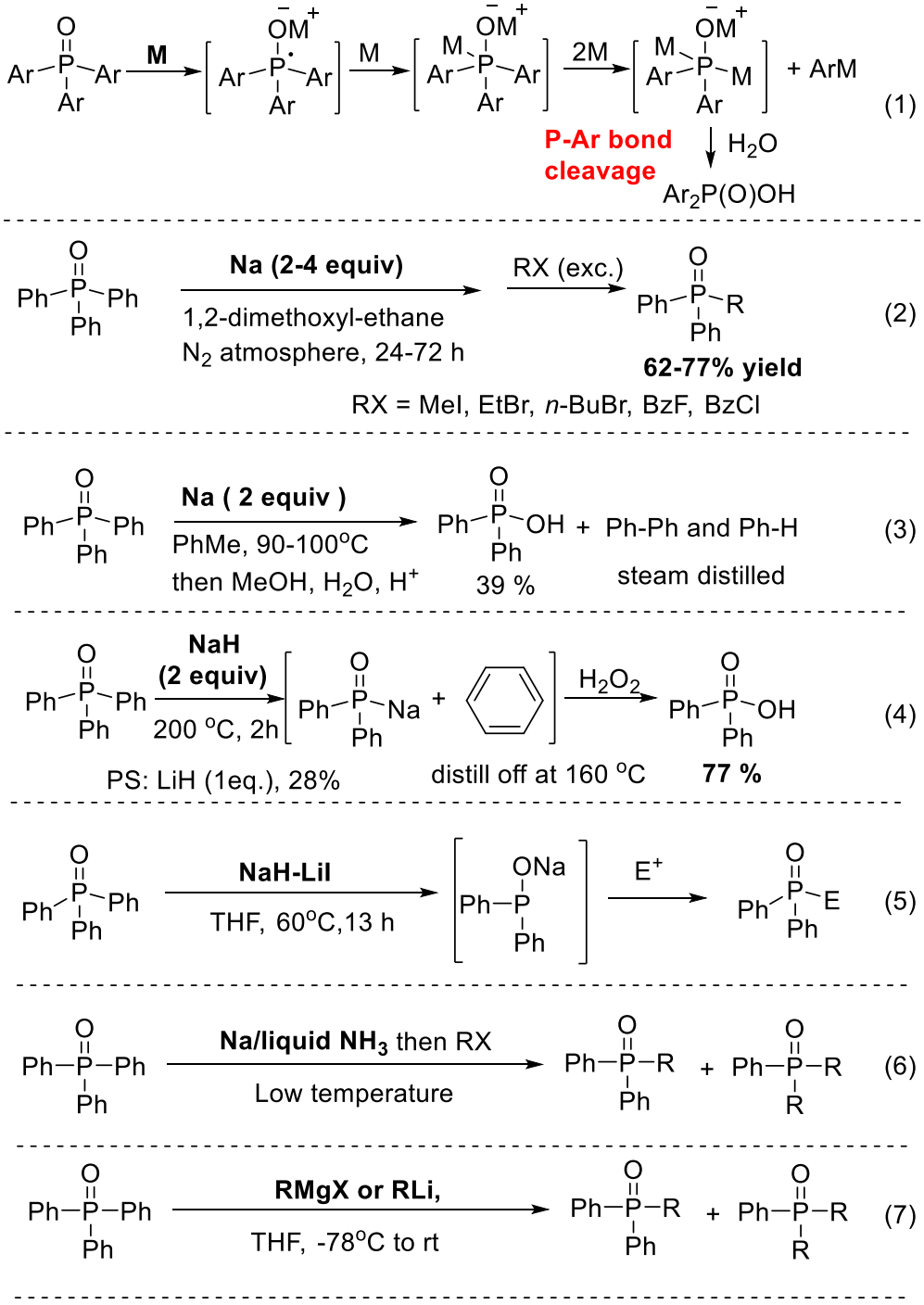
Scheme 1.10 Reduction of $Ph_3P(O)$ in the industry and laboratory



several reviews.[10c-d] Very recently, electroreduction has been reported to reduce phosphine oxides.[10e] However, all these solutions had to introduce the toxic and environmentally friendly organohalide reagents that would arise secondary pollutions, additionally, the expensive reducing agents and harsh reduction conditions heavily limited their practical application in the industry.

On the other hand, directly using triphenylphosphine oxide as starting material to prepare new organophosphorus compounds is a straightforward solution (Scheme 11). In 1953, Pohlemann was the first to discover the phenomenon that colourless tertiary arylphosphine oxide in xylole treating with an alkali metal resulted to a brown solution, and then identified the cleavage of P-C bond occurred in the process (eq 1).[11a] In 1959, Hoffmann and coworkers discovered that by reacting $Ph_3P(O)$ with excessive metallic sodium in 1,2-dimethoxyl-ethane under nitrogen, the P-Ph bond could be cleft, quenching the reaction mixture with organic halide (R'X, R = Me, Et, *n*-Bu, Benzyl etc.) gave the corresponding diphenyl(alkyl)phosphine oxide in 62-77 yields (eq 2).[11b-c] In the meantime, Horner also reported a similar P-C bond cleaving reaction with sodium using toluene as solvent that finally obtained a moderated yield of diphenylphosphinic acid (eq 3).[11d] One year later, Horner employed sodium hydride NaH to conduct the similar reaction, 77% yield of product could be achieved,[11e] however, the heating temperature was up to 200 ^oC (eq 4). To improve the reaction efficiency and gentle the harsh conditions, very recently, Chiba and co-authors found that, by using sodium hydride-iodide composite (NaH-LiI), $Ph_3P(O)$ was readily converted to sodium phosphinite intermediate via P-C bond cleavage at 60 ^oC, and subsequent quenching reactions with electrophiles resulted a range of functionalize new phosphine oxides in good yields (eq 5).[11f] After that, employing sodium dispersed in liquid ammonia turned out to be an efficient approach to transform $Ph_3P(O)$ to diphenylphosphinite ion (Ph_2PO^-), and the alkylation or arylation derivatives ($Ph_2P(O)R$) was easily accessed. However, in addition to the tedious process under low temperature, *tert*-butyl alcohol was required to neutralize the co-generated base (eq 6).[11g-h] Apart from the metallic sodium, the reactive organometallic reagents including the organolithium (RLi) and Grignard reagents (RMgX) were capable of modifying $Ph_3P(O)$ via P-Ph bond cleavage through nucleophilic substitutions that resulted to the diphenyl(alkyl) phosphine oxides or dialkyl(phenyl)phosphine oxides, even the cyclic dibenzophosphole oxide compounds by treating with PhLi under reflux conditions could be delivered (eq7), however, the low conversion and poor selectivity limited its practical application.[11i-k]

Scheme 1.11 Direct transformation of $Ph_3P(O)$



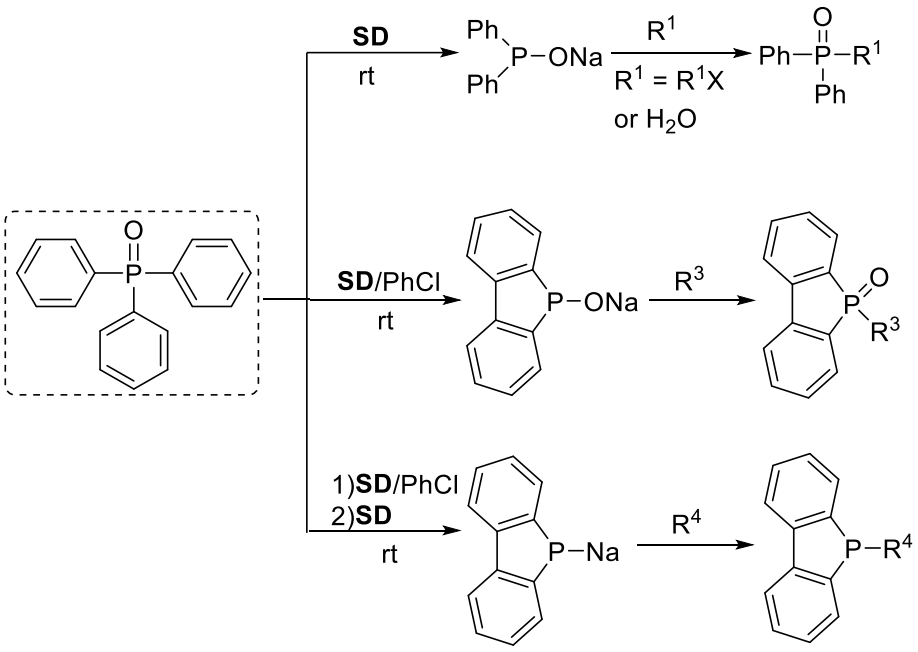
1.4 Themes of this thesis: efficient utilization of $Ph_3P(O)$ to valuables

The waste problem associated with triphenylphosphine oxide is still severe although so many solutions has been developed, because of the low efficiency and high cost. In the current study, by employing a cheap and earth-abundant metallic sodium (sodium finely dispersed in paraffin oil with μm-scale particles, hereafter abbreviated as SD) as the key reagent, triphenylphosphine oxide could be used as the starting material that is

selectively transformed to diverse valuable organophosphorus compounds in high efficacy.

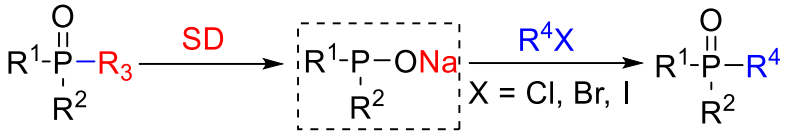
Chapter 2 disclosed the selective conversion of triphenylphosphine oxide to three reactive organophosphorus intermediates—sodium diphenylphosphinite, sodium 5H-benzo [b]phosphindol-5-olate and sodium benzo[b]phosphindol-5-ide—that efficiently give the corresponding functional organophosphorus compounds in good yields (Scheme 1.12). The initial discovery, reaction conditions optimization, mechanism depiction, and the relevant applications were presented.

Scheme 1.12 Selective conversion of $Ph_3P(O)$ by SD



In Chapter 3, several important problems left in chapter 1 were solved (Scheme 1.13). First, the SD-mediated P-C bond cleavage was smoothly extended to the reaction of other pentavalent phosphine oxides $R_3P(O)$, and the selectivity of P-alkyl bond and P-aryl bond by sodium was also discussed. On the other hand, among the three alkali metals M (M = Li, Na and K) investigated, sodium exhibited the best efficacy and selectivity for converting triphenylphosphine oxide $Ph_3P(O)$ to diphenylphosphinite $Ph_2P(OM)$. In addition, the destiny of co-generated PhNa from the reaction of $Ph_3P(O)$ with Na was disclosed. Last, the reactivity of Ph_2PONa toward alkyl halides and aryl halides was completed. The mechanism of P-C bond cleavage by Na was discussed.

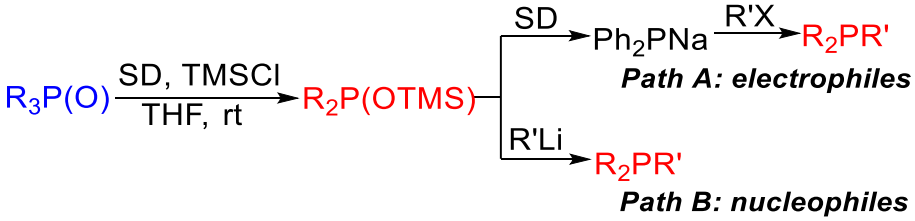
Scheme 1.13 The reactions of tertiary phosphine oxides with sodium



R^1, R^2 = Ph, alkyl, alkoxyl
R^3 = Ph, alkoxyl
R^4 = alkyl, aryl

In Chapter 4, as mentioned in chapter 1, sodium 5H-benzo [b]phosphindol-5-olate could be readily reduced to sodium benzo[b]phosphindol-5-ide, I wondered whether the corresponding sodium diphenylphosphinite Ph_2PNa would be also generated from $Ph_3P(O)$ by deeper investigation. Therefore, in this chapter (Scheme 1.14), by introducing trimethylsilyl chloride (TMSCl), the pentavalent phosphoryl compounds $R_3P(O)$ such as triphenylphosphine oxides, secondary phosphine oxides etc., were readily converted to the corresponding $R_2P(OTMS)$ intermediates, that can further react efficiently with SD and then with an electrophile R'X, or directly with a nucleophile R'Li to produce the corresponding trivalent phosphines R_2PR'. By this strategy chiral phosphines could also be obtained with high stereospecificity. The mechanism of P-R (R = C or O) bond cleavage of phosphine oxides was discussed.

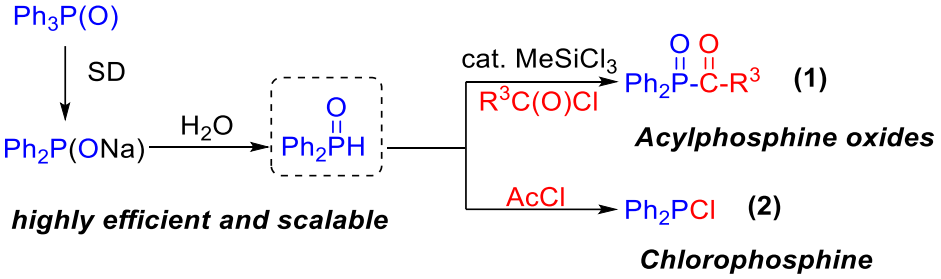
Scheme 1.14 Reduction transformation of P(V) to P(III) (From $R_3P(O)$ to R_2PR')



Chapter 5, by using diphenylphosphine oxide $Ph_2P(O)H$ as starting material that could be efficiently and prepared from $Ph_3P(O)$ in large scale, two highly valuable industrial products, acylphosphine oxides and chlorophosphines were readily synthesized respectively. By treating with acyl chlorides and using chlorosilanes as addictive or catalyst, $Ph_2P(O)H$ could be converted to acylphosphine oxides in high yields (Scheme 1.15, eq 1). A series of acyl chlorides coupled with secondary phosphine oxides smoothly by the strategies. On the other hand, direct treatment of diphenylphosphine oxide with a simple acetyl chloride resulted to diphenylphosphine chloride, the strategy could be also appliable to transform other secondary

phosphine oxides to the corresponding phosphine chlorides in good efficiency (Scheme 1.15, eq 2). These both transformations largely further broaden the utilization of $Ph_3P(O)$.

Scheme 1.15 Applications: synthesis of acylphosphine oxides and chlorophosphines



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Chapter 2 Conversion of Triphenylphosphine Oxide to Organophosphorus *via* Selective Cleavage of P-C, P-O, and C-H Bonds with Sodium

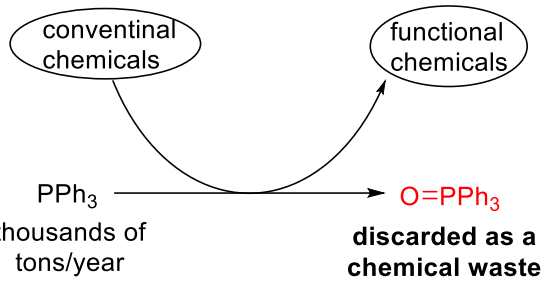
Abstract

Over half a century, thousands of tons of triphenylphosphine oxide $Ph_3P(O)$ have been produced every year from the chemical industries as a useless chemical waste. Herein, I disclose efficient transformations of $Ph_3P(O)$ with the cheap resource-abundant metallic sodium fine dispersed in paraffin oil (SD Na). $Ph_3P(O)$ can be easily and selectively transformed to three reactive organophosphorus intermediates (sodium diphenylphosphinite, sodium 5H-benzo[b]phosphindol-5-olate and sodium benzo[b]phosphindol-5-ide that efficiently give the corresponding functional organophosphorus compounds in good yields. These functional organophosphorus compounds are difficult to prepare but highly industrially useful compounds. Therefore, now $Ph_3P(O)$ is no longer a chemical waste but a precious starting material for highly valuable phosphorus compounds.

2.1. Introduction

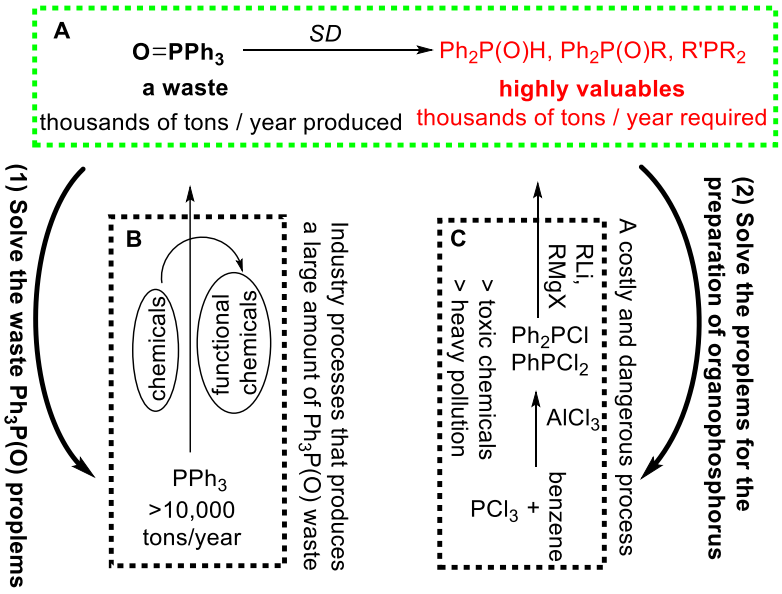
Triphenylphosphine oxide $Ph_3P(O)$ is a chemically stable compound that is primarily generated, tens of thousands tons a year, as a by-product from the chemical industries, during the preparation of valuable fine chemicals, such as vitamins, pharmaceuticals, agrochemicals etc, and bulk chemicals such as butanols, using triphenylphosphine PPh_3 as an oxophilic reagent or ligand for a metal catalyst (Scheme 2.1).[1-9] A well-known serious problem associated with $Ph_3P(O)$ is, thousands of tons of this compound are discarded as useless chemical waste because of its limited utilities. This situation has lasted for more than half a century, and has become a big concern from both industry and academia sides.[10-11] In order to solve this problem, extensive studies have been carried out world widely. Among them, the reduction of triphenylphosphine oxide $Ph_3P(O)$ to its original form triphenylphosphine Ph_3P is most studied.[12] However, either hard conditions or expensive reductants are required in order to break the strong P=O bond. Therefore, a practically operable way that can settle the triphenylphosphine oxide problem has not been found yet. [13-16]

Scheme 2.1 Triphenylphosphine Ph_3P ends up with its corresponding stable oxide $Ph_3P(O)$



Herein I disclose an effective solution to this longstanding problem that by simply treating with the cheap, resource-abundant metallic sodium (sodium fine dispersed in paraffin oil with μm-scale sizes; hereafter abbreviated as SD) at 25 °C, triphenylphosphine oxide $Ph_3P(O)$, the so far discarded chemical waste, can be transformed, easily and selectively, to a variety of organic phosphorus compounds (phosphoryl compounds and phosphines) that are widely used valuable chemicals in the industry (Scheme 2.2, A).[17] It is noted that the current process for the production of these organophosphorus compounds is rather dirty, energy-consuming and dangerous since it starts from the highly toxic benzene and phosphorus trichloride (Scheme 2.1, C).[18-19] Heavy pollution problems also associate with their preparation because of the poor efficiency. Therefore, the present new finding not only solves the waste $Ph_3P(O)$ problem (**1**) but also solves the problems associated with the preparation of other useful organophosphorus compounds (**2**).

Scheme 2.2 Comparison between the traditional methods and this new methods for the highly valuable phosphorus compounds[a]

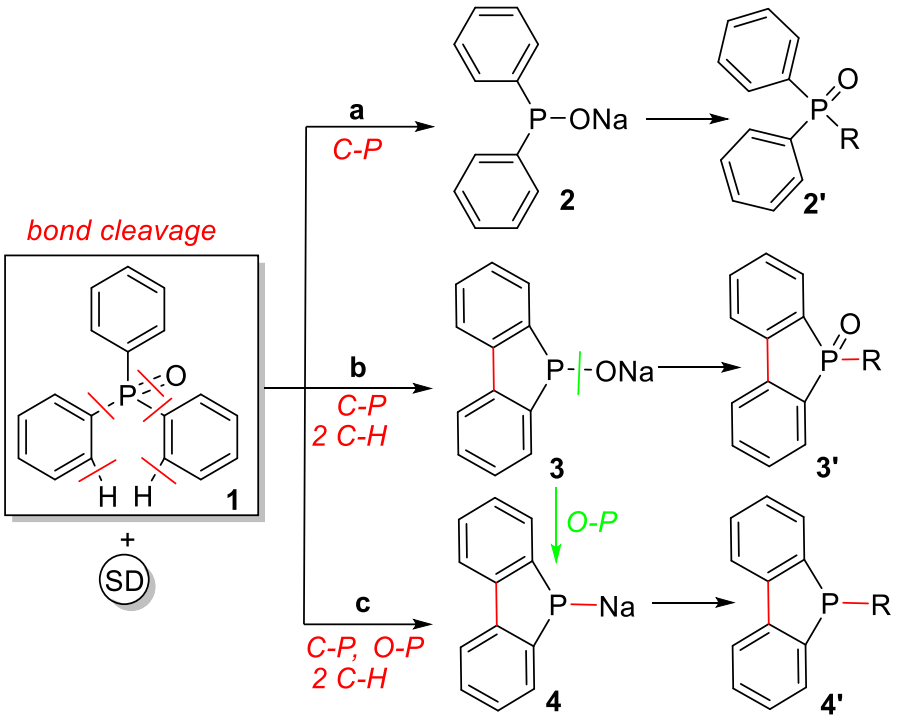


[a]**A** Transformation of $Ph_3P(O)$ to a variety of organic phosphorus compounds by SD. **B** A vast amount of $Ph_3P(O)$ is produced and

discarded as a useless chemical waste. **C** Costly and dangerous methods for the preparation of organophosphorus compounds.

Thus, as depicted in Scheme 2.3, starting from triphenylphosphine oxide **1**, by cleaving one C-P bond, sodium diphenylphosphinite **2** was generated quantitatively. This intermediate **2** was easily transformed to the corresponding phosphine oxides **2'** (**a**). On the other hand, by slightly changing the conditions, very interestingly, sodium 5H-benzo[b]phosphindol-5-olate **3** was generated in high yields *via* one C-P and two C-H bonds cleavage (**b**). More interestingly, the O-P bond in intermediate **3** could be further cleft to sodium benzo[b]phosphindol-5-ide **4** quantitatively (**c**). Thus, by simply treating with metallic sodium, triphenylphosphine oxide could readily produce three kinds of highly valuable phosphorus compounds.

Scheme 2.3 Unexpected easy conversion of $Ph_3P(O)$ to valuable organic phosphorus compounds[a]



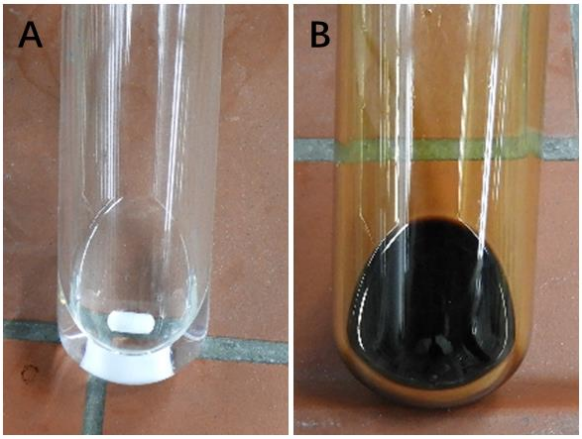
[a]These transformations provide solutions both to the waste $Ph_3P(O)$ problem and the preparation of organophosphorus compounds through selective C-P, C-H and O-P bond cleavage of triphenylphosphine oxide by SD under mild conditions. Condition a: **1** and SD in THF at 25 °C; Condition b: SD/PhCl then **1** at 25 °C, THF; Condition c: SD/PhCl, **1**, then SD at 25 °C, THF.

2.2 Results and discussion

2.2.1 Reactions of $Ph_3P(O)$ with metallic sodium.

I accidently discovered this rapid reaction of $Ph_3P(O)$ with metallic sodium as I added $Ph_3P(O)$ to THF that contains trace amount of metallic sodium initially used for its drying. The originally transparent colorless THF solution of $Ph_3P(O)$ (Scheme 2.4, A) instantly changed to yellow and then brown (Scheme. 2.4, B) at 25 ^oC! This clear color change is a strong indication that a rapid chemical reaction takes place between $Ph_3P(O)$ and sodium. Indeed, this is true. A subsequent experiment surprisingly revealed that, at 25 ^oC, upon adding sodium to $Ph_3P(O)$ dissolved in THF, an exothermic reaction took place rapidly and the starting material $Ph_3P(O)$ was completely consumed after 2 h! (Scheme 2.5, equation (1)).

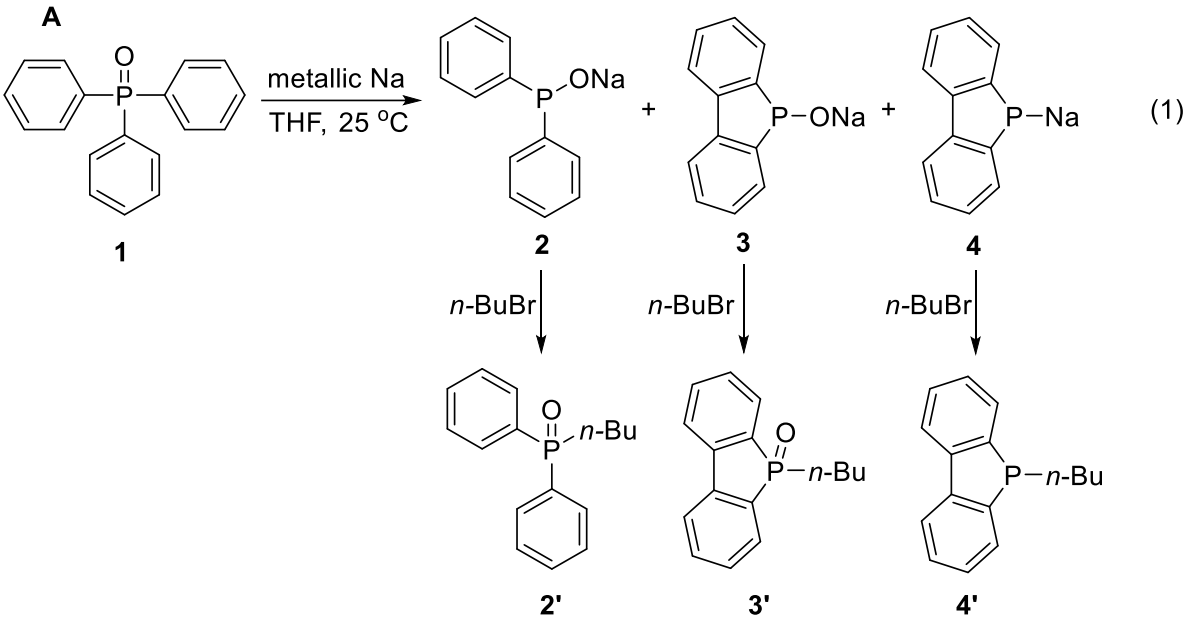
Scheme 2.4 Reactions of $Ph_3P(O)$ with metallic sodium. **A** $Ph_3P(O)$ dissolved in THF. **B** $Ph_3P(O)$ dissolved in THF in the presence of Na.



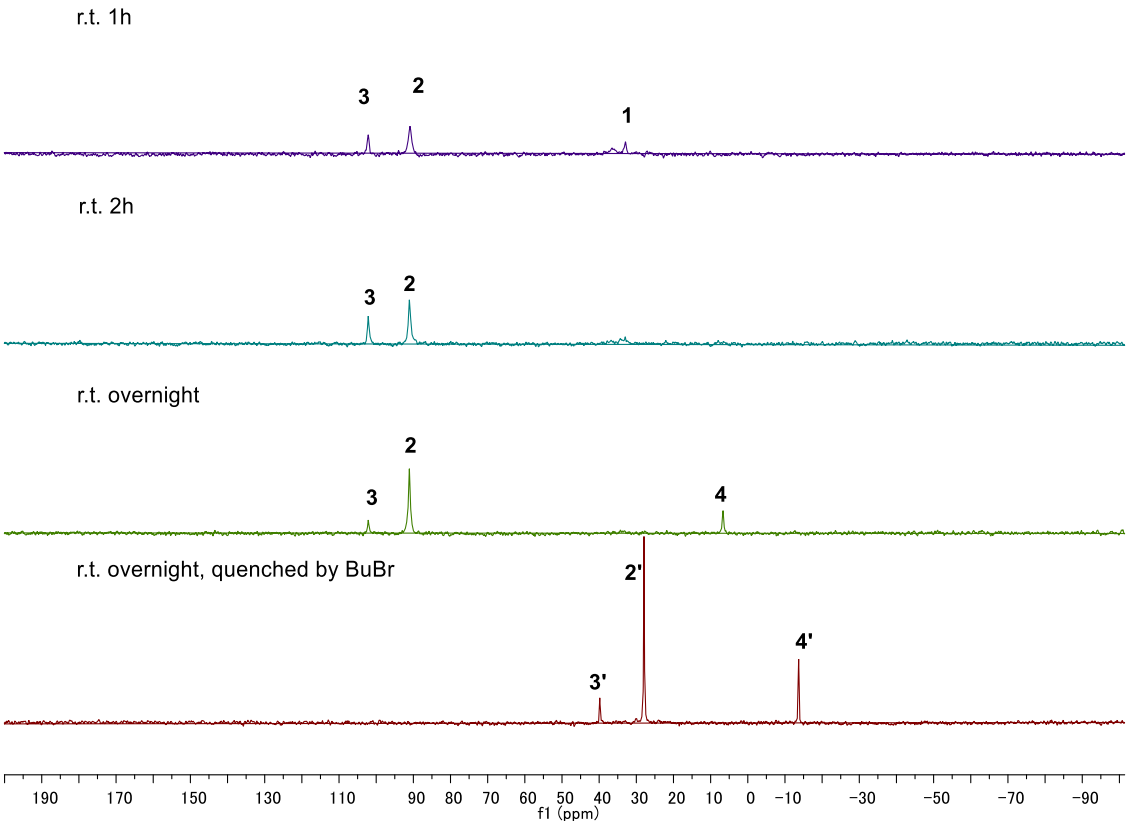
This easy conversion of $Ph_3P(O)$ by sodium was rather unexpected considering that until now literatures all had to conduct this reaction in a highly reducing medium by dissolving sodium in liquid ammonia (the Birch reduction medium) at low temperatures.[13-14] In addition to the tedious process under the Birch reduction system, that requires difficult handling and operating techniques, yields and selectivity of the desired products were also not satisfactory. A NaH/LiI composite system was recently reported to break down the C-P bond of triarylphosphine oxides. However, NaH is a rather costly reagent. Moreover, a long-time heating (overnight at 60^oC) was required.[16]

As shown in Scheme 2.5, metallic sodium (2.5 mmol), cut to small pieces, was added to $Ph_3P(O)$ (0.5 mmol) dissolved in THF (3 mL) at 25 ^oC (equation (1)). The color of the reaction mixture soon changed to brown. After stirring for 2 hours, ^{31}P NMR spectroscopy showed that the starting material $Ph_3P(O)$ at 32.9 ppm almost disappeared, and three new signals emerged at 91.1 ppm (compound **2**) and 102.1 ppm (compound **3**) and 6.7 ppm (compound **4**) after overnight stirring. In order to identify these compounds, *n*-BuBr was added to the solution and

Scheme 2.5 The reaction of triphenylphosphine oxide with sodium lump[a] that was monitored by ^{31}P NMR



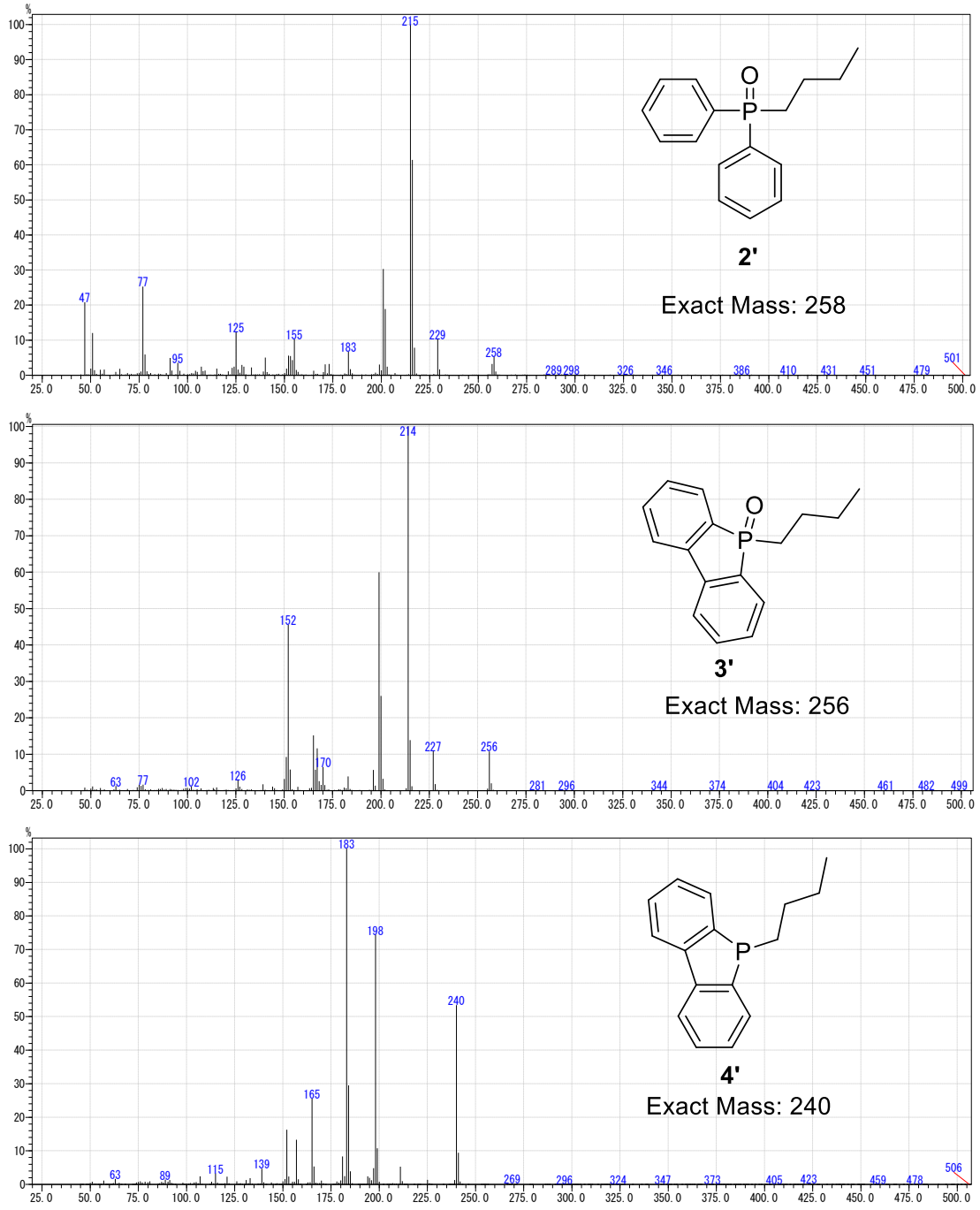
B. Monitored by ^{31}P NMR spectroscopy



[a]**A** reaction conditions: 0.5 mmol $Ph_3P(O)$ was dissolved in 3 mL THF, and 2.5 mmol metallic Na was added at 25 °C. **B** The reaction mixture was stirred for 1 hour, 2 hours and overnight and monitored by ^{31}P NMR, respectively.

2', **3'** and **4'** were obtained in 70%, 8%, and 21%, respectively (Initially characterized by GCMS, see Scheme 2.6), confirming that the new generated phosphorus species are sodium diphenylphosphinite (**2**), sodium 5H-benzo[b]phosphindol-5-olate (**3**) and sodium benzo[b]phosphindol-5-ide (**4**).

Scheme 2.6. MS (ESI) spectra copy of **2'**, **3'** and **4'**

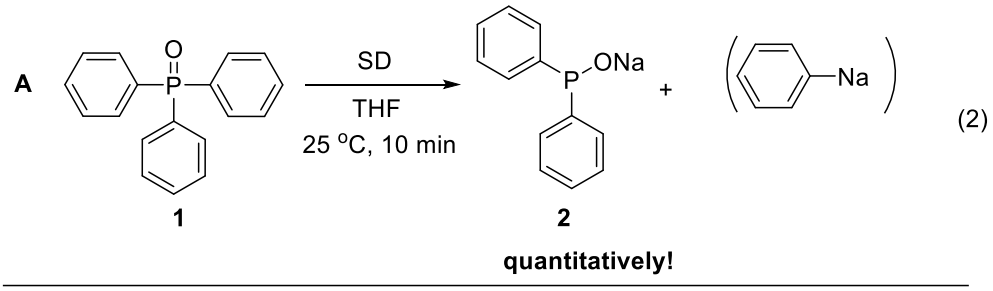


2.2.2 Selective generation of 2: the realization for the ready transformation of $Ph_3P(O)$ to $Ph_2P(O)H$ and $Ph_2P(O)R$.

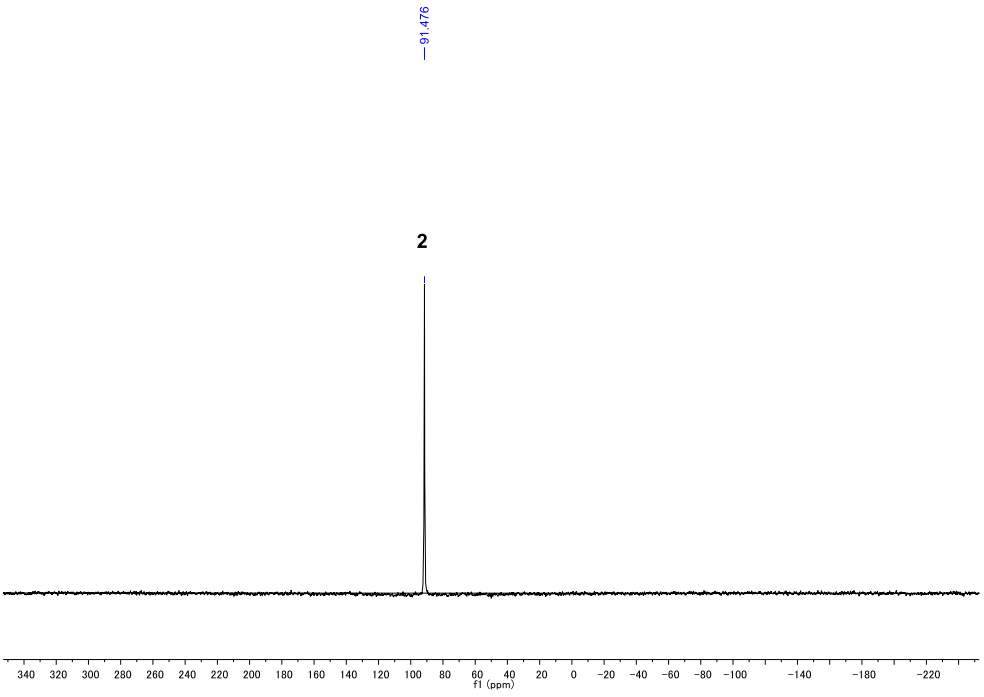
More excitingly, in addition to the disclosure of the event that $Ph_3P(O)$ could readily react with sodium under mild conditions, the reaction conditions for the generation of the three phosphorus species **2**, **3** and **4** were tunable, so that these three active phosphorus species could be highly selectively formed, respectively.

First, instead of sodium lump, when sodium powder dispersed in paraffin oil (average particle size < 10 μm, here below abbreviated as SD)[20] was used, I can produce compound **2** exclusively within a few minutes. Thus, 2.5 mmol SD was added to 1.0 mmol $Ph_3P(O)$ in 5 mL THF at 25 °C (Scheme 2.7, A). After 10 minutes, the corresponding sodium diphenylphosphinite (**2**, δ = 91.5 ppm) was produced exclusively and quantitatively! No side products could be detected at all (Scheme 2.7, B).

Scheme 2.7 Selective transformation to of **1** to sodium diphenylphosphinite **2**.



B ***^{31}P NMR spectra copy of the crude reaction solution***



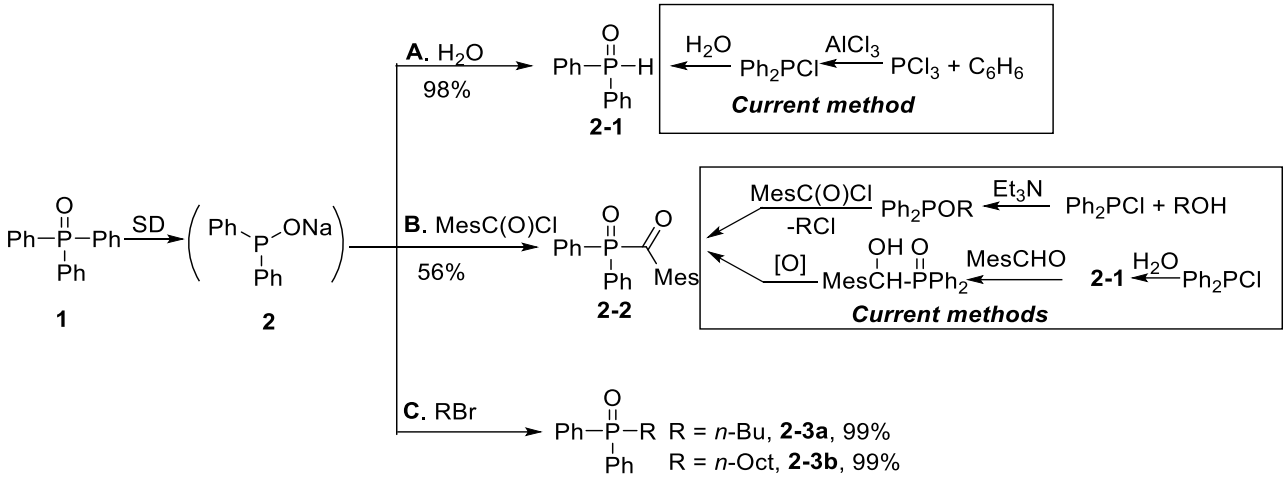
As to the molar ratios of sodium *vs* $Ph_3P(O)$, I found that more than 2 equivalents of sodium are necessary for the selective complete conversion of $Ph_3P(O)$ to $Ph_2P(ONa)$. For example, under similar conditions, when one equivalent SD was used, 12% $Ph_3P(O)$ remained unchanged, and $Ph_2P(ONa)$ and **3** were obtained in 60% and 28% yield, respectively, as determined by ^{31}P NMR spectroscopy. Therefore, the reaction should proceed,

being similar to that under the super reducing medium Na/NH_3,[13-14] via the cleavage of one C-P bond of $Ph_3P(O)$ by two equivalents of sodium generating an equimolar $Ph_2P(ONa)$ and PhNa (vide infra).

This easy and quantitative conversion of **1** $Ph_3P(O)$ to **2** $Ph_2P(O)Na$ guaranteed its application as an industrially useful reaction because, now, diphenylphosphine oxide $Ph_2P(O)H$, a widely used but rather expensive industrial chemical, can be easily prepared from the waste chemical $Ph_3P(O)$! Diphenylphosphine oxide $Ph_2P(O)H$[21] is widely employed as a versatile starting material for the synthesis of a lot of valuable organophosphorus compounds. This compound is currently industrially produced via the hydrolysis of Ph_2PCl. However, Ph_2PCl is prepared from a rather inefficient Friedel-Crafts reaction of PCl_3 and benzene using $AlCl_3$ that releases a large amount of wastes (more than 3 tones wastes in order to produce one tone product).[18-19] As shown in Scheme 2.8, by simply added water, the intermediate sodium phosphinite **2** developed above could quantitatively give $Ph_2P(O)H$ **2-1 (** A). It is noted that $Ph_2P(O)H$ is also a starting material for the preparation of 2,4,6-trimethylbenzoyldipenylphosphine oxide (TPO). TPO is an important photoinitiator and thousands of tons of TPO are broadly used in the realm of photopolymerization.[22] This compound is industrially prepared by two methods: 1) Michaelis–Arbuzov reaction of alkoxyphosphine with acyl chloride[23-24] and 2) oxidation of α-hydroxyphosphine oxide generated by the addition of $Ph_2P(O)H$ to the aldehyde[25] (Scheme 2.8, B). I found that TPO could be conveniently generated directly using $Ph_2P(O)Na$ **2** that can eliminate the isolation of $Ph_2P(O)H$ and other steps for the synthesis of TPO (Scheme 2.8, B). For example, by adding Ph_2PONa **2** to 2,4,6-trimethylbenzoyl chloride (MesC(O)Cl) in THF at 0 °C, the desired product TPO **2-2** was obtained in 56% yield. Beyond its practical utility, it is noted that this reaction is the first example for the preparation of TPO and analogues by the direct nucleophilic substitution reactions with an acylchloride because all of the literature attempts generated side products rather than the desired product TPO.[22-25]

Finally, Ph_2PONa can also efficiently react with an organohalide to give the corresponding phosphine oxide in high yield, which is useful in organic synthesis, metal extraction etc. (Scheme 2.8, C).[26-27] Although the nucleophilic substitution reaction of Ph_2PONa with RBr generating $Ph_2P(O)R$ is a known reaction, the high yield of $Ph_2P(O)R$ with a slightly excess RBr is surprising considering that an equimolar PhNa is also generated in the reaction mixture but does not interfere in the nucleophilic substitution reaction (vide infra).

Scheme 2.8 Utility of sodium diphenylphosphinite **2**.[a]

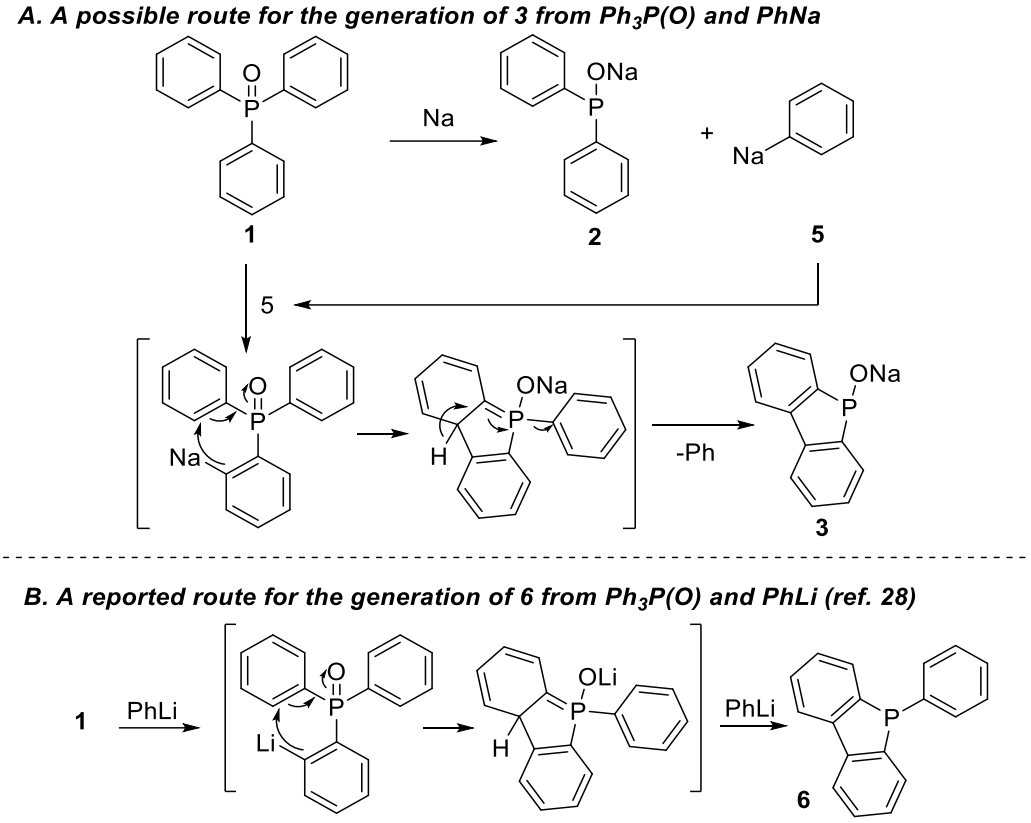


[a]Reaction conditions: Ph_2PONa **2** was prepared from 1.0 mmol $Ph_3P(O)$ in 5 mL solvent and 2.5 mmol SD according to the standard procedure. **A** 2.0 mL saturated aqueous NH_4Cl solution was added to Ph_2PONa **2** (1.0 mmol, in 1,4-dioxane) at 25 °C. **B** Ph_2PONa **2** (1.0 mmol, in THF) was added to MesC(O)Cl (1.5 mmol) at 0 °C. **C** An alkyl halide (1.2 mmol) was added to Ph_2PONa **2** (1.0 mmol, in THF) at 0 °C. Isolated yield.

2.2.3 Selective generation of 3: a practical way for converting $Ph_3P(O)$ to functional materials.

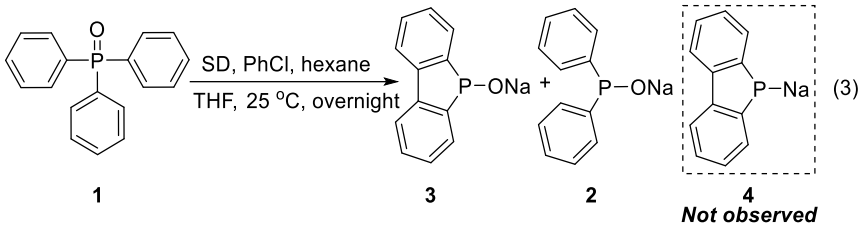
Fixing the optimized conditions for the selective generation of **3** was not as easy as **2**. The study hardly progressed until I eventually realized that PhNa should be the key for its generation (Scheme 2.9). Thus, I anticipated that sodium 5H-benzo[b]phosphindol-5-olate **3**, would be formally generated by dehydrogenative cyclization. Since PhNa **5** was generated during the reaction of $Ph_3P(O)$ with Na, PhNa might act as a base to react with $Ph_3P(O)$ to give **3** via cyclization.[28-29] An early literature reported that the reaction of PhLi with $Ph_3P(O)$ in THF under reflux overnight gave 5-phenyl-5H-benzo[b]phosphindole **6** rather than **3** (Scheme2.9, B).[28] Although not fully understood at present, this difference in reactivity between PhLi and PhNa is very interesting since . It should be noted that while the current reaction with PhNa took place rapidly at room temperature, the reaction with PhLi required a long-time heating.[28]

Scheme 2.9 Possible mechanisms for the generation of **3** (A) and **6** (B) (ref. 28).



This was indeed the case. When $Ph_3P(O)$ (0.45 mmol dissolved in 2 mL THF) was added to PhNa (1.0 mmol prepared from 2.0 mmol SD with 1.1 mmol PhCl) at 25 °C (Table 2.1, Eq. 3),[20] 5H-benzo[b]phosphindol-5-olate **3** (δ = 101.7 ppm) was generated predominantly (Table 2.1, run 1). By quenching the organophosphorus species with *n*-OctBr, **3'b** was obtained in 77% yield together with **2-3b** generated via the reaction of **2** (11%), respectively, as determined by ^{31}P NMR spectroscopy. Efforts had been devoted to improving the yield and selectivity of **3**. Switching the ratio of $Ph_3P(O)$ **1** and PhNa to 0.33:1 leaded to lower yield and selectivity of **3** (Table 2.1, run 2). When a solid PhNa was added to $Ph_3P(O)$ dissolved in THF, **3** and **2** were generated in 42% and 38% respectively (Table 2.1, run 3). Interestingly, by increasing the amount of $Ph_3P(O)$ to 0.9 mmol, nearly an equimolar ratio to PhNa, a similar yield of **3** could be obtained (See Scheme 2.16), indicating that only one equivalent of PhNa is required for the generation of **3** in the reaction, which not only significantly improved the efficiency of the use of PhNa (Table 2.1, run 4), but also sustained the proposed mechanism (Scheme 2.9). The selectivity was not further improved either under a lower or higher temperature (Table 2.1, runs 5-6).

Table 2.1 Selective transformation of $Ph_3P(O)$ to sodium 5H-benzo[b]phosphindol-5-olate **3**[a]

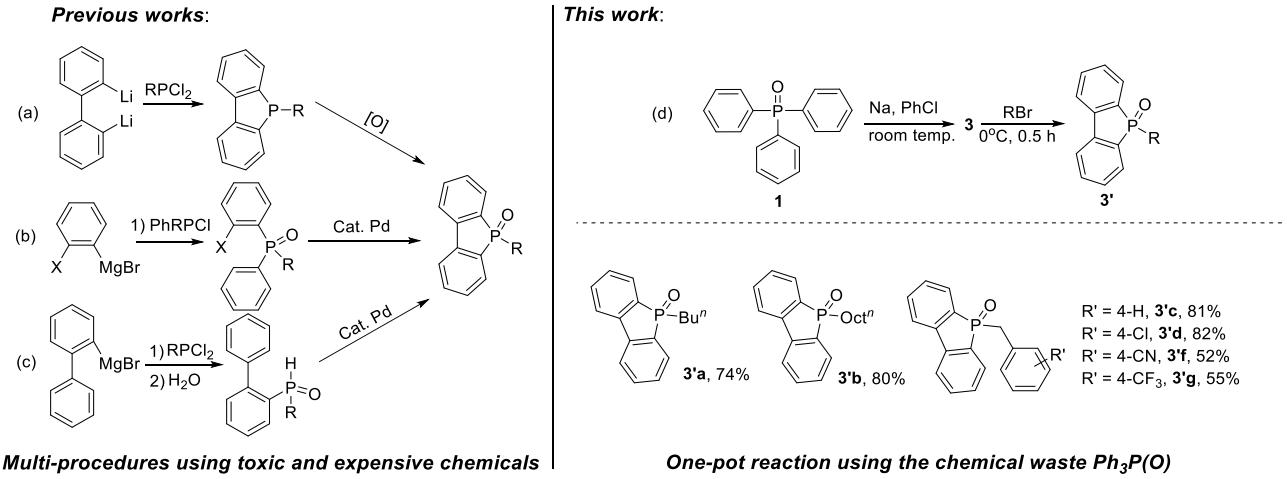


run	$Ph_3P(O)$	PhNa	temperature	Conversion of **1** (yield of **3** and **2**)
1	0.45 mmol	1.0 mmol	25 °C	88% (77% of **3**, 11% of **2**)
2	0.33 mmol	1.0 mmol	25 °C	85% (41% of **3**, 44% of **2**)
3	0.45 mmol	1.0 mmol	25 °C	80% (42% of **3**, 38% of **2**)
4	**0.90 mmol**	**1.0 mmol**	**25 °C**	**100% (82% of 3, 18% of 2)**
5	0.90 mmol	1.0 mmol	0 °C	42% (39% of **3**, 3% of **2**)
6	0.90 mmol	1.0 mmol	40 °C	86% (64% of **3**, 12% of **2**)

[a]Reaction conditions: PhNa was generated in situ by the reaction of SD (2.0 mmol) with PhCl (1.1 mmol) in 2.0 mL hexane at 25 °C for 1 h. A specified amount of $Ph_3P(O)$ dissolved in 2.0 mL THF was then added into PhNa at 25 °C and the mixture was stirred for overnight. Yields were estimated from ^{31}P NMR spectroscopy based on **1** used. [b]Solid PhNa was used.

Molecules with dibenzophosphole framework have great potentials as novel optical and electrical materials.[30] As shown in Scheme 2.10, old procedures for the synthesis of dibenzophosphole oxides mainly relied on metathesis reaction between dilithiated biphenyl with $RPCl_2$ followed by oxidation (a).[31] Recently, a palladium-catalyzed intramolecular arylation of ortho-halodiphenylphosphine (b) and intramolecular dehydrogenative cyclization of secondary hydrophosphine oxides (c) have been developed. [32-33] All these approaches had to use the toxic phosphine chlorides, and the processes are tedious. As shown in Scheme 2.10, the sodium 5H-benzo[b]phosphindol-5-olate **3** derived from $Ph_3P(O)$ was easily transformed to the corresponding dibenzophosphole oxides in moderate to high yields. Functional groups like Cl, CN, CF_3 are well tolerable. Therefore, an efficient way for the generation of these useful dibenzophosphole oxides by using the chemical waste $Ph_3P(O)$ was established.

Scheme 2.10 Efficient synthesis of dibenzophosphole oxides from the chemical waste $Ph_3P(O)$.[a]

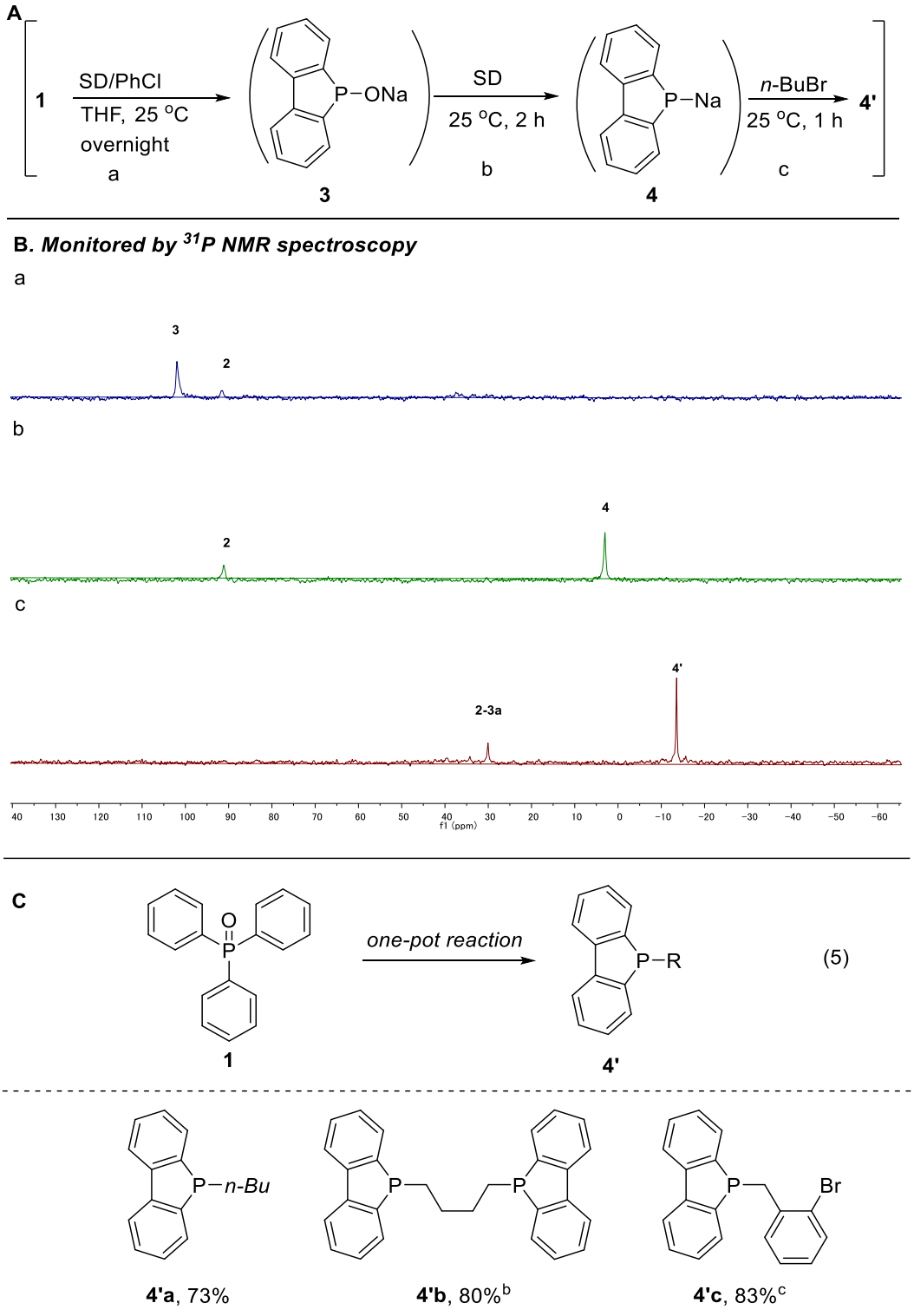


[a]Reaction conditions: PhNa was generated in situ by adding PhCl (1.1 mmol) to a suspension of SD (2.0 mmol in 2.0 mL hexane) at 25 °C for 1 h. $Ph_3P(O)$ dissolved in THF (2.0 mL) was added into the above PhNa suspension and stirred for overnight. RBr (1.5 mmol) was then added at 0 °C and stirred for 0.5 h. Isolated yield.

2.2.4 Selective generation of 4: a rare example for P=O reduction by sodium.

A more fascinating phenomenon is that even the trivalent phosphole **4** can be selectively generated starting from $Ph_3P(O)$ (Scheme 2.11). Thus, during the study on further possible reactions with metallic sodium of **2** and **3**, I surprisingly found that although no reaction took place with **2**, **3** reacted quickly to give **4**! Thus, ^{31}P NMR showed that after the addition of SD to **3** at 25 °C for a few minutes, the signal of **3** completely disappeared and a new signal of **4** at 3.0 ppm appeared. As expected, the subsequent addition of *n*-BuBr to the mixture gave compound **4'** (δ = -13.5 ppm) which was fully characterized by comparing with an authentic sample prepared separately.[34] This protocol is amenable to use dibromides as electrophiles for the synthesis of bisphosphole **4'b**. Since the reaction of sodium benzo[b]phosphindol-5-ide **4** with an alkyl bromide is faster than that with an aromatic bromide, **4'c** could be selectively generated. Therefore, by carrying out a one-pot reaction, the so far chemical waste $Ph_3P(O)$ could also be easily converted to phosphole **4'** (Scheme 2.11, Equation (5))! This is also a rare example for converting phosphine oxide (P(V)) to phoshine (P(III)) that usually requires highly reactive reducing reagents such as $LiAlH_4$ and hydrosilances, or under harsh conditions, in order to break down the robust P-O bond.[12-16]

Scheme 2.11 Selective transformation of $Ph_3P(O)$ to sodium benzo[b]phosphindol-5-ide **4**.[a]

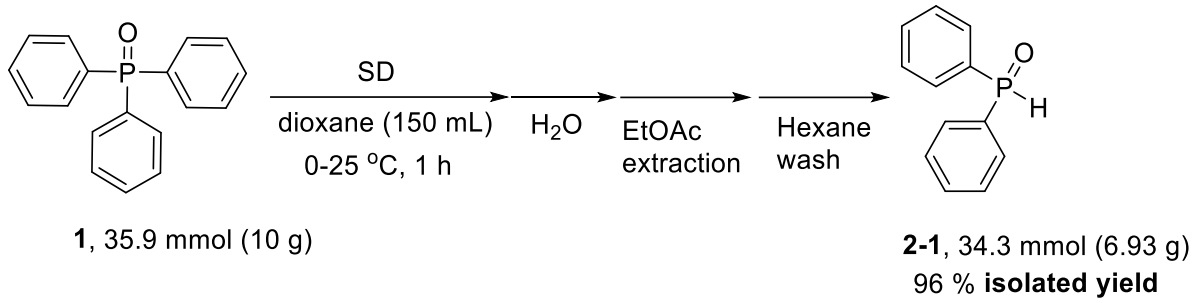


[a]Reaction conditions in **A**:(a) sodium H-benzo[b]phosphindol-5-olate **3** was generated in situ from $Ph_3P(O)$ (0.9 mmol) and PhNa (1.0 mmol); (b) SD (2.5 mmol) was then added and stirred for 2h; (**c)** *n*-BuBr (2.0 mmol) was added to the mixture and stirred for 1 h. **B** The reaction was monitored by ^{31}P NMR. **C** One-pot conversion of $Ph_3P(O)$ to phosphle **4'**. Isolated yield. [b]0.4 mmol of BrC_4H_8Br was added. [c]The product was oxidized by H_2O_2 for easy isolation.

2.2.5 A 10 g- scale reaction.

As demonstrated by a lab-scale reaction, the present method is easily applicable to a large-scale preparation of the phosphorus compound (Scheme 2.12). For example, after treating 10g of $Ph_3P(O)$ **1** with 90 mmol SD (2.5 equiv.) at 25 °C, water was added. The mixture was simply extracted with EtOAc, washed by hexane and passed through a short silica gel column. A spectroscopically pure diphenylphosphine oxide **2-1** was obtained as a white solid (6.93 g, 96 % yield).

Scheme 2.12 10 g-scale transformation of $Ph_3P(O)$ to $Ph_2P(O)H$.



1, 35.9 mmol (10 g)

2-1, 34.3 mmol (6.93 g)
96 % **isolated yield**

2.3 Conclusion

In conclusion, I disclosed for the first time that the C-P bond of $Ph_3P(O)$ could be so easily and efficiently cleft by metallic sodium under normal conditions without using the dangerous super reducing media (sodium dissolved in ammonia Na/NH_3). Three basic reactive organophosphorus intermediates **2, 3, 4** can be highly selectively generated from the combination of $Ph_3P(O)$ with metallic sodium, that give the corresponding organophosphorus compounds efficiently. The industrial markets for these organophosphorus compounds derivatives, that are difficult to prepare by other methods, is large enough to consume up all of the $Ph_3P(O)$ produced as a chemical waste from the chemical industry. Therefore, $Ph_3P(O)$ is no longer a waste but a precious chemical stock for highly valuable functional organophosphorus compounds. I believe that this finding can settle the $Ph_3P(O)$ problem that has annoyed people for half a century.

2.4 Experimental Section

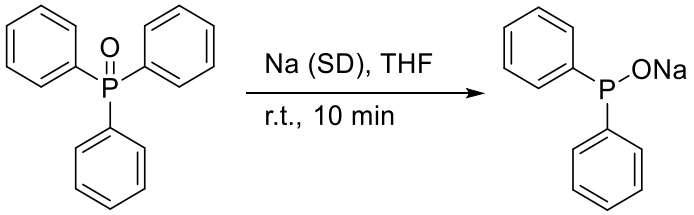
2.4.1 General Information

All reactions were carried out in oven dried Schlenk tubes under argon atmosphere. All materials were purchased and used without further purification. The sodium I used was dispersed in paraffin oil with an

average particle size smaller than 10 μm and a concentration of 10 mol/L. ^{1}H NMR spectra were recorded on JEOL JNM-ECS400 (400 MHz) FT NMR in $CDCl_3$ with Me_4Si as an internal standard. ^{13}C NMR spectra were taken on JEOL JNM-ECS400 (100 MHz) FT NMR system in $CDCl_3$. ^{31}P NMR spectra were taken on JEOL JNM-ECX400 (162 MHz) FT NMR system in $CDCl_3$ with 85% H_3PO_4 solution as an external standard. MS (ESI) data were obtained on SHIMADZU GC-MS 2010 plus. HPLC (recycle GPC) method for isolation was performed on JAPAN ANALYTICAL INDUSTRY LC-908. The HPLC was a recycling preparative HPLC (Gel permeation chromatography) with two columns (20 mm I.D. -600 mm L; JAIGEL-1H and JAIGEL-2H). All the products were purified by the same conditions: $CHCl_3$ as eluent, flow rate: 4.0 mL/min, and the spectra was recorded at a moving paper in the speed of 60 mm/h. Melting points were measured on OptiMelt by SRS.

2.4.2 General procedure for selective transformation of $Ph_3P(O)$ to 2, 3, 4

A. General method A for selective transformation of $Ph_3P(O)$ to sodium diphenylphosphinite 2 and its derivatives



1 **2**

Fig 2.1 Conversion of $Ph_3P(O)$ **1** to sodium diphenylphosphinite **2**

Under the argon atmosphere (1 atm), 1.0 mmol triphenylphosphine oxide **1** (278 mg) was dissolved in 5 mL solvent (THF or 1,4-dioxane), and then 2.5 mmol SD (Sodium Dispersed, 0.25 mL) was added in dropwise by syringe within 10 seconds. The mixture was stirred under room temperature for 10 minutes. After reaction, excessive solid Na was separated from the solution by centrifugation, product *sodium diphenylphosphinite* **2** was determined by ^{31}P NMR with a signal at 91 ppm in quantitative yield (Fig 2.1).

(1) For the synthesis of $Ph_2P(O)H$:

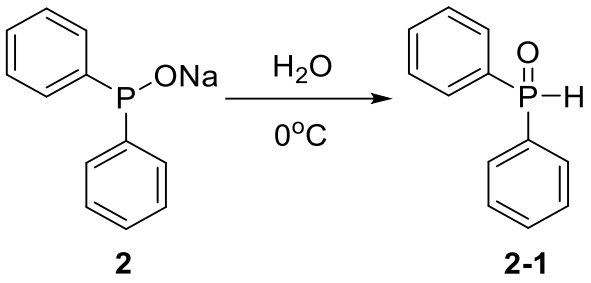


Fig 2.2 Conversion of $Ph_2P(ONa)$ **2** to $Ph_2P(O)H$ **2-1**

According to general method A, sodium diphenylphosphinite **2** was obtained in 1,4-dioxane instead of THF for higher yield. Under argon (1 atm), 1.0 mmol Ph_2PONa (dioxane solution) was quenched by 2.0 mL saturated aqueous NH_4Cl solution and extracted with EtOAc (3 mL×3), the combined organic layer was dried over anhydrous Na_2SO_4, then filtered and evaporated. The crude product was washed by Hexane (5 mL×3) via a silica column to remove the oil derived from SD and eluent with EtOAc to give crude products. And recrystallization (5.0 mL Hexane + 2 mL $CHCl_3$ at -20°C) afforded analytically pure $Ph_2P(O)H$ **2-1** in quantitative yield (Fig 2.2).

(2) For the synthesis of $Ph_2P(O)C(O)Mes$:

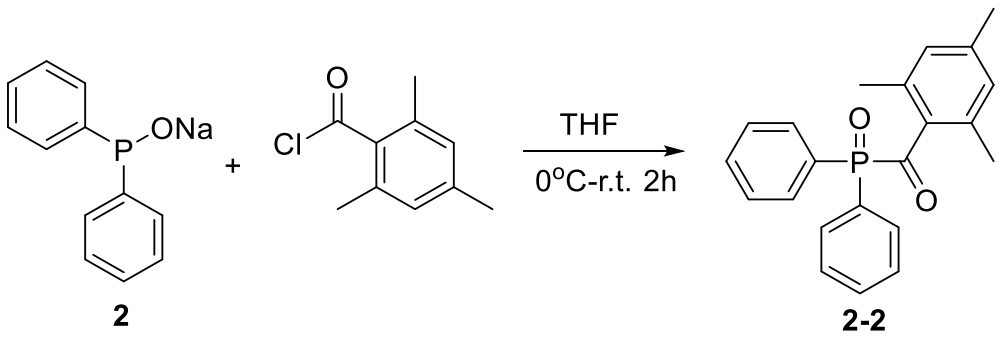
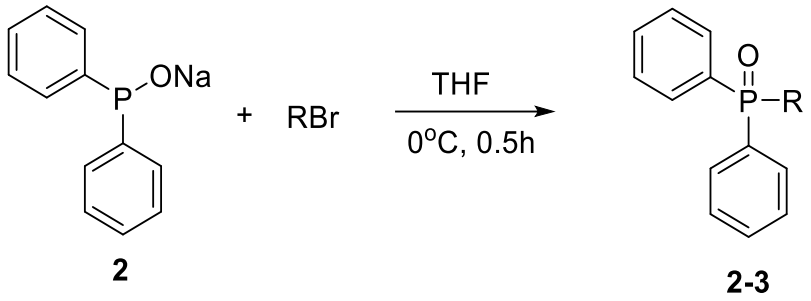


Fig 2.3 Conversion of $Ph_2P(ONa)$ **2** to TPO **2-2**

Under argon (1 atm), 1.0 mmol Ph_2PONa (THF solution) was added dropwise to 1.5 mmol MesC(O)Cl dissolved in 5.0 mL THF at 0°C, after stirring for 2 hours at room temperature, the mixture was quenched by 5.0 mL saturated aqueous NH_4Cl solution and extracted with EtOAc (5 mL×3), the combined organic layer was dried over anhydrous Na_2SO_4, then filtered and evaporated. The residues were passed through a silica chromatographic column (particle size 37-54 μm) using ethyl acetate/petroleum ether (1:4) as an eluent to afford analytically pure **2-2** product in 56% isolated yield (Fig 2.3).

(3) For the synthesis of $Ph_2P(O)R$:



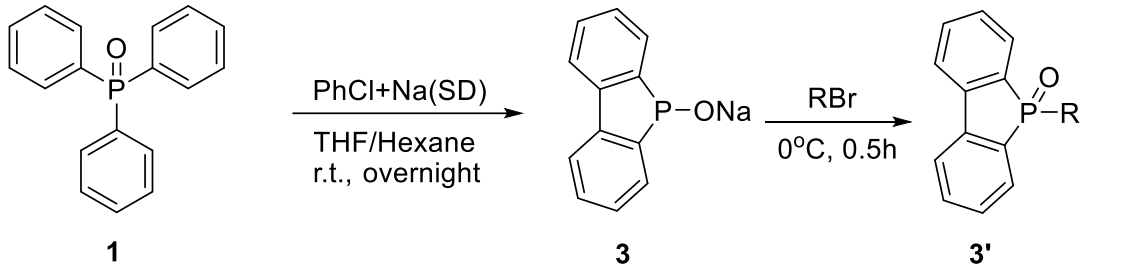
2 **2-3**

Fig 2.4 Conversion of $Ph_2P(ONa)$ **2** to diphenylalkylphosphine oxides **2-3**

Under argon (1 atm), 1.2 mmol electrophilic reagents RBr was added dropwise to 1.0 mmol Ph_2PONa (THF solution) at 0°C. After stirring for 0.5 h, the mixture was washed by 5.0 mL saturated aqueous NH_4Cl solution, and then extracted with EtOAc (5 mL×3), the combined organic layer was dried over anhydrous Na_2SO_4, then filtered and evaporated. The residues were diluted in $CHCl_3$ and isolated by HPLC (polystyrene-based column, $CHCl_3$ as eluent, flow rate = 4.0 mL/min) to afford analytically pure **2-3** products (Scheme 2.4).

B. General method B for selective transformation of $Ph_3P(O)$ to sodium 5H-benzo[b]phosphindol-5-olate 3 and its derivatives

Under the argon (1 atm), to a solution of 2.0 mmol sodium dispersion (0.2 mL) in 2 mL of hexane was added 1.1 mmol PhCl (112 μL) and the mixture was stirred at room temperature for 1 h until the color of mixture turned deep purple. And then the solution of 0.9 mmol $Ph_3P(O)$ (250 mg) dissolved in 2 mL of THF was added to the above PhNa/hexane solution *via* syringe within 10 seconds. The reaction proceeded under room temperature for overnight. The selective product *sodium 5H-benzo[b]phosphindol-5-olate* **3** was determined by ^{31}P-NMR with a signal at 101 ppm. And then the mixture of **3** was quenched with 1.5 mmol RBr at 0°C and stirred for 0.5 h, washed by saturated aqueous NH_4Cl solution, extracted with EtOAc (5 mL×3), the combined organic layer was dried over anhydrous Na_2SO_4, then filtered and evaporated. The residues were diluted in $CHCl_3$ and isolated by HPLC (polystyrene-based column, $CHCl_3$ as eluent, flow rate = 4.0 mL/min) to afford analytically pure **3'** products (Fig 2.5).



^{31}P NMR spectroscopies for Table 1, run 4

The crude reaction solution

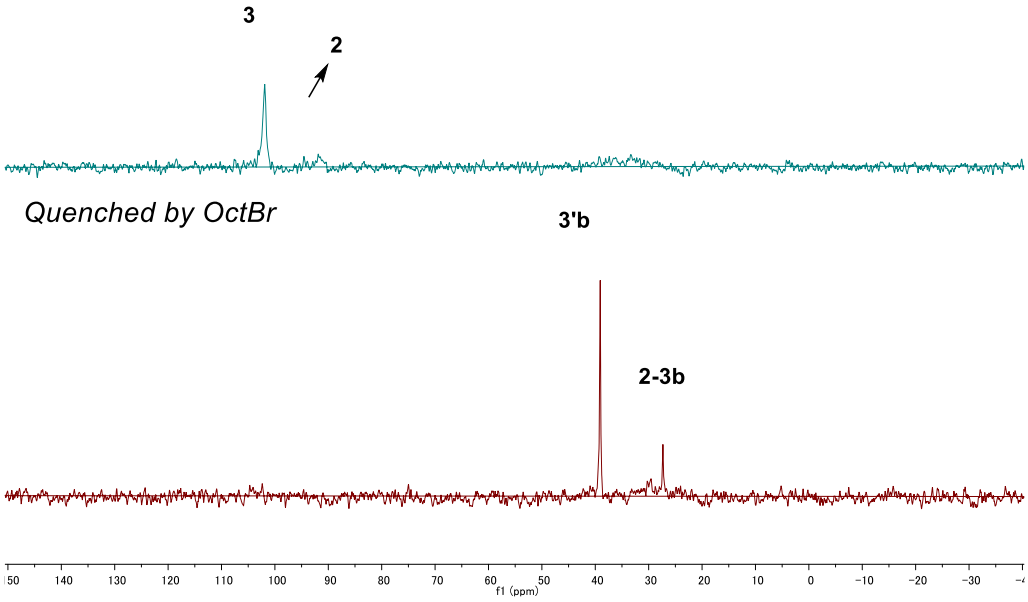


Fig. 2.5 Conversion of $Ph_3P(O)$ to *sodium 5H-benzo[b]phosphindol-5-olate* **3** and quenching with alkyl bromides

C. General method C for selective transformation of $Ph_3P(O)$ to sodium benzo[b]phosphindol-5-ide 4 and its derivative

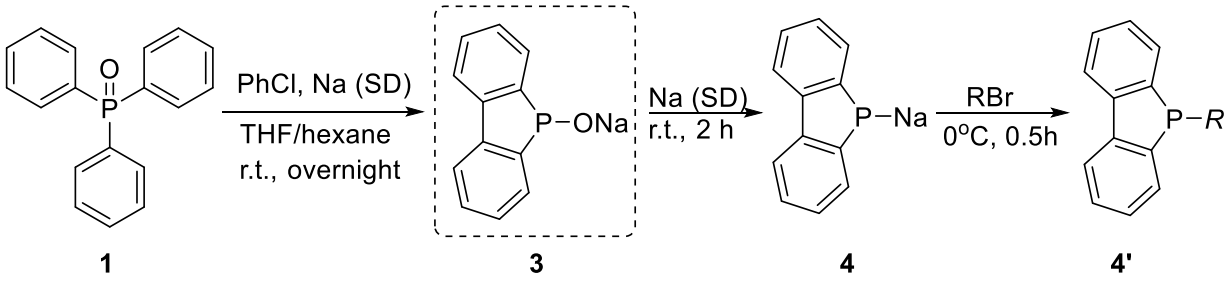


Fig 2.6 Conversion of $Ph_3P(O)$ to *sodium benzo[b]phosphindol-5-ide* **4** and quenching with alkyl bromides

Under the argon atmosphere (1 atm), to a solution of 2.0 mmol sodium dispersion (0.2 mL) in 2 mL of

hexane was added 1.1 mmol PhCl (112 μL) and the mixture was stirred at room temperature for 1h until the color of mixture turned deep purple. And then the solution of 0.9 mmol $Ph_3P(O)$ (250 mg) dissolved in 2 mL of THF was added to the above PhNa solution *via* syringe within 10 seconds. The reaction proceeded under room temperature for overnight affording the solution of **3**, and then 2.5 mmol sodium dispersion (0.25 mL) was added and the mixture was stirred at room temperature for 2 h. The selective product *sodium benzo[b]phosphindol-5-ide* **4** were determined by ^{31}P-NMR with a signal at 3.0 ppm and quenching with RBr affording 5-alkyl-5H-benzo[b]phosphindole **4'**. The residues were diluted in $CHCl_3$ and isolated by HPLC (polystyrene-based column, $CHCl_3$ as eluent, flow rate = 4.0 mL/min) to afford analytically pure **4'** products (Fig 2.6).

D. Scale-up synthesis of $Ph_2P(O)H$

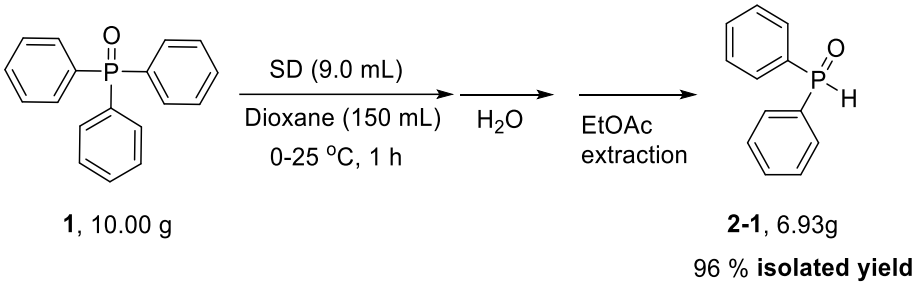
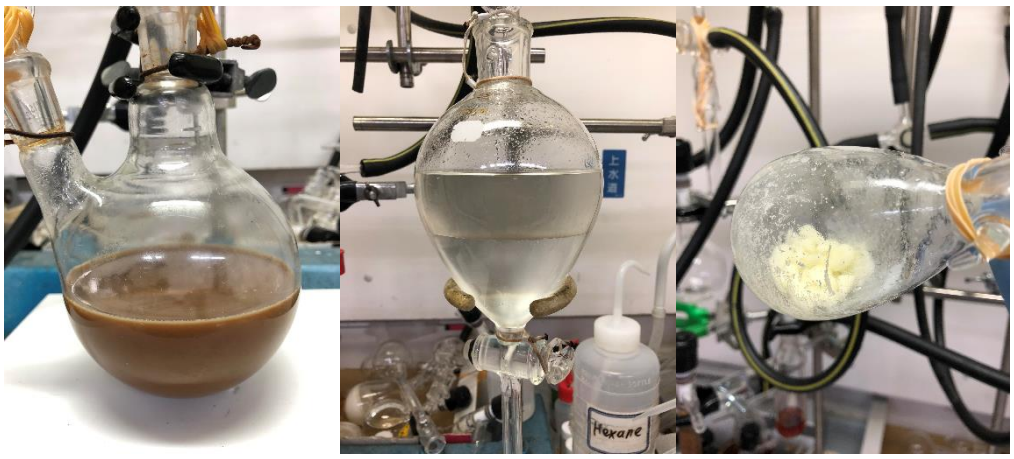


Fig 2.7 10g-scale up synthesis of $Ph_2P(O)H$ from $Ph_3P(O)$

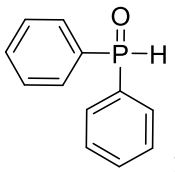
Under the argon atmosphere (1 atm), 10.0 g triphenylphosphine oxide **1** (35.93 mmol) was dissolved in 150 mL 1,4-dioxane, and then 9.0 mL SD (Sodium Dispersed, 90 mmol) was added in dropwise at 0°C. After stirring for 1 hour under room temperature (**A**). The Ph_2PONa (dioxane solution) was quenched by 150 mL saturated aqueous NH_4Cl solution and extracted with EtOAc (100 mL×3) (**B**). The combined organic layer was dried over Na_2SO_4, then filtered and evaporated. The crude product was washed with hexane by column chromatography to remove the oil derived from SD, then elution with EtOAc to give the crude product. Evaporation of EtOAc and recrystallization (100 mL Hexane + 10 mL $HCCl_3$ at -20°C) afforded analytically pure $Ph_2P(O)H$ **2-1** (6.93 g) in 96 % isolated yield (**C**) (Fig 2.7).



(A) **(B)** **(C)**

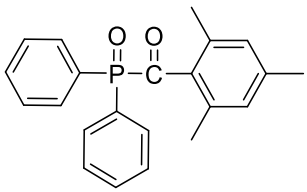
Fig. 2.8 (A) $Ph_3P(O)$ and SD (dioxane), (B) Quenched with H_2O, (C) pure $Ph_2P(O)H$

2.4.3 Characterization and analytical data of products



2-1

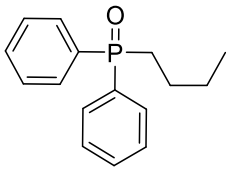
Diphenylphosphine oxide (2-1). According to the general procedure A-1, purification by recrystallization afforded **2-1** (197mg, 98% yield) as a pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 0.5 H), 7.69–7.64 (m, 4H), 7.54–7.50 (m, 2H), 7.47–7.43 (m, 4.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.62 (d, $J_{P\text{-}C}$ = 2.6 Hz), 131.55 (d, $J_{P\text{-}C}$ = 100.8 Hz), 130.76 (d, $J_{P\text{-}C}$ = 11.4 Hz), 128.96 (d, $J_{P\text{-}C}$ = 12.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 21.91. MS (ESI) m/z: ($[M]^+$) Calcd for $C_{12}H_{11}OP$ 202, found 202. Melting Point: 42.9-45.5 °C. This compound is known and in agreement with the literature data: Lhermet, R., Moser, E., Jeanneau, E., Olivier-Bourbigou, H. & Breuil, P. A. R. *Chem. Eur J*. **2017**, *23*, 7433–7437.



2-2

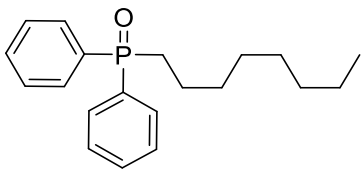
(diphenylphosphoryl)(mesityl)methanone (2-2). According to the general procedure A-2, purification by silica column chromatography afforded **2-2** (195 mg, 56% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.96 (m, 4H), 7.58–7.47 (m, 6H), 6.80 (s, 2H), 2.25 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 220.23 (d, $J_{P\text{-}C}$ = 61.3 Hz), 140.68, 136.35 (d, $J_{P\text{-}C}$ = 39.7 Hz), 135.00, 132.47 (d, $J_{P\text{-}C}$ = 2.6 Hz), 131.99 (d, $J_{P\text{-}C}$ = 8.6 Hz), 129.85 (d, $J_{P\text{-}C}$ = 92.8 Hz), 129.00, 128.81 (d, $J_{P\text{-}C}$ = 11.6 Hz), 21.31, 19.78. ^{31}P NMR (162 MHz, $CDCl_3$): δ 13.78. MS (ESI) m/z: ($[M]^+$) Calcd for $C_{22}H_{21}O_2P$ 348, found 348. Melting Point: 82.4-86.3°C. This compound is known and in agreement with the literature data: (a) Lechtken, P., Buethe, I., Jacobi, M., & Trimborn, W. *US Patent* 4,298,738, 1981; (b) Wang Z., Wang Y., Wang Y., Song H. Preparation method of acyl phosphine oxide compound. *CN Patent* 103159796, 2011.



2-3a

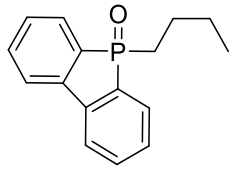
Butyldiphenylphosphine oxide (**2-3a**). According to the general procedure A-3, purification by HPLC (standard conditions) afforded **2-3a** (255 mg, 99% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72–7.67 (m, 4H), 7.48–7.39 (m, 6H), 2.25–2.18 (m, 2H), 1.59–1.51 (m, 2H), 1.42–1.33 (m, 2H), 0.84 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.31 (d, $J_{P\text{-}C}$ = 97.2 Hz), 131.67 (d, $J_{P\text{-}C}$ = 2.4 Hz), 130.83 (d, $J_{P\text{-}C}$ = 9.2 Hz), 128.66 (d, $J_{P\text{-}C}$ = 11.4 Hz), 29.56 (d, $J_{P\text{-}C}$ = 71.8 Hz), 24.17 (d, $J_{P\text{-}C}$ = 15.0 Hz), 23.55 (d, $J_{P\text{-}C}$ = 3.8 Hz), 13.66; ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.07. MS (ESI) m/z: ($[M]^+$) Calcd for $C_{16}H_{19}OP$ 258, Found 258; Melting Point: 91.5-93.2 °C. This compound is known and in agreement with the literature data: Huang, T., Chen, T., & Han, L. B. *J. Org. Chem.* **2018***, 83,* 2959–2965.



2-3b

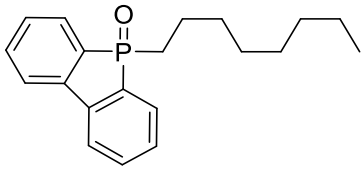
Octyldiphenylphosphine oxide (2-3b). According to the general procedure A-3, purification by HPLC (standard conditions) afforded **2-3b** (310 mg, 99% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.68 (m, 4H), 7.49-7.40 (m, 6H), 2.25–2.19 (m, 2H), 1.64–1.54 (m, 2H), 1.39–1.32 (m, 2H), 1.26–1.19 (m, 8H), 0.82 (t, 3H, J = 14.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.34 (d, $J_{P\text{-}C}$ = 157.0 Hz), 131.66 (d, $J_{P\text{-}C}$ = 2.1 Hz), 130.84 (d, $J_{P\text{-}C}$ = 9.4 Hz), 128.66 (d, $J_{P\text{-}C}$ = 11.6 Hz), 31.82, 31.05 (d, $J_{P\text{-}C}$ = 14.6 Hz), 30.18, 29.47, 29.28 (d, $J_{P\text{-}C}$ = 1.4 Hz), 22.66, 21.48 (d, $J_{P\text{-}C}$ = 3.8 Hz), 14.14; ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.08 . MS

(ESI) m/z: ([M]$^+$) Calcd for $C_{20}H_{27}OP$ 314, Found 314; Melting Point: 62.5-63.9°C. This compound is known and in agreement with the literature data: Wang, F., Qu, M., Chen, F., Xu, Q., & Shi, M. *Chem. Comm.* **2012**, *48,* 8580–8582.



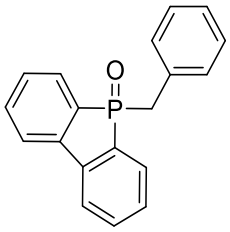
3'a

5-buylbenzo[b]phosphindole 5-oxide (3'a). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'a** (170 mg, 74% yield) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.77 (m, 4H), 7.57 (t, 2H, J = 7.6 Hz), 7.44–7.40 (m, 2H), 2.11–2.04 (m, 2H), 1.57–1.47 (m, 2H), 1.40–1.30 (m, 2H), 0.84 (t, 3H, J = 14.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.27 (d, $J_{P\text{-}C}$ = 20.6 Hz), 133.19, 132.12 (d, $J_{P\text{-}C}$ = 100.2 Hz), 129.48 (d, $J_{P\text{-}C}$ = 9.2 Hz), 129.20 (d, $J_{P\text{-}C}$ = 10.6 Hz) , 121.27 (d, $J_{P\text{-}C}$ = 9.4 Hz), 30.10 (d, $J_{P\text{-}C}$ = 69.4 Hz), 24.17(d, $J_{P\text{-}C}$ = 3.0 Hz), 24.11 (d, $J_{P\text{-}C}$ = 22.4 Hz), 13.58; ^{31}P NMR (162 MHz, $CDCl_3$): δ 44.37. MS (ESI) m/z: ([M]$^+$) Calcd for $C_{16}H_{17}OP$ 256, Found 256. This compound is known and in agreement with the literature data: Vedejs, E., & Marth, C. *Tetrahedron Lett.* **1987**, *28*, 3445–3448.



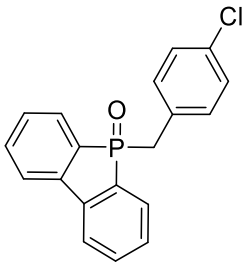
3'b

5-octylbenzo[b]phosphindole 5-oxide (3'b). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'b** (224 mg, 80% yield) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83–7.75 (m, 4H), 7.55 (t, 2H, J = 7.2 Hz), 7.42–7.37 (m, 2H), 2.09–2.01 (m, 2H), 1.56–1.46 (m, 2H), 1.30–1.17 (m, 10H), 0.82 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.25 (d, $J_{P\text{-}C}$ = 20.8 Hz), 133.23, 132.07 (d, $J_{P\text{-}C}$ = 100.4 Hz), 129.47 (d, $J_{P\text{-}C}$ = 9.4 Hz), 129.20 (d, $J_{P\text{-}C}$ = 10.6 Hz) , 121.30 (d, $J_{P\text{-}C}$ = 9.6 Hz), 31.773, 30.90 (d, $J_{P\text{-}C}$ = 15.2 Hz), 30.66, 29.97, 29.01 (d, $J_{P\text{-}C}$ = 1.6 Hz), 22.64, 22.13 (d, $J_{P\text{-}C}$ = 3.4 Hz), 14.13; ^{31}P NMR (162 MHz, $CDCl_3$): δ 44.36. . MS (ESI) m/z: ([M]$^+$) Calcd for $C_{20}H_{25}OP$ 312, Found 312.



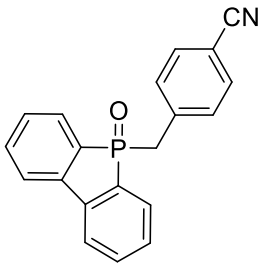
3'c

5-benzylbenzo[b]phosphindole 5-oxide (3'c). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'c** (210 mg, 81% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.66 (m, 2H), 7.57–7.49 (m, 4H), 7.36–7.31 (m, 2H), 7.18–7.17 (m, 3H), 7.05–7.03 (m, 2H), 3.41 (d, 2H, J = 15.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.11 (d, $J_{P\text{-}C}$ = 44.0 Hz), 133.34, 131.19 (d, $J_{P\text{-}C}$ = 102.2 Hz), 131.34 (d, $J_{P\text{-}C}$ = 7.8 Hz), 129.92 (d, $J_{P\text{-}C}$ = 14.2 Hz), 129.95, 129.00 (d, $J_{P\text{-}C}$ = 10.8 Hz) , 128.43 (d, $J_{P\text{-}C}$ = 2.4 Hz), 127.00 (d, $J_{P\text{-}C}$ = 3.2 Hz), 121.17 (d, $J_{P\text{-}C}$ = 9.8 Hz), 38.42 (d, $J_{P\text{-}C}$ = 64.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 40.31. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{19}H_{15}OP$ 290, Found 290. Melting Point: 129.7-136.1 °C. This compound is known and in agreement with the literature data: (a) Allen, D. W., & Hutley, B. G. *Zeitschrift für Naturforschung B* **1979**, *34*, 1116-1120; (b) Ezzell, B. R., & Freedman, L. D. *J. Org. Chem.***1969**, *34*, 1777–1780.



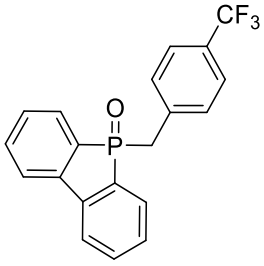
3'd

5-(4-chlorobenzyl)benzo[b]phosphindole 5-oxide (3'd). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'd** (239 mg, 82% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.68 (m, 2H), 7.59–7.51 (m, 4H), 7.37–7.33 (m, 2H), 7.14 (d, 2H, J = 8.4 Hz), 6.96–6.94 (m, 2H), 3.38 (d, 2H, J = 15.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.11 (d, $J_{P\text{-}C}$ = 21.4 Hz), 133.49, 132.21 (d, $J_{P\text{-}C}$ = 169.8 Hz), 131.29 (d, $J_{P\text{-}C}$ = 14.9 Hz), 130.15 (d, $J_{P\text{-}C}$ = 38.5 Hz), 129.88, 129.79, 129.10 (d, $J_{P\text{-}C}$ = 10.5 Hz) , 128.55 (d, $J_{P\text{-}C}$ = 2.1 Hz), 121.27 (d, $J_{P\text{-}C}$ = 9.8 Hz), 37.81 (d, $J_{P\text{-}C}$ = 64.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 40.02. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{16}H_{14}ClOP$ 324, Found 324. Melting Point: 75.6-80.3 °C.



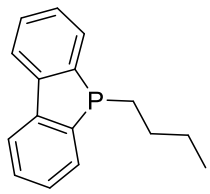
3'e

4-((5-oxidobenzo[b]phosphindol-5-yl)methyl)benzonitrile (3'e). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'e** (146 mg, 52% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.67 (m, 2H), 7.59–7.53 (m, 4H), 7.43 (d, 2H, J = 8.0 Hz), 7.39–7.35 (m, 2H), 7.11–7.09 (m, 2H), 3.48 (d, 2H, J = 15.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.04 (d, $J_{P\text{-}C}$ = 21.8 Hz), 137.27 (d, $J_{P\text{-}C}$ = 7.9 Hz), 133.77, 132.05 (d, $J_{P\text{-}C}$ = 2.5 Hz), 130.06 (d, $J_{P\text{-}C}$ = 5.1 Hz), 129.75 (d, $J_{P\text{-}C}$ = 9.0 Hz), 129.25 (d, $J_{P\text{-}C}$ = 10.7 Hz) , 121.38 (d, $J_{P\text{-}C}$ = 10.1 Hz), 118.68, 110.95 (d, $J_{P\text{-}C}$ = 3.5 Hz), 38.91 (d, $J_{P\text{-}C}$ = 62.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 39.22. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{20}H_{14}NOP$ 315, Found 315. Melting Point: 167.3-183.5 °C.



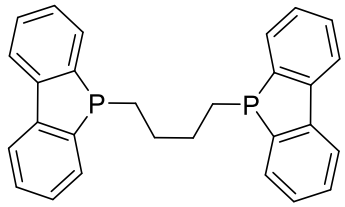
3'f

5-(4-(trifluoromethyl)benzyl)benzo[b]phosphindole 5-oxide (3'f). According to the general procedure B, purification by HPLC (standard conditions) afforded **3'f** (177 mg, 55% yield) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.66 (m, 2H), 7.57–7.50 (m, 4H), 7.43 (d, 2H, J = 8.4 Hz), 7.36–7.33 (m, 2H), 7.15 (d, 2H, J = 6.8 Hz), 3.44 (d, 2H, J = 15.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.04 (d, $J_{P\text{-}C}$ = 21.6 Hz), 135.74 (d, $J_{P\text{-}C}$ = 7.9 Hz), 133.62 (d, $J_{P\text{-}C}$ = 1.5 Hz), 131.22, 130.23 (d, $J_{P\text{-}C}$ = 5.2 Hz), 129.76 (d, $J_{P\text{-}C}$ = 9.0 Hz), 129.16 (d, $J_{P\text{-}C}$ = 10.7 Hz) , 125.28 (d, $J_{P\text{-}C}$ = 6.4 Hz), 125.28, 121.33 (d, $J_{P\text{-}C}$ = 10.1 Hz), 38.48 (d, $J_{P\text{-}C}$ = 62.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 39.23. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{20}H_{14}F_3OP$ 358, Found 358. Melting Point: 155.1-157.0 °C.



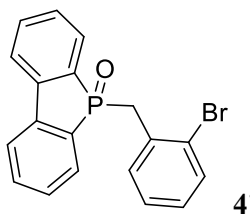
4'a

5-butyl-5H-benzo[b]phosphindole (4'a). According to the general procedure C, purification by HPLC (standard conditions) afforded **4'a** (158 mg, 73% yield) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96–7.91 (m, 2H), 7.78–7.71 (m, 2H), 7.50–7.44 (m, 2H), 7.39–7.34 (m, 2H), 1.82–1.78 (m, 2H), 1.44–1.31 (m, 4H), 0.87 (t, 2H, J = 13.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.84, 143.39 (d, $J_{P\text{-}C}$ = 5.3 Hz), 130.00 (d, $J_{P\text{-}C}$ = 20.1 Hz), 128.35, 127.17 (d, $J_{P\text{-}C}$ = 7.4 Hz), 121.44, 29.49 (d, $J_{P\text{-}C}$ = 17.7 Hz) , 28.12 (d, $J_{P\text{-}C}$ = 8.0 Hz), 24.23 (d, $J_{P\text{-}C}$ = 10.5 Hz), 13.79. ^{31}P NMR (162 MHz, $CDCl_3$): δ -13.66. MS (ESI) m/z: ($[M]^+$) Calcd for $C_{16}H_{17}P$ 240, Found 240. This compound is known and in agreement with the literature data: Cornforth, J., Cornforth, R. H., & Gray, R. T. Synthesis of substituted dibenzophospholes. Part 1. *J. Chem. Soc., Perkin Trans. 1* ,**1982**, 2289–2297.



4'b

1,4-bis(5H-benzo[b]phosphindol-5-yl)butane (4'b). According to the general procedure C (note: 0.4 mmol 1,4-dibromobutane was added), purification by HPLC (standard conditions) afforded **4'b** (152 mg, 80% yield) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, 4H, J = 8.0 Hz), 7.69–7.66 (m, 4H), 7.47–7.43 (m, 4H), 7.35–7.31 (m, 4H), 1.70 (t, 4H, J = 8.0 Hz), 1.39–1.33 (m, 4H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.85, 143.0 (d, $J_{P\text{-}C}$ = 5.5 Hz), 129.95 (d, $J_{P\text{-}C}$ = 21.4 Hz), 128.40, 127.19 (d, $J_{P\text{-}C}$ = 7.6 Hz), 121.41, 29.20 (d, $J_{P\text{-}C}$ = 18.6 Hz), 27.26 (t, $J_{P\text{-}C}$ = 8.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ -13.82. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{27}H_{22}P_2$ 408, Found 408.



4'c

5-(2-bromobenzyl)benzo[b]phosphindole 5-oxide (**4'c**). According to the general procedure C, the product was oxidized by 1 mL 30 % H_2O_2 before isolation, purification by HPLC (standard conditions) afforded **4'c** (274 mg, 83% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.68 (m, 2H), 7.61–7.52 (m, 4H), 7.40 (d, 1H, J = 8.0 Hz), 7.36–7.32 (m, 3H), 7.17 (t, 1H, J = 7.6 Hz), 7.06–7.02 (m, 1H), 3.69 (d, 2H, J = 15.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.10 (d, $J_{P\text{-}C}$ = 21.9 Hz), 133.44 (d, $J_{P\text{-}C}$ = 1.5 Hz), 132.91 (d, $J_{P\text{-}C}$ = 2.4 Hz), 131.85 (d, $J_{P\text{-}C}$ = 31.4 Hz), 131.60 (d, $J_{P\text{-}C}$ = 4.5 Hz), 130.61, 129.96 (d, $J_{P\text{-}C}$ = 8.9 Hz), 129.07 (d, $J_{P\text{-}C}$ = 10.7 Hz), 128.65 (d, $J_{P\text{-}C}$ = 3.4 Hz), 127.47 (d, $J_{P\text{-}C}$ = 2.8 Hz), 125.14 (d, $J_{P\text{-}C}$ = 6.7 Hz), 121.14 (d, $J_{P\text{-}C}$ = 10.1 Hz), 37.97 (d, $J_{P\text{-}C}$ = 63.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 39.63. MS (ESI) m/z: ([M]$^+$) Calcd. for $C_{19}H_{14Br}OP$ 368, Found 368.

2.5 References and notes

[1] The chemical waste triphenylphosphine oxide $Ph_3P(O)$ **1** was predominantly generated from the chemical industries as an end-up compound of triphenylphoshine Ph_3P. Ph_3P is the most popularly used organic phosphorus compound, and more than thousands of tons of this compound is manufactured every year (https://hpvchemicals.oecd.org/UI/handler.axd?id=898195ab-9e1a-44f3-9f08-d823481a2c40). It is used in a number of famous organic synthetic reactions such as the Mitsunobu, Staudinger, Wittig, Rauhut-Currier and Appeal reactions for the production of vitamins, pharmaceuticals and agrochemicals. Triphenylphosphine is also the most important ligand for organometal catalysts, as exemplified by the Wilkinson catalyst $RhCl(PPh_3)_3$ for hydrogenation, the palladium catalyst $Pd(PPh_3)_4$ for couplings, and the metal catalysts for hydroformylation producing aldehydes (the Oxo synthesis) etc. These Ph_3P eventually ends up as $Ph_3P(O)$.

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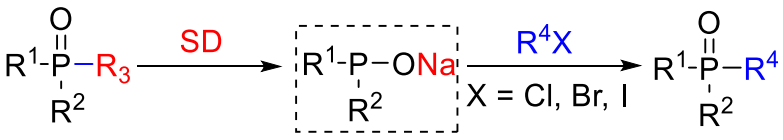
Chapter 3 Studies on the Generality of P-C Bond Cleavage of Phosphine Oxides by Sodium

Abstract

A detailed study on the sodium-mediated transformations of phosphine oxides *via* cleavages of C-P and C-O bonds was carried out. Among the three alkali metals M (M = Li, Na and K) investigated, sodium exhibited the best efficacy and selectivity for converting triphenylphosphine oxide $Ph_3P(O)$ to diphenylphosphinite $Ph_2P(OM)$. The co-generated PhNa from the reaction of $Ph_3P(O)$ with Na, was quickly decomposed by THF to give sodium vinylate that was relatively inert towards electrophiles such as alkyl halides. Selective cleavage took place on P-Ph bonds for $Ph_2P(O)R$ where R = Me, *n*-Bu, and *i*-Pr, whereas cleavages of P-R bonds were also observed for R = *t*-Bu and Bn. 1,4-Dioxane was a better solvent than THF. By carrying out the reactions of $Ph_2P(O)R$ with sodium in 1,4-dioxane followed by quenching the mixture with *n*-BuBr, the corresponding PhP(O)R*n*-Bu could be generated in high yield. PhP(O)*n*-Bu_2 also reacted similarly via the cleavage of the P-Ph bond, however, *n*-$Oct_3P(O)$ did not react at all. On the other hand, the P-O bonds were also efficiently cleft for $Ph_2P(O)OR$ and $PhP(O)(OR)_2$ to produce the corresponding phosphine oxides, $Ph_2P(O)$*n*-Bu and PhP(O)*n*-Bu_2, respectively. However, $(PhO)_3P(O)$ only gave a trace amount of desired *n*-$Bu_3P(O)$ under similar conditions. Other electrophiles of primary and secondary alkyl halides R^4X (X = Cl, Br, I) could be used to react with Ph_2PONa to generate the corresponding alkyldiphenylphosphine oxides in good to excellent yields. Furthermore, by using a palladium catalyst, aryl halides ArX (X = Cl, Br, I), especially the electron-rich aryl chlorides that usually exhibited low reactivity, were capable of coupling with $Ph_2P(ONa)$ to produce the corresponding diphenyl(aryl)phosphine oxides in good yields.



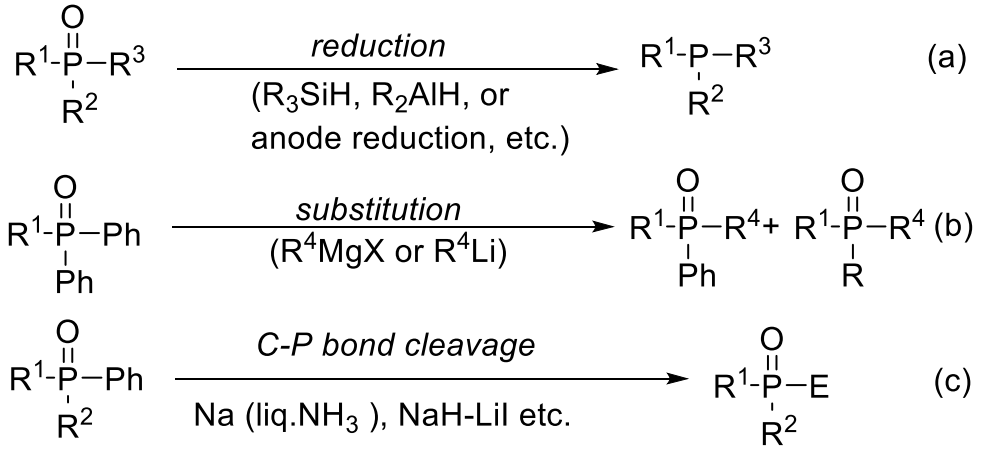
R^1, R^2 = Ph, alkyl, alkoxyl
R^3 = Ph, alkoxyl
R^4 = alkyl, aryl

3.1 Introduction

Triorganylphosphine oxides $R_3P(O)$ have long been used as metal extractants.[1] They are also used in the extraction of acids from industrial wastewaters.[2] A large amount of these compounds and related are also used as novel flame retardants.[3] Compared to the traditional phosphate esters $(RO)_3P(O)$-based flame retardants, the triorganylphosphine oxides $R_3P(O)$-based ones are resistant to hydrolysis, and therefore, are more suitable for materials for electronic devices such as the printed circuit boards that require good electronic insulation. Triorganylphosphine oxides $R_3P(O)$ also have applications in organic synthesis.[4] In particular, the recent studies on the application of $R_3P(O)$ as organocatalysts have been attracted great attention.[5] However, their preparations are still immature due to the limited methods for C-P bond formations.[6]

Up to date, the reductions of phosphine oxides $R_3P(O)$ to its original form phosphines R_3P have been most studied (Scheme 3.1a).[7] In the laboratories, silanes have been frequently used for the reductions.[7a-c] Organolithium and Grignard reagents can react with $Ar_3P(O)$ to give the corresponding substitution products,[8] though there are limitations (Scheme 3.1b). Although lack of efficiency and convenience, the C-P bond of $Ph_3P(O)$ could be cleft by using sodium dissolved in liquid ammonia.[9] Recently, NaH-LiI was found to be a good reagent for this C-P bond cleavage (Scheme 3.1c).[10]

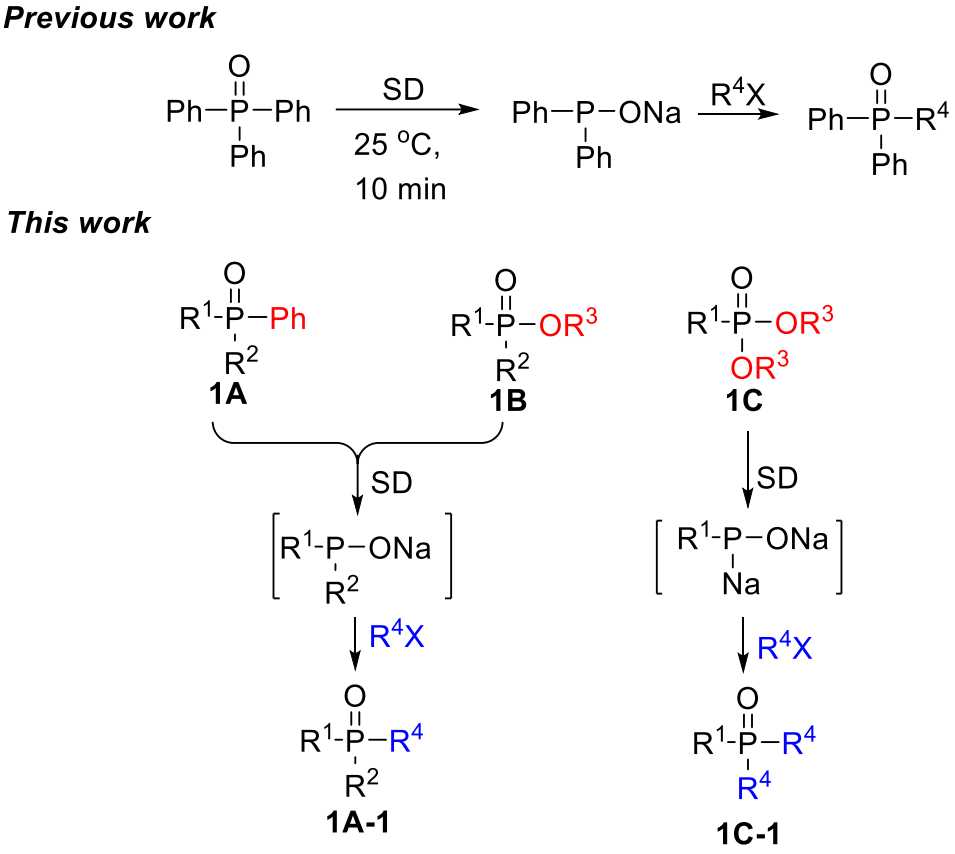
Scheme 3.1 Representative Methods for the Conversion of Phosphine Oxides



It is well known that every year, a large amount of tertiary phosphine oxides $R_3P(O)$ are produced as byproduct from the chemical industry through the Wittig reaction,[11] Mitsunobu reaction,[12] Appel reaction[13] and so on. Because of the chemical stability of $R_3P(O)$,[14] their utilities as chemical starting materials are limited and a lot of them have to be discarded as useless wastes.[15] Very recently, I have briefly disclosed that $Ph_3P(O)$

can be instantly converted to diphenylphosphinite ($Ph_2P(ONa)$) quantitatively at room temperature by using the abundant & cheap sodium (sodium finely dispersed in paraffin oil with μm-scale sizes, hereafter abbreviated as SD).[16] Herein I report the details of the reaction. This method is a rather general way for the preparation of phosphine oxides. As shown in Scheme 3.2, in addition to $Ph_3P(O)$, the method can be applied to other phosphine oxides **1A**, phosphinates **1B** and phosphonates **1C** to produce the corresponding phosphine oxides in high yields.

Scheme 3.2 Easy Preparation of Phosphine Oxides via the Ready Cleavage of C-P and O-P bonds by SD



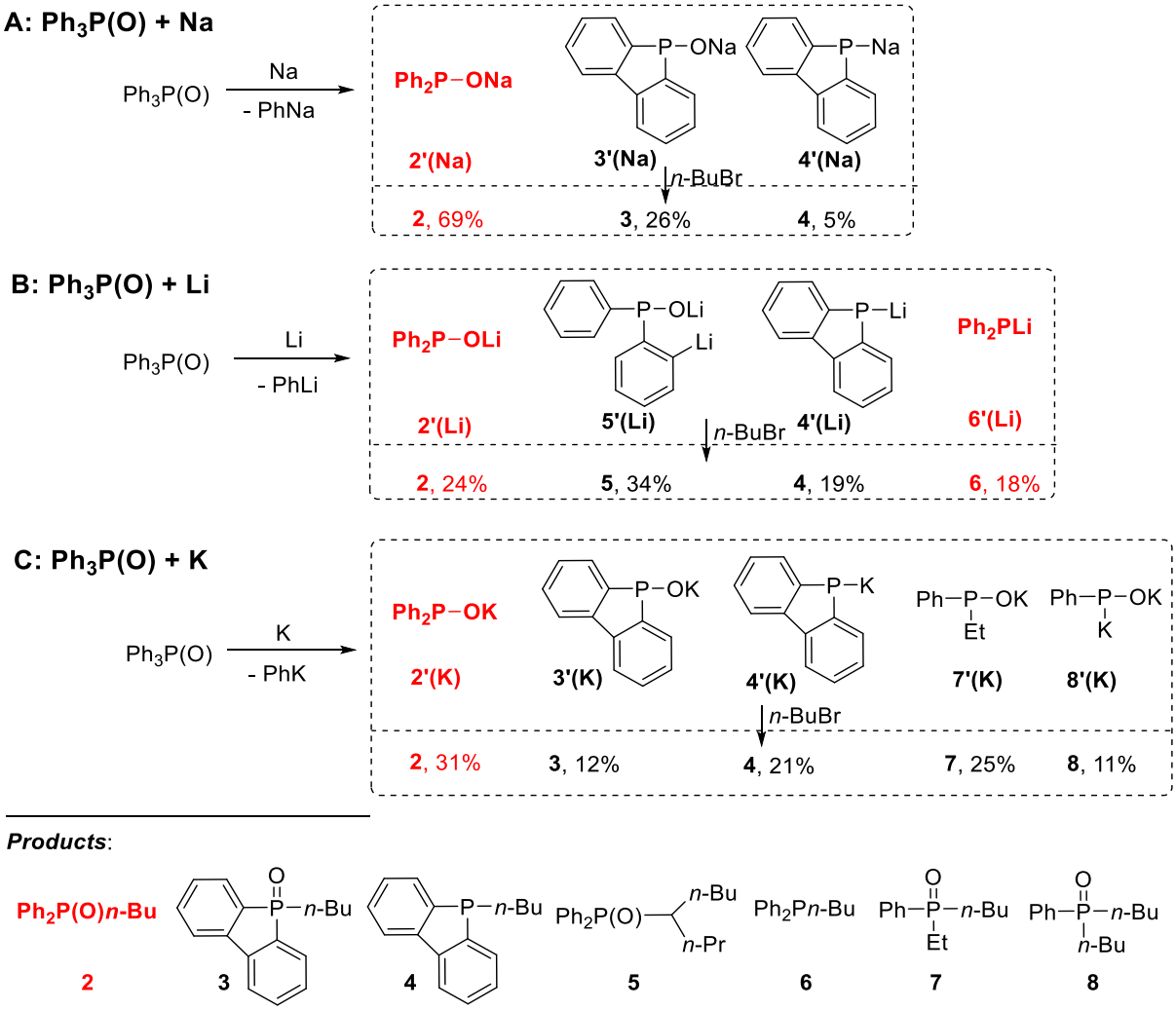
3.2 Results and Discussion

3.2.1 Comparison between Li, Na and K.

It has been briefly disclosed that, in addition to sodium, lithium also reacted with $Ph_3P(O)$ to give $Ph_2P(OLi)$ though the efficiency was low.[16a] Therefore, it is interesting to know the difference in reactivity of the three alkali metals lithium, sodium and potassium. Under argon atmosphere, 2.5 equivalents of the corresponding alkali metal cut into small pieces was added to $Ph_3P(O)$ dissolved in 5 mL THF at room temperature. All the

three alkali metals could react quickly with $Ph_3P(O)$ as the initially colorless solution of $Ph_3P(O)$ instantly changed to brown. The mixture was stirred at room temperature overnight, and then quenched with *n*-butyl bromide, and analyzed by GC-Mass and ^{31}P NMR spectroscopies (Scheme 3.3).

Scheme 3.3 Reactions of $Ph_3P(O)$ with Alkali Metals.[a]

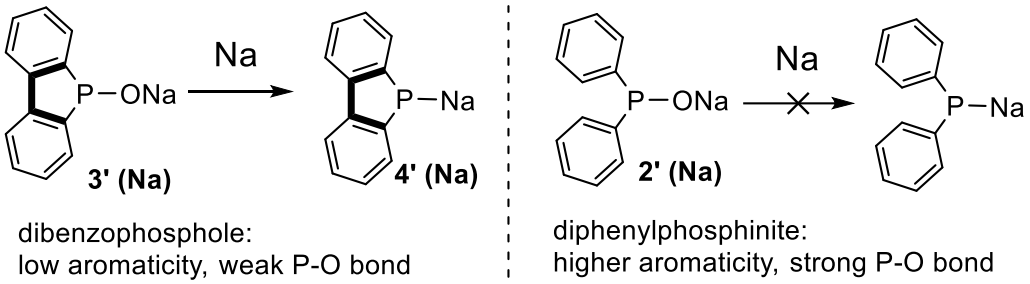


[a]Reaction conditions: under argon atmosphere, $Ph_3P(O)$ (1.0 mmol), alkali metal (2.5 mmol), THF (5.0 mL), 25 °C, overnight. Then *n*-BuBr (2.0 mmol), 25 °C, 0.5 h. Yields refer to ^{31}P-NMR yields based on $Ph_3P(O)$ used.

As reported before,[16a] the reaction of $Ph_3P(O)$ with sodium after quenching by *n*-BuBr produced *n*-butyldiphenyl phosphine oxide $Ph_2P(O)n$-Bu **2**, 5-butyldibenzophosphole 5-oxide **3** and 5-butyldibenzophosphole **4**, via the reactions of the corresponding sodium salts of **2'(Na)**, **3'(Na)**, and **4'(Na)**, in 69%, 26% and 5% yields, respectively. Compound **2'(Na)** was generated via the cleavage of $Ph_3P(O)$'s P-Ph bond by sodium, while **3'(Na)** was from the reaction of $Ph_3P(O)$ with PhNa and **4'(Na)** was from the

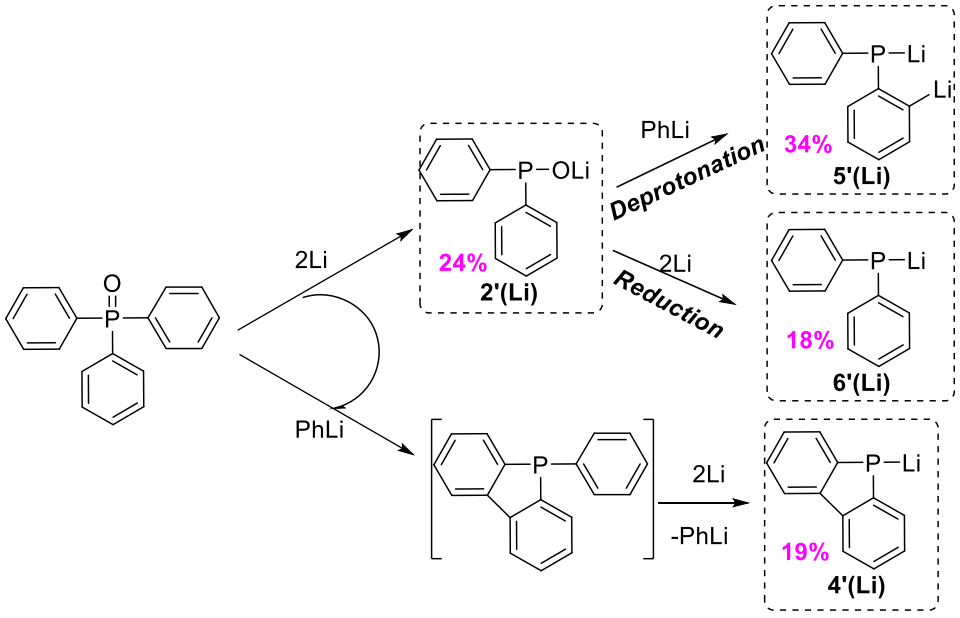
reduction of **3'(Na)** by sodium.[16] However, Ph_2PNa derived from Ph_2PONa via deoxygenation was not detected. The difference may result from the weaker P-O bond strength of cyclic **3'(Na)** in comparison to that of **2'(Na)**, because the phosphole structure of **3'(Na)** possesses lower aromatic characteristic (only has a conjugates diene),[16b] which leads to lower conjugation effect of the electrons among the P-O bond and the phenyl rings. On the other side, **2'(Na)** possesses higher aromaticity that strength the P-O bond, so the deoxygenation was hard to proceed. (Scheme 3.4).

Scheme 3.4 Comparison of the reduction of two PONa intermediates by sodium



Under similar conditions, the reaction of $Ph_3P(O)$ with lithium produced four phosphorus compounds, **2**, **5**, **4** and **6** in 24%, 34%, 19% and 18% yields, respectively. The dibenzophosphole oxide **3** observed with sodium could not be detected. Instead, two new phosphorus compounds **5**[28] and **6** via **5'(Li)** and **6'(Li)**, respectively,[24] that were not observed for sodium, were generated.

Scheme 3.5 The reactions occurred between $Ph_3P(O)$ with Li



The new intermediate **5'(Li)** should arise via the reaction of **2'(Li)** with PhLi, and **6'(Li)** was from the

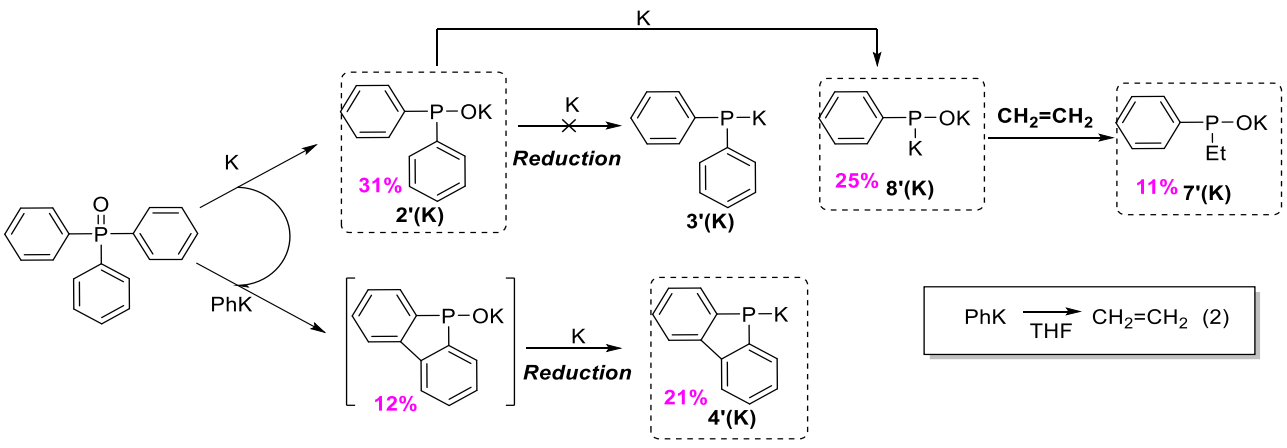
reduction of **2'(Li)** by lithium. Since PhLi could not be trapped by THF (PhNa reacted with THF easily, refer to Scheme 3.5, so the reactions with Na was associated with less side reactions), thus the side reaction of PhLi with $Ph_3P(O)$ and **2'(Li)** forming the corresponding **4'(Li)** and **5'(Li)** took place, respectively (Scheme 3.5). Worth noticing is that, the smooth reduction of **2'(Li)** to **6'(Li)** was due to that the reduction potential of lithium ($E^0(Li^+/Li)$ = -3.045 V) is higher than that of sodium ($E^0(Na^+/Na)$ = -2.714 V) and potassium ($E^0(K^+/K)$ = -2.925 V). And the reduction potentials are consistent to the experimental results that sodium and potassium (see the reaction of $Ph_3P(O)$ with K, the reduction product Ph_2PK of **2'(K)** was also not detected in the reaction mixture, Scheme 3.6) failed to reduce diphenylphosphinite Ph_2POM to diphenylphosphide Ph_2PM (M = Na or K), only lithium could facilitate the deoxygenation of Ph_2POLi to Ph_2PLi. (Eq 1)

$$Ph_2P{-}OM \xrightarrow[-\ M_2O]{2M} Ph_2P{-}M \qquad (1)$$

M = Li, ***observed* (18%)**
M = Na or K, ***not detected***

When it came to potassium, it gave a different result to both lithium and sodium to give five compounds **2**, **3**, **4, 7** and **8** (Scheme 3.6). Both **7** and **8** were new compounds that were not observed with Li and Na. Such a compound of **8** could not be detected from the reactions with Li and Na, showing that K is more reactive than Na and Li, and even two P-Ph bonds of $Ph_3P(O)$ could be cleft by potassium. In addition, the formation of **7** was not observed with Li and Na either. A reaction as shown in eq 2 was assumed to take place for the generation of ethylene (*vide infra*) that lead to the formation of **7'(K)** from **8'(K)**.[17]

Scheme 3.6 The reactions occurred between $Ph_3P(O)$ with K



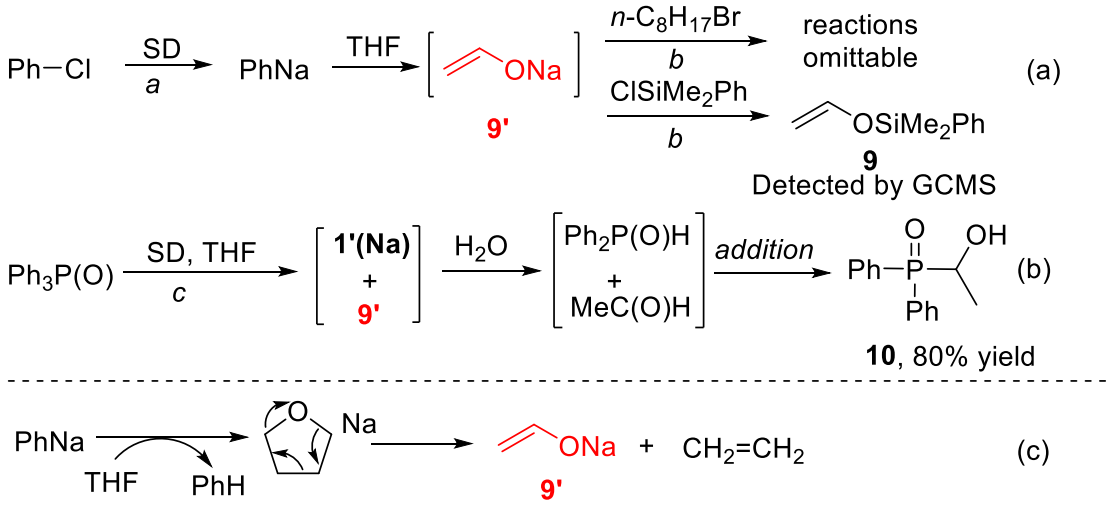
Therefore, it is concluded that, as to the selective C-P bond cleavage of $Ph_3P(O)$ to generate $Ph_2P(OM)$, *Na*

is better than Li and K,[18] because the heavy side reactions aroused by PhLi and the excessively reactivity of K that could break two P-Ph bonds.

3.2.2 The destiny of PhNa co-generated from the reaction of $Ph_3P(O)$ with sodium

As shown above in Scheme 3.3, one equivalent of PhNa was co-generated from the reaction of $Ph_3P(O)$ with SD in THF. Although it is known that, unlike PhLi generated using lithium (Scheme 3.3B) that is stable in THF and stay there in the solution, the generated PhNa is so reactive and should decompose quickly in THF at room temperature.[17] However, detailed reactions of the decomposition of PhNa by THF were not clear.[17c] To clarify this decomposition, PhNa was generated separately from PhCl and SD in THF, and then the solution was quenched with electrophiles *n*-$C_8H_{17}Br$ and $PhMe_2SiCl$, respectively (Scheme 3.7a). Although reactions with *n*-$C_8H_{17}Br$ were omittable,[19] to our surprise, a silylvinyl ether **9** was detected, indicating the formation of the vinylate **9'** from the reaction! However, the exact yield of **9'** was hard to be determined due to its rather easy decomposition of **9** with water. Fortunately, this intermediate could be trapped by the in situ generated $Ph_2P(O)H$ as shown in Scheme 3.7b. Thus 80% yield of **10**, formed by the easy addition of $Ph_2P(O)H$ to acetaldehyde under basic conditions,[20] was obtained that unambiguously confirmed that **9'** was the main sodium alkoxide generated from the reaction of PhNa with THF (Scheme 3.7c).[17]

Scheme 3.7 The Decomposition of PhNa by THF.[a]



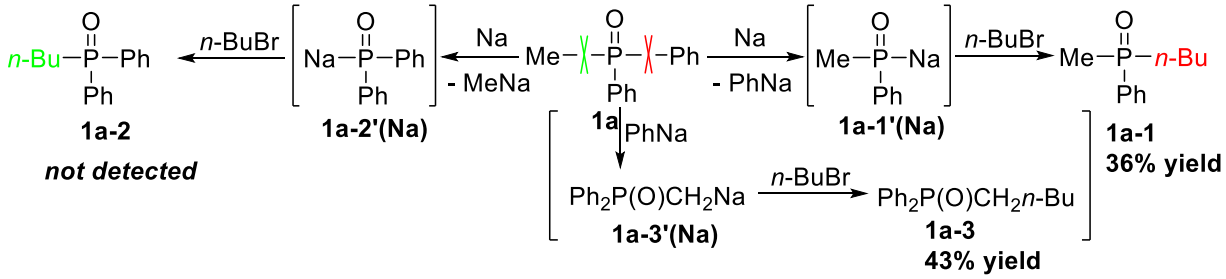
[a]Conditions: a) PhCl (1.0 mmol), SD (2.0 mmol), THF (5.0 mL), 25 °C, 1 h. b) Electrophiles (1.2 mmol), 25 °C, 0.5 h. c) $Ph_3P(O)$ (1.0mmol), SD (2.5 mmol), THF (5 mL), 25 °C, 10 min.

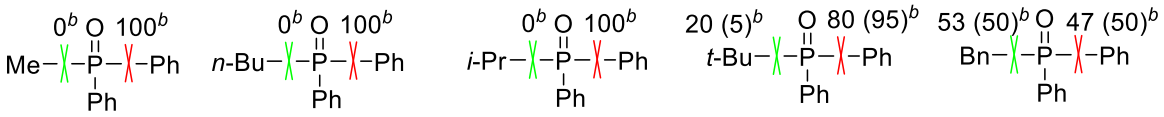
Therefore, vinylate **9'** was the main co-product in the solution of $Ph_2P(ONa)$ generated from $Ph_3P(O)$ and SD. The fortunate thing is that, unlike PhLi (Scheme 3.3b), the presence of **9'** affects little the following reactions of $Ph_2P(ONa)$ with an electrophile[21] such as RX because of the relatively low reactivity of **9'** and the relatively high reactivity of $Ph_2P(ONa)$, i.e. in most cases $Ph_2P(ONa)$ generated from $Ph_3P(O)$ and SD can be used as it to react with other electrophiles even in the presence of **9'**.[16]

3.2.3 Selectivity on the C-P bond cleavage of diphenyl(alkyl)phosphine oxides by sodium

As shown in Scheme 3.8, the C-P bond cleavage of unsymmetrical diphenyl(alkyl)phosphine oxides was studied. All these phosphine oxides reacted similarly to $Ph_3P(O)$ to generate the corresponding $R_2P(ONa)$. As exemplified by the reaction of $Ph_2P(O)Me$ **1a**, to the phosphine oxide in THF was added 1 equiv of SD at room temperature to generate an orange solution. The mixture was stirred for 1 h and then quenched by an excess amount of *n*-BuBr. Compound **1a-1** was obtained in 36% GC yield, but compound **1a-2** could not be detected at all. As expected, compound **1a-3** via the reactions of PhNa and **1a** was also obtained in 43% yield. By conducting similar reactions, the selectivity on the C-P bond cleavage of diphenyl(alkyl)phosphine oxides $Ph_2P(O)R$ (P-Ph vs P-R) was determined. Thus, while cleavage on P-Ph bond took place exclusively with Me, *n*-Bu and *i*-Pr groups, interestingly, for $Ph_2P(O)t$-Bu, the selectivity of P-Ph vs P-*t*-Bu is 80/20, and for $Ph_2P(O)Bn$, the selectivity even became 47/53, showing that it is equally easy to break the P-Bn bond and the P-Ph bond.

Scheme 3.8 Selectivity of the C-P bond Cleavage[a]





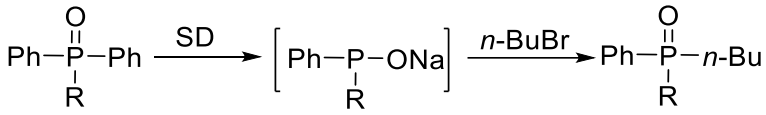
[a]Reaction conditions: $Ph_2P(O)R$ (0.3 mmol), THF (2.0 mL), SD (0.3 mmol), 25 °C, 1 h. Then excessive *n*-BuBr, 25 °C, 0.5 h. Yields were determined by GC. [b]The ratio of P-R bond and P-Ph bond cleavage was determined by GC. The data in parentheses were collected

in 1,4-dioxane.

3.2.4 Scope and limitations

In order to make the present SD-mediated C-P bond cleavage of phosphine oxides a general method for the synthesis of organophosphine oxides, the first thing I have to do is to fix the problem of the co-generation of the side product of $Ph_2P(O)R$ by the abstraction of the α-protons by PhNa as exemplified by $Ph_2P(O)Me$ (Scheme 3.8). Since the generation of the side product **1a-3'(Na)** by PhNa (Scheme 3.8) is a competition reaction to the generation of the aimed product **1a-1'(Na)** by Na, the use of an excess amount of Na should suppress its formation. As shown in Table 3.1, by treating 0.3 mmol of $Ph_2P(O)Me$ **1a** dissolved in THF with 1.0 mmol of SD (3.3 equiv) at room temperature overnight, 62% yield of the desired product **3a** could be obtained (run 1). The yield of **1a-1** increased to 78% by carrying a similar reaction at 60 °C (run 2). Furthermore, when I used 1,4-dioxane as the solvent, 71% yield of **1a-1** was obtained at room temperature (run 3). Finally, almost a quantitative yield of **1a-1** could be obtained by carrying out the reaction in dioxane at 60 °C (run 4). $Ph_2P(O)$*n*-Bu reacted similarly, and PhP(O)*n*-Bu_2 **1b-1** was obtained in 90% yield and quantitatively at 25 °C (run 5) and 60 °C (run 6), respectively.

Table 3.1 Reaction Condition Optimization of $Ph_2P(O)R$ with SD[a]



1 **1(Na)** **1-1**

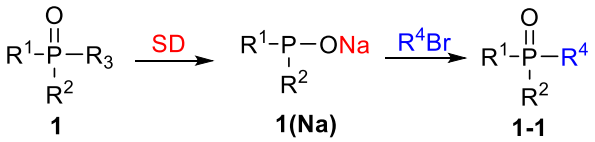
Run	R	Temp. (°C)	Solvent	Yield of **1-1**[b]
1	Me	25	THF	62 %
2	Me	60	THF	78 %
3	Me	25	1,4-dioxane	71 %
4	Me	60	1,4-dioxane	98 %
5	*n*-Bu	25	1,4-dioxane	90 %
6	*n*-Bu	60	1,4-dioxane	99 %

[a]Reaction conditions: **1** (0.3 mmol), SD (1.0 mmol), solvent (2.0 mL), indicated temperature, overnight, and then *n*-BuBr (0.4 mmol), 25 °C, 0.5 h. [b]^{31}P-NMR yield based on **1** used.

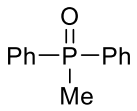
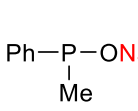
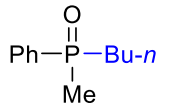
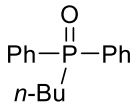
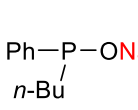
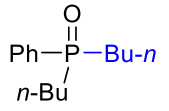
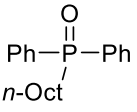
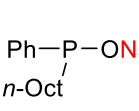
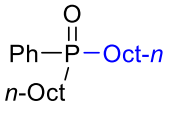
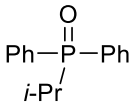
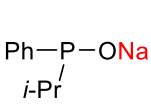
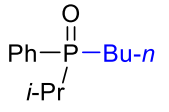
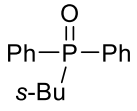
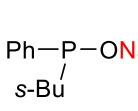
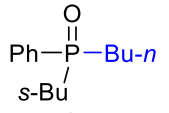
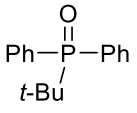
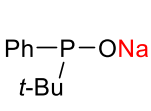
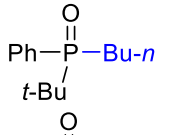
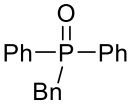
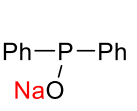
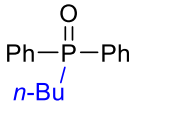
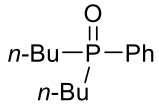
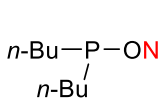
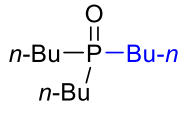
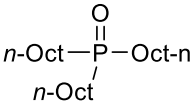
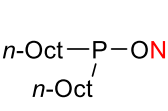
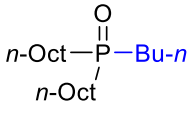
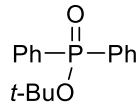
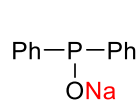
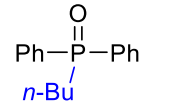
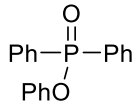
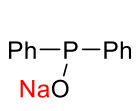
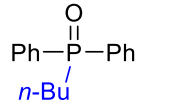
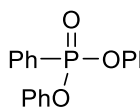
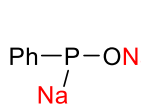
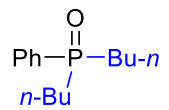
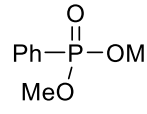
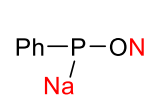
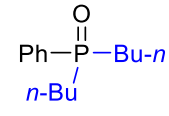
To demonstrate the generality of the above reaction as an efficient synthetic tool for the preparation of phosphine oxides, as depicted in Table 3.2, the reactions of representative phosphine oxides and related were investigated. Highly selective Ph-P bond cleavage of diphenyl(alkyl)phosphine oxides $Ph_2P(O)R$ took place efficiently, where R can be methyl (run 1), primary (runs 2 and 3), secondary (run 4 and 5) and tertiary (run 6) alkyl groups, to produce the corresponding PhRP(ONa) that was trapped by alkyl bromide to give the corresponding new phosphine oxides in good to excellent yields. However, benzyldiphenylphosphine oxide $Ph_2P(O)CH_2Ph$ gave complicated results under similar conditions (run 7) due to the bad selectivity of the C-P bond cleavages (Scheme 5) and the easier deprotonation of the benzyl proton of $Ph_2P(O)CH_2Ph$ by a base. After carrying out an extensive study on the optimization of the reaction conditions, I found that by conducting the reaction in 1,4-dioxane at 100 °C, the $Ph_2P(O)$*n*-Bu **1g-1**, assumed from the P-Bn bond cleavage, was obtained in 53% yield.[22] Dibutylphenylphosphine oxide could be also used as the substrate, and the Ph-P bond was selectively cleft (run 8). However, trioctylphosphine oxide did not react even at a higher temperature (run 9).

In addition to tertiary phosphine oxides, the reactions of phosphinic (runs 10 and 11), phosphonic (runs 12 and 13) and phosphoric (run 14) esters were also examined. Only the products via the cleavage of the P-O bonds were obtained. Thus, diphenylphosphinates like $Ph_2P(O)O$*t*-Bu and $Ph_2P(O)OPh$ generated Ph_2PONa in high yield (runs 10 and 11). Surprisingly, with diphenyl phenylphosphonate $PhP(O)(OPh)_2$, the two P-O bonds could be readily broken and the product $PhP(O)$*n*-Bu_2 assumed via the reaction of PhP(Na)ONa and *n*-BuBr was obtained in good yield (run 12). However, under similar conditions, dimethyl phenylphosphonate $PhP(O)(OMe)_2$ gave a complex mixture and only 31% $PhP(O)$*n*-Bu_2 was obtained (runs 13). Last, although triphenyl phosphate $(PhO)_3P(O)$ also reacted with SD rapidly, the result was very complicated and only trace amount of *n*-$Bu_3P(O)$ could be detected (run 14).

Table 3.2 Conversion of Phosphine Oxides to Other Organophosphorus by SD.[a]

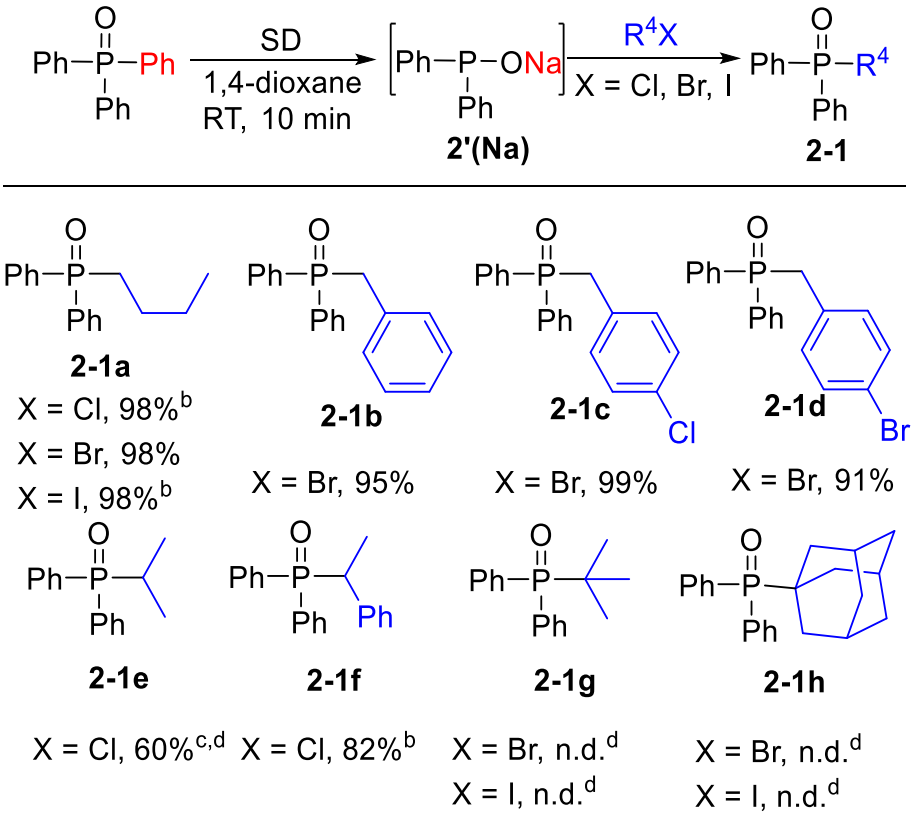


1 **1(Na)** **1-1**

run	**1**	**1(Na)**	**1-1**/yield
1			 **1a-1**, 89%
2			 **1b-1**, 92%
3[b]			 **1c-1**, 96%
4			 **1d-1**, 92%
5			 **1e-1**, 99%
6			 **1f-1**, 90%
7			 **1g-1**, 53%
8			 **1h-1**, 87%
9			 **1i-1**, not detected
10			 **1g-1**, 93%
11			 **1g-1**, 85%
12[c]			 **1b-1**, 69%
13[c,d]			 **1b-1**, 31%
14[e]			**1h-1**, trace

[a]Reaction conditions: **1** (0.3 mmol), SD (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 24 h. Then *n*-BuBr (0.4 mmol), 25 °C, 0.5 h. Isolated yield. [b]*n*-OctBr (0.4 mmol) was used. [c]SD (1.8 mmol), *n*-BuBr (0.8 mmol). [d]Yield was determined by ^{31}P NMR based on **1m** used. [e]SD (2.4 mmol), *n*-BuBr (1.0 mmol).

Table 3.3 Scope of Alkyl Halides.[a]



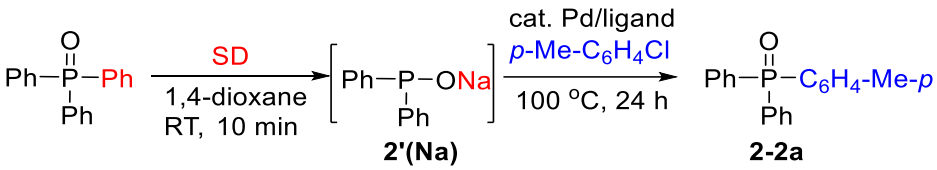
[a]Reaction conditions: $Ph_3P(O)$ (0.2 mmol), SD (0.5 mmol), 1,4-dioxane (1.0 mL), 25 °C, 10 min. Then R^4X (0.3 mmol), 25 °C, 0.5 h. Isolated yield. [b]60 °C, overnight. [c]15-crown-5 ether (0.2 mmol) was added at step 2. [d]100 °C, overnight.

Apart from using the simple *n*-BuBr as electrophile, as outlined in Table 3.3, *n*-BuCl and *n*-BuI could also be used as electrophiles for trapping $Ph_2P(ONa)$ to generate the corresponding products in almost quantitative yields, though heating is required for *n*-BuCl due to its low reactivity. The electrophilic reagents were readily extended to other primary alkyl bromides with functional groups such as Cl and Br (**2-1b–d**) as well as secondary alkyl chlorides (**2-1e** and **2-1f**). Unfortunately, treatment of $Ph_2P(ONa)$ with tertiary alkyl halides such as *t*-butyl and admantyl halides led to complex mixture and no desired products could be obtained at all (**2-1g** and **2-1f**).

In order to extend the utilization of $Ph_2P(ONa)$ in organic synthesis, I wondered if it can be used in the cross-coupling reactions with aryl halides ArX replacing $Ph_2P(O)H$ for the preparation of diphenyl(aryl)phosphine oxides. To our knowledge, the conventional transition metal-catalyzed couplings of $Ph_2P(O)H$ with the reactive aryl bromides or aryl iodides were fully studied,[23] however, the reactions with the less reactive aryl chlorides, especially the electron-rich aryl chlorides were limited.[24] Therefore, in this work, I dedicated to investigating the reactions of Ph_2PONa with ArCl.[25]

Delightfully, as shown in Table 3.4, without adding any base, by simply heating the mixture of 0.2 mmol of $Ph_2P(ONa)$ in situ generated from $Ph_3P(O)$ and SD and 1 equivalent of *p*-MeC_6H_4Cl in the presence of 5 mol % of $Pd(OAc)_2$, the expected coupling product $Ph_2P(O)C_6H_4$-Me-*p* **2-2a** was produced in 78% yield (Table 3.4,

Table 3.4 Reaction Conditions Optimization.[a]



run	metal	ligand	Yield[b] (**2-2a**)/%
1	$Pd(OAc)_2$	-	78
2	$Pd(OAc)_2$	Ph_3P	88
3	$Pd(OAc)_2$	dppf	79
4	$Pd(OAc)_2$	dppb	90
5	$Pd(OAc)_2$	dppm	86
6	$Pd(PPh_3)_2Cl_2$	-	94 (85)
7	$Ni(dppp)Cl_2$	-	trace

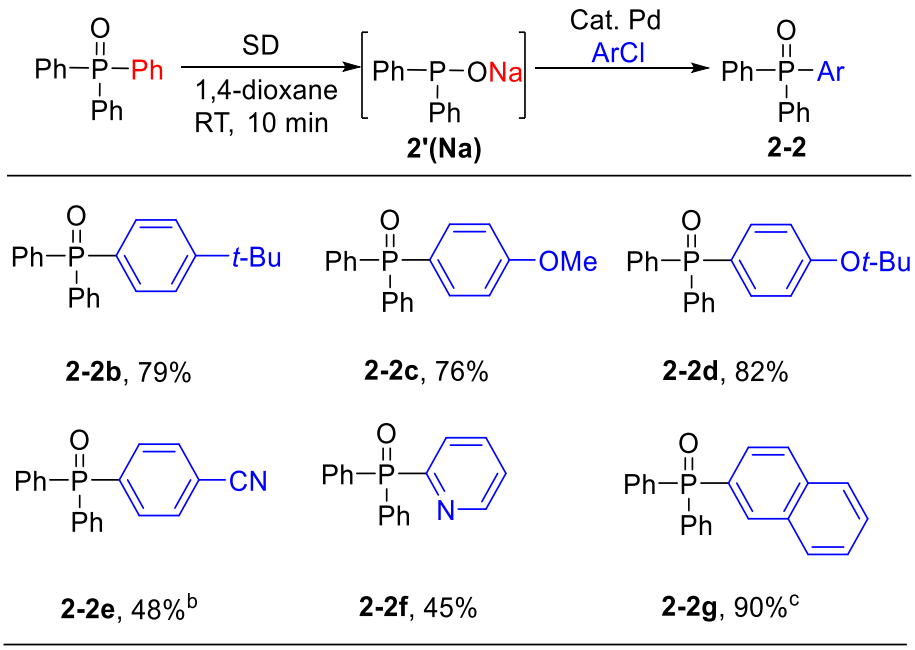
[a]Reaction conditions: $Ph_3P(O)$ (0.2 mmol), SD (0.5 mmol), 1,4-dioxane (1.0 mL), 25 °C, 10 min. Then Pd/ligand (5 mol %) and *p*-Me-C_6H_4Cl (0.2 mmol) was sequentially added, 100 °C, 24 h. [b]GC yield using decane as an internal standard, isolated yield in parentheses.

run 1). Further study showed that introducing phosphine ligands could improve the reaction efficiency (Table 3.4, runs 2–5). Finally, I found that $Pd(Ph_3P)_2Cl_2$ was an efficient catalyst for this coupling reaction (Table 4, run 6), whereas $Ni(dppp)Cl_2$ exhibited very low catalytic activity for this coupling (Table 3.4, run 7).

The Pd-catalyzed coupling reaction can be readily applied to a variety of other aryl chlorides. For example, the electron-rich aryl chlorides including those with *tert*-butyl, methoxyl and *tert*-butoxyl groups on the benzene ring, were suitable substrates for this conversion, affording the corresponding coupling adducts in high yields (Table 3.5, **2-2b**–**2-2d**). 2-pyridyl chloride was also tolerated in this catalyzed reaction and formed

the products in moderate yield (Table 3.5, **2-2f**). The catalyst loading could be reduced to 2 mol % without reducing the reaction's efficacy, since 1 mmol of 2-chloronaphthalene was readily phosphorylated to produce **2-2g** in 90% yield.

Table 3.5 Palladium-Catalyzed Cross-Coupling Reactions of Ph_2PONa and Aryl Halides.[a]



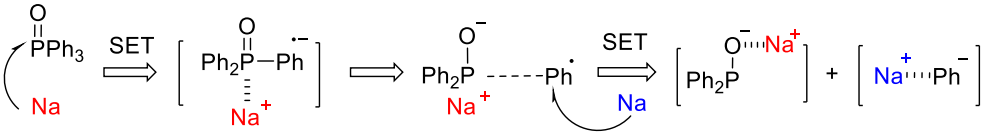
[a]Reaction conditions: $Ph_3P(O)$ (0.2 mmol), SD (0.5 mmol), 1,4-dioxane (1.0 mL), 25 °C, 10 min. Then $Pd(Ph_3P)_2Cl_2$ (5 mol %) and ArX (0.2 mmol) was sequentially added, 100 °C, 24 h. Isolated yield. [b]$Pd(OAc)_2$/dppf (5 mol %) was used. [c] $Ph_3P(O)$ (1.0 mmol), SD (2.5 mmol), 1,4-dioxane (5.0 mL), 25 °C, 10 min. And then $Pd(Ph_3P)_2Cl_2$ (2 mol %), 2-chloronaphthalene (1.0 mmol), 120 °C, 30 h.

3.2.5 Mechanism of the P-C Bond Cleavage

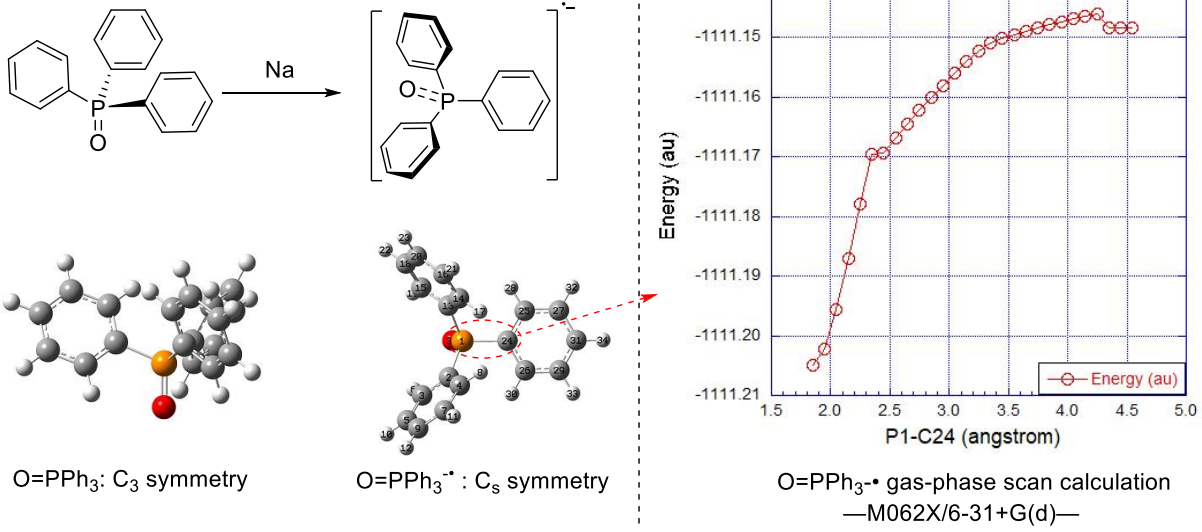
As for the mechanism of cleaving P-R bond of organophosphine oxides (Scheme 3.9), I first figured out the reaction mechanism of $Ph_3P(O)$ with sodium. As depicted in scheme 3.9A, I supposed that single electron transfer (SET) of Na to $Ph_3P(O)$ formed the radical anion intermediate $[Ph_3PO]^{-\bullet}Na^+$,[26] it should be noted that, of the three P-C bonds in the radical anion, the P-C bond located on the Cs mirror surface is slightly longer than the other two P-C bonds, thus weaking one P-Ph bond strength, as observed by the DFT calculation results that an increase in energy of about 36 kcal·mol^{-1} was observed with the extension of the P-C bond (Scheme 3.9B). Subsequently, the decomposition of the radical anion along with a P-Ph bond cleavage generated the corresponding $[Ph_2PO^-Na^+]$ intermediate and phenyl radical Ph• since the path a for generating phenyl radical

Scheme 3.9 Mechanism study

A. Possible Mechanism of P-C bond Cleavage.

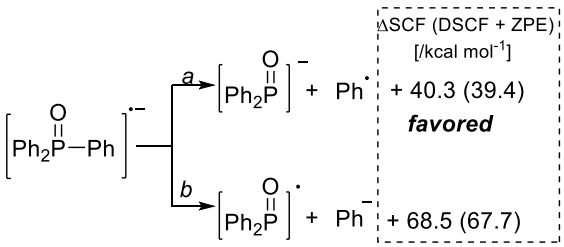


B. $Ph_3P(O)^{\bullet-}$ radical anion gas phase scan calculation.

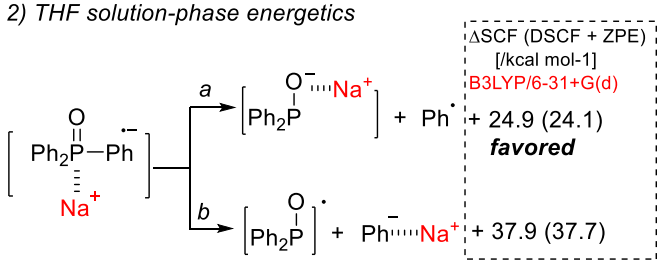


C. $Ph_3P(O)^{\bullet-}$ radical anion decomposition

1) Gas-phase energetics



2) THF solution-phase energetics



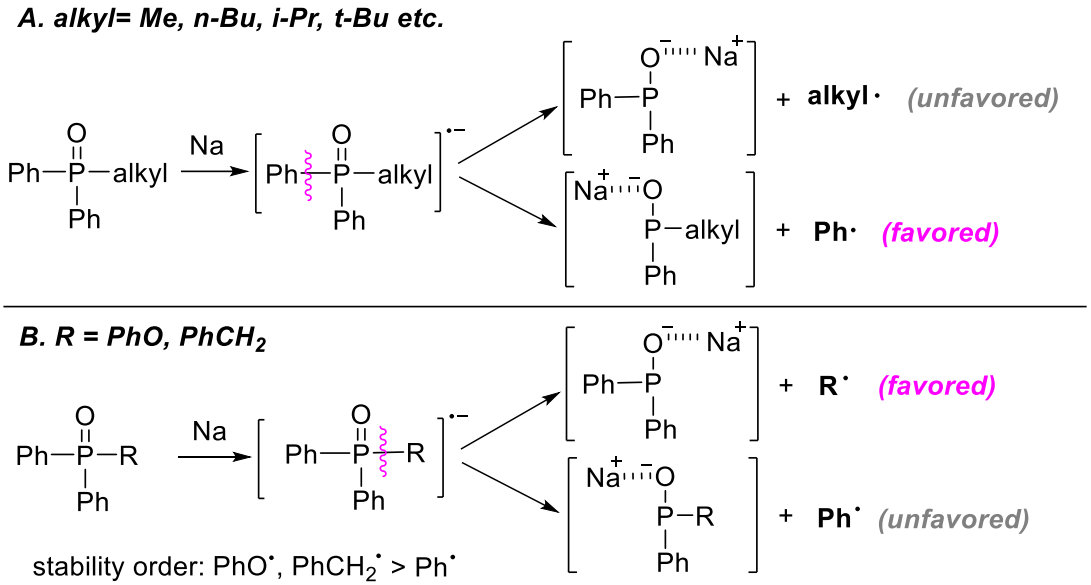
D. $Ph_3P(O)$'s reaction energetics (THF-solution-phase)

	B3LYP/6-31 + G(d)		M062X/6-31 + G(d)	
	ΔH	*ΔG*	*ΔH*	*ΔG*
$Ph_3P(O)$ + Na	0.0	0.0	0.0	0.0
$Ph_3P(O)^{\bullet-}Na^+$	-17.3	-9.7	-24.1	-16.4
$Ph_2P(O)^-Na^+$ + $Ph^\bullet$	6.8	1.2	8.6	3.2
$Ph_2P(O)^-Na^+$ + Ph^-Na^+	-51.3	-49.4	-59.2	-54.1

is favored in comparison to the path b for phenyl anion, according to the calculation (Scheme 3.9C). And finally, second SET of a molecule of sodium resulted to the $R^1R^2PO^-Na^+$ and R^-Na^+. The Gibbs energy profiles of the reaction of $Ph_3P(O)$ with Na indicated that the overall process is exothermic, which is consistent to the experiment phenomenon (Scheme 3.9D).

With respect to the diphenyl(alkyl)phosphine oxides, the observed experimental results showed P-Ph bond was dominantly broken (Table 3.2, run 1-6), which means one of the P-Ph bond of the radical anion intermediate $[Ph_2RPO]^{-\bullet}Na^+$ was preferable to be longer and easier to be broken (Scheme 3.10A). But on the contrary, when it came to diphenyl(alkoxy)phosphine oxide $Ph_2P(O)OR$ or diphenyl(benzyl)phosphine oxide $Ph_2P(O)CH_2Ph$, P-R bond, instead of P-Ph bond, was preferably cleft, demonstrating that P-R bond preferably became longer and weaker in the radical anion intermediate $[Ph_2RPO]^{-\bullet}Na^+$ (Scheme 3.10B). It could also be explained by the stability order of the radicals ($Ph^\bullet < Bn^\bullet < PhO^\bullet$)[27] that lead to the decomposed species ($Ph_2PO^-Na^+$ and $R^\bullet$) with lower Gibbs energy.

Scheme 3.10 P-R bond cleavage of other phosphine oxides



3.3 Conclusions

In summary, I have studied the sodium-mediated P-C and P-O bond's selective cleavage of tertiary phosphine oxides in detail. In contrast to Li, K and Mg, sodium shows the best efficiency and selectivity for cleaving C-Ph bond of triphenylphosphine oxide to generate phosphinite. The destiny of PhNa co-generated from P-Ph bond cleavage as well as the selectivity of P-Ph and P-R (alkyl group) bond cleavage were disclosed. A variety of phosphine oxides, reacted with SD efficiently to give P-ONa intermediates via P-C or P-O bond cleavage, and subsequent reactions of the P-ONa intermediates with a variety of alkyl halides and aryl halides afforded the corresponding new phosphine oxides in moderate to high yields. This protocol provided a new

route for the preparation of unsymmetric phosphine oxides compounds. The mechanism study indicated that P-C bond or P-O bond cleavage depends on the R group.

3.4 Experimental Section

3.4.1 General Information

The reactions were carried out in oven dried Schlenk tubes under argon atmosphere. The sodium I used was dispersed in paraffin oil with an average particle size smaller than 10 μm and a concentration of ~10.0 mol/L. MS (ESI) data were obtained on SHIMADZU GC-MS 2010 plus. The High-resolution ESI mass spectra were obtained on Bruker micrOTOF II. Column chromatography was performed using Silica Gel 60 N (TCI, spherical, neutral). HPLC (recycle GPC) isolation was performed using JAPAN ANALYTICAL INDUSTRY LC-908, equipped with two preparative columns (20 mm × 600 mm; JAIGEL-1H and JAIGEL-2H). $CHCl_3$ (flow rate: 4.0 mL/min) was used as eluent. ^{1}H, ^{13}C, and ^{31}P NMR were recorded on a JEOL JNM-ECS400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, and 162 MHz for ^{31}P NMR spectroscopy). Chemical shifts for ^{1}H NMR are referred to internal Me_4Si (0 ppm) and reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. Chemical shifts for ^{31}P NMR were relative to H_3PO_4 (85% solution in D_2O, 0 ppm). The melting points were obtained on SRS OptiMelt. All DFT calculations were carried out using Gaussian 09 programs.

3.4.2 Typical Experimental Procedure for the Synthesis of Phosphine Oxides 1a-1 from 1a by SD

Under argon atmosphere, to a stirring solution of diphenyl(methyl)phosphine oxide **1a** (0.3 mmol, 1 equiv., 64.8 mg) in 1,4-dioxane (2.0 mL) was added SD (1.0 mmol, 3.3 equiv., 0.1 mL) *via* a syringe. The mixture was then stirred at 60 ºC for 24 h. After removal of the excessive Na by filtration, *n*-BuBr (0.4 mmol, 1.33 equiv., 43 μL) was added, and further stirring the mixture was continued for 0.5 h. After that, the resulting mixture was filtered and concentrated under vacuum. Next, the obtained residue was directly eluted with hexane via a silica gel column and then eluted with MeOH to give the crude product, which was then diluted in $CHCl_3$ and purified by GPC to afford pure product **1a-1** (52.3 mg, 0.267 mmol, 89 % yield).

3.4.3 Experimental Procedure for 2 mmol-Scale Synthesis of Phosphine Oxides 1b-1 from 1b by SD

Under argon atmosphere, to a stirring solution of diphenyl(butyl)phosphine oxide **1b** (2.0 mmol, 1 equiv, 516.2 mg) in 1,4-dioxane (10.0 mL) was added SD (8.0 mmol, 4 equiv, 0.8 mL) *via* a syringe. The mixture was then stirred at 60 °C for 48 h. After removal of the excessive Na by filtration, *n*-BuBr (3.0 mmol, 1.5 equiv, 161 μL) was added, and further stirring the mixture for 2 h. After that, the resulting mixture was filtered and concentrated under vacuum. Next, the residue was then purified by flash column chromatography on silica gel with hexane/ethyl acetate (1:1) to give the desired product **1b-1** (409.6 mg, 1.72 mmol, 86% yield).

3.4.4 Typical Experimental Procedure for Pd-catalyzed coupling reaction of $Ph_2P(ONa)$ with p-MeC_6H_4Cl generating diphenyl(p-tolyl)phosphine oxide 2-2a

Under argon atmosphere, to a stirring solution of triphenylphosphine oxide (0.2 mmol, 1 equiv, 55.6 mg) in 1,4-dioxane (1.0 mL) was added SD (0.5 mmol, 2.5 equiv, 50.0 μL) *via* a syringe. The mixture was then stirred at 25 °C for 10 min. After removal of the excessive Na by filtration, $Pd(Ph_3P)Cl_2$ (5 mol %, 7.0 mg) and *p*-MeC_6H_4Cl (0.2 mmol, 1.0 equiv, 24.0 μL) was sequentially added, and further stirring the mixture at 100 °C for 24 h. After that, the resulting mixture was filtered and concentrated under vacuum. Next, the obtained residue was directly eluted with hexane via a silica gel column and then eluted with MeOH to give the crude product, which was then diluted in $CHCl_3$ and purified by GPC to afford pure product **2-2a** (49.7mg, 0.17 mmol, 85 % yield).

3.4.5 Comparison Experimental Procedure for the Treatments of $Ph_3P(O)$ with Alkali Metals (Na, Li, K, Mg)

Under argon atmosphere, to a solution of $Ph_3P(O)$ (1.0 mmol, 278.0 mg) in THF (5 mL) was added alkali (Li, Na, K) or alkaline-earth (Mg) metal (2.5 mmol) cut into tiny pieces, after stirring the mixture at room temperature for 24 h, excessive *n*-BuBr was added, and then the resulting mixture was analyzed by ^{31}P NMR, GC, and GCMS.

3.4.6 Synthesis of Compound 5 by Literature Method.[28]

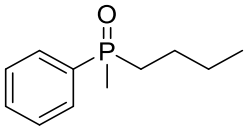
Under argon atmosphere, *s*-BuLi (2.0 mmol, 1.04 mol/L solution in hexane, 2.0 mL) was added in dropwise to the stirred solution of $Ph_2P(O)$*n*-Bu (1.0 mmol, 258.0 mg) in THF (4.0 mL) at -78 °C, after stirring for 30

min, the reaction mixture was warmed to 0 ºC, *n*-BuBr (2.0 mmol, 215 μL) was added and stirring the mixture for another 30 min. After that, the mixture was quenched by saturated NH_4Cl aqueous solution (5 mL) at 0 ºC and extracted with CH_2Cl_2 (5 mL × 3), then the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was diluted in $CHCl_3$ and purified by GPC to afford pure product **5** (238 mg, 0.76 mmol, 76% yield).

3.4.7 Synthesis of Compound 10

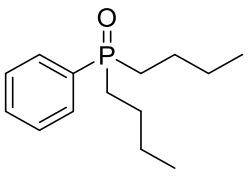
Under argon atmosphere, to a stirring solution of $Ph_3P(O)$ (1.0 mmol, 1 equiv.) in THF (5.0 mL) was added SD (3.0 mmol, 3 equiv., 0.3 mL) *via* a syringe. After stirring the mixture at room temperature for 0.5 h, saturated NH_4Cl aqueous solution (5.0 mL) was added and then extracted with EtOAc (5 mL ×3), the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was eluted with hexane via a silica gel column and then eluted with MeOH to give the crude product, which was then diluted in $CHCl_3$ and purified by GPC to afford pure product **10** (196 mg, 0.80 mmol, 80 % yield).

3.4.8 ^{1}H and ^{13}C NMR and ^{31}P NMR Spectral Data of the Products



1a-1

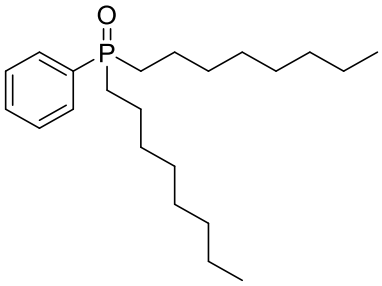
Butyl(methyl)(phenyl)phosphine oxide **(1a-1)**. White solid: 52.3 mg, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.65 (m, 2H), 7.49–7.42 (m, 3H), 2.01–1.80 (m, 2H), 1.67 (d, 3H, J = 12.4 Hz), 1.59–1.48 (m, 1H), 1.46–1.39 (m, 1H), 1.38–1.29 (m, 2H), 0.83 (t, 3H, J = 7.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 133.6 (d, $J_{p\text{-}c}$ = 95.3 Hz), 131.7 (d, $J_{p\text{-}c}$ = 2.1 Hz), 130.1 (d, $J_{p\text{-}c}$ = 9.0 Hz), 128.7 (d, $J_{p\text{-}c}$ = 11.3 Hz), 31.5 (d, $J_{p\text{-}c}$ = 70.1 Hz), 24.0 (d, $J_{p\text{-}c}$ = 15.1 Hz), 23.72 (d, $J_{p\text{-}c}$ = 4.0 Hz), 16.0 (d, $J_{p\text{-}c}$ = 69.4 Hz), 13.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 39.0. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{11}H_{17}OP$ 196, Found 196. This compound is known.[8]



1b-1

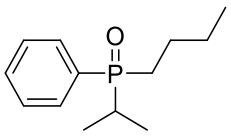
Dibutyl(phenyl)phosphine oxide **(1b-1).** White solid: 65.7 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ

7.59–7.64 (m, 2H), 7.49–7.43 (m, 3H), 2.00–1.77 (m, 4H), 1.64–1.53 (m, 2H), 1.44–1.28 (m, 6H), 0.84 (t, 6H, J = 7.2 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.6 (d, $J_{p\text{-}c}$ = 91.4 Hz), 131.5 (d, $J_{p\text{-}c}$ = 2.4 Hz), 130.5 (d, $J_{p\text{-}c}$ = 8.6 Hz), 128.7 (d, $J_{p\text{-}c}$ = 11.1 Hz), 29.7 (d, $J_{p\text{-}c}$ = 68.1 Hz), 24.2 (d, $J_{p\text{-}c}$ = 14.4 Hz), 23.6 (d, $J_{p\text{-}c}$ = 4.2 Hz), 13.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 41.6. MS (ESI) m/z: ([M]$^+$) Calcd. for $C_{14}H_{23}OP$ 238, Found 238. This compound is known.[29a]



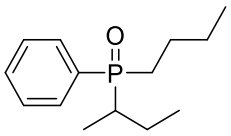
1c-1

Dioctyl(phenyl)phosphine oxide **(1c-1).** White solid: 100.8 mg, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.62 (m, 2H), 7.49–7.41 (m, 3H), 1.97–1.76 (m, 5H), 1.63–1.50 (m, 2H), 1.44–1.17 (m, 21H), 0.83–0.79 (m, 6H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.5 (d, $J_{p\text{-}c}$ = 91.9 Hz), 131.5 (d, $J_{p\text{-}c}$ = 1.8 Hz), 130.5 (d, $J_{p\text{-}c}$ = 8.7 Hz), 128.6 (d, $J_{p\text{-}c}$ = 11.2 Hz), 31.8, 31.1, 30.9, 29.9 (d, $J_{p\text{-}c}$ = 67.9 Hz), 29.1, 22.6, 21.5 (d, $J_{p\text{-}c}$ = 3.8 Hz), 14.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ 42.0. MS (ESI) m/z: ([M]$^+$) Calcd. for $C_{22}H_{39}OP$ 350, found 350. This compound is known.[29b, 29c]



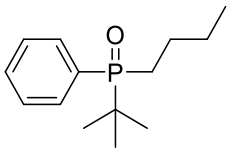
1d-1

Butyl(isopropyl)(phenyl)phosphine oxide **(1d-1).** Colorless oil: 61.8 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.61 (m, 2H), 7.48–7.40 (m, 3H), 2.05–1.95 (m, 2H), 1.83–1.80 (m, 1H), 1.61–1.54 (m, 1H), 1.37–1.25 (m, 3H), 1.16 (dd, 3H, J_1 = 15.6 Hz, J_2 = 6.8 Hz), 0.88 (dd, 3H, J_1 = 16.0 Hz, J_2 = 7.2 Hz), 0.81 (t, 3H, J = 7.2 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 131.9, 131.4 (d, $J_{p\text{-}c}$ = 2.3 Hz), 131.0 (d, $J_{p\text{-}c}$ = 8.2 Hz), 128.5 (d, $J_{p\text{-}c}$ = 10.7 Hz), 28.6 (d, $J_{p\text{-}c}$ = 68.9 Hz), 26.4 (d, $J_{p\text{-}c}$ = 66.1 Hz), 24.2 (d, $J_{p\text{-}c}$ = 13.7 Hz), 23.5 (d, $J_{p\text{-}c}$ = 4.2 Hz), 15.8 (d, $J_{p\text{-}c}$ = 1.1 Hz), 15.2 (d, $J_{p\text{-}c}$ = 2.4 Hz), 13.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 46.4. HRMS (ESI-TOF): m/z: ([M+Na]$^+$) Calcd. for $C_{13}H_{21}OPNa$ 247.1228, Found 247.1224.



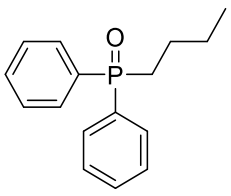
1e-1

Sec-butyl(butyl)(phenyl)phosphine oxide **(1e-1).** White solid: 70.6 mg, 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.59 (m, 2H), 7.44–7.39 (m, 3H), 2.04–1.89 (m, 1H), 1.82–1.72 (m, 2H), 1.55–1.54 (brs, 1H), 1.37–1.18 (m, 4H), 1.13 (dd, 2H, J_1 = 16.0 Hz, J_2 = 7.2 Hz), 0.98–0.70 (m, 8H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 131.3, 131.0 (d, $J_{p\text{-}c}$ = 5.3 Hz), 130.9 (d, $J_{p\text{-}c}$ = 5.6 Hz), 128.5 (dd, J_1 = 10.5 Hz, J_2 = 2.5 Hz), 35.5 (dd, J_1 = 68.2 Hz, J_2 = 10.1 Hz), 26.6 (d, $J_{p\text{-}c}$ = 65.6 Hz), 24.2 (d, $J_{p\text{-}c}$ = 13.8 Hz), 23.4, 22.3 (d, $J_{p\text{-}c}$ = 52.0 Hz), 13.6, 8.4 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz), 11.8 (d, $J_{p\text{-}c}$ = 52.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 46.0. MS (ESI) m/z: ([M]$^+$) Calcd. for $C_{14}H_{23}OP$ 238, found 238. This compound is known.[29d]



1f-1

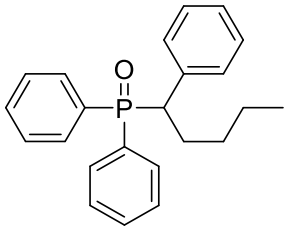
Tert-butyl(butyl)(phenyl)phosphine oxide **(1f-1).** White solid: 64.3 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.60 (m, 2H), 7.48–7.40 (m, 3H), 2.00–1.90 (m, 2H), 1.67–1.54 (m, 1H), 1.42–1.21 (m, 3H), 1.07 (d, 9H, J = 14.0 Hz), 0.82 (t, 3H, J = 7.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 131.9 (d, $J_{p\text{-}c}$ = 7.7 Hz), 131.4 (d, $J_{p\text{-}c}$ = 2.5 Hz), 130.9 (d, $J_{p\text{-}c}$ = 9.3 Hz), 130.2 (d, $J_{p\text{-}c}$ = 85.6 Hz), 128.7 (d, $J_{p\text{-}c}$ = 11.4 Hz), 128.3 (d, $J_{p\text{-}c}$ = 10.4 Hz), 32.7 (d, $J_{p\text{-}c}$ = 68.1 Hz), 24.6brs, 24. (d, $J_{p\text{-}c}$ = 13.9Hz), 23.6 (d, $J_{p\text{-}c}$ = 4.2 Hz), 22.7 (d, $J_{p\text{-}c}$ = 64.4 Hz), 13.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 50.3. MS (ESI) m/z: ([M]+) Calcd. for $C_{14}H_{23}OP$ 238, found 238. This compound is known.[8]



1g-1

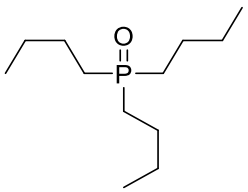
Diphenyl(butyl)phosphine oxide **(1g-1)**. White solid: 41.0 mg, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.69 (m, 4H), 7.48–7.42 (m, 6H), 2.27–2.20 (m, 2H), 1.63–1.53 (m, 2H), 1.44–1.35 (m, 2H), 0.86 (t, 3H,

J = 7.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 133.3 (d, $J_{p\text{-}c}$ = 96.9 Hz), 131.7 (d, $J_{p\text{-}c}$ = 2.1 Hz), 130.9 (d, $J_{p\text{-}c}$ = 9.2 Hz), 128.7 (d, $J_{p\text{-}c}$ = 11.4 Hz), 29.6 (d, $J_{p\text{-}c}$ = 71.8 Hz), 24.2 (d, $J_{p\text{-}c}$ = 15.1 Hz), 23.6 (d, $J_{p\text{-}c}$ = 3.7 Hz), 13.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.1. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{16}H_{19}OP$ 258, Found 258. This compound is known.[29e]



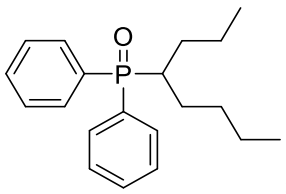
1g-3

Diphenyl(1-phenylpentyl)phosphine oxide **(1g-3)**. White solid: 44.9 mg, 43% yield. mp 205–208 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92–7.87 (m, 2H), 7.56–7.49 (m, 3H), 7.42–7.38 (m, 2H), 7.32–7.28 (m, 1H), 7.22–7.13 (m, 7H), 3.41–3.35 (m, 1H), 2.18–2.06 (m, 1H), 1.92–1.82 (m, 1H), 1.25–1.09 (m, 4H), 0.73 (t, 3H, J = 7.2 Hz). ^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 136.1 (d, $J_{p\text{-}c}$ = 5.2 Hz), 132.8 (d, $J_{p\text{-}c}$ = 27.0 Hz), 131.4 (d, $J_{p\text{-}c}$ = 8.3 Hz), 131.2 (d, $J_{p\text{-}c}$ = 1.9Hz), 131.1 (d, $J_{p\text{-}c}$ = 8.7 Hz), 129.9 (d, $J_{p\text{-}c}$ = 5.8 Hz), 128.7 (d, $J_{p\text{-}c}$ = 10.9 Hz), 128.0 (d, $J_{p\text{-}c}$ = 11.4 Hz), 126.9 (d, $J_{p\text{-}c}$ = 2.2 Hz), 47.0 (d, $J_{p\text{-}c}$ = 67.0 Hz), 30.0 (d, $J_{p\text{-}c}$ = 12.9 Hz), 28.8, 22.2, 13.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.5. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{23}H_{25}OPNa$ 371.1541, Found 371.1538.



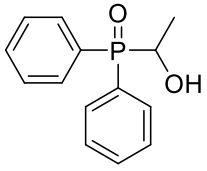
1h-1

Tributylphosphine oxide **(1h-1).** White solid: 56.9 mg, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.62–1.55 (m, 6H), 1.53–1.41 (m, 6H), 1.39–1.27 (m, 6H), 0.86–0.81 (m, 9H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 27.7 (d, $J_{p\text{-}c}$ = 64.7 Hz), 24.3 (d, $J_{p\text{-}c}$ = 14.1 Hz), 23.8 (d, $J_{p\text{-}c}$ = 3.3 Hz), 13.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 49.1. MS (ESI) m/z: ($[M]^+$) Calcd. for $C_{12}H_{27}OP$ 218, found 218. This compound is known.[8]



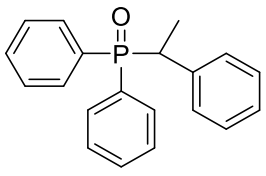
5

***Octan-4-yldiphenylphosphine oxide* (5).** Preparation by literature method.[28] White solid: 238 mg, 76% yield). mp 151–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81–7.76 (m, 4H), 7.48–7.42 (m, 6H), 2.25–2.16 (m, 1H), 1.73–1.59 (m, 2H), 1.56–1.39 (m, 4H), 1.25–1.13 (m, 4H), 0.80–0.75 (m, 6H); ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 133.2 (dd, J_1 = 93.6 Hz, J_2 = 2.9 Hz), 131.4 (d, $J_{p\text{-}c}$ = 2.4 Hz), 131.0 (dd, J_1 = 8.5 Hz, J_2 = 1.1 Hz), 128.6 (d, $J_{p\text{-}c}$ = 11.1 Hz), 37.1 (d, $J_{p\text{-}c}$ = 70.3 Hz), 30.3 (d, $J_{p\text{-}c}$ = 9.2 Hz), 29.9, 27.3, 22.8, 21.3 (d, $J_{p\text{-}c}$ = 9.4 Hz), 14.3, 13.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ 37.3. HRMS (ESI-TOF): m/z: ([M+Na]$^+$) Calcd. for $C_{20}H_{27}OPNa$ 337.1697, Found 337.1698.



10

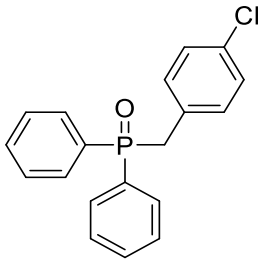
***(1-Hydroxyethyl)diphenylphosphine oxide* (10)**. White solid: 196.7 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.83 (m, 2H), 7.78–7.73 (m, 2H), 7.50–7.38 (m, 6H), 4.88 (brs, 1H), 4.57–4.52 (m, 1H), 1.39 (dd, 3H, J_1 = 15.6 Hz, J_2 = 7.2 Hz). ^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 132.5 (d, $J_{p\text{-}c}$ = 8.0 Hz), 132.1 (d, $J_{p\text{-}c}$ = 8.9 Hz), 132.0 (d, $J_{p\text{-}c}$ = 3.6 Hz), 131.6 (d, $J_{p\text{-}c}$ = 8.9 Hz), 130.7 (d, $J_{p\text{-}c}$ = 8.2 Hz), 129.8, 128.6 (d, $J_{p\text{-}c}$ = 10.6 Hz), 128.5 (d, $J_{p\text{-}c}$ = 10.7 Hz), 66.7 (d, $J_{p\text{-}c}$ = 84.0 Hz), 17.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.6. This compound is known.[8]



2-1b

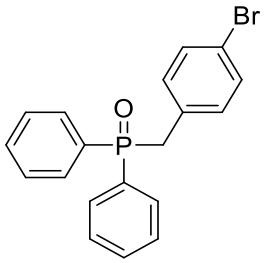
***Benzyldiphenylphosphine oxide* (2-1b)**. White solid: 55.5 mg, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.65 (m, 4H), 7.50–7.39 (m, 6H), 7.16–7.08 (m, 5H), 3.64 (d, 2H, J = 13.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.4 (d, $J_{p\text{-}c}$ = 98.5 Hz), 131.9 (d, $J_{p\text{-}c}$ = 2.3 Hz), 131.3 (d, $J_{p\text{-}c}$ = 9.2 Hz), 130.2 (d, $J_{p\text{-}c}$ = 5.4

Hz), 128.6, 128.5, 128.45 (d, $J_{p\text{-}c}$ = 1.9 Hz), 126.8 (d, $J_{p\text{-}c}$ = 1.7 Hz), 38.2 (d, $J_{p\text{-}c}$ = 66.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.0. This compound is known.[30a]



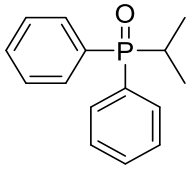
2-1c

(4-Chlorobenzyl)diphenylphosphine oxide **(2-1c)**. White solid: 64.6 mg, 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.65 (m, 4H), 7.53–7.48 (m, 2H), 7.45–7.41 (m, 4H), 7.14 (d, 2H, J = 8.4 Hz), 7.04–7.01 (m, 2H), 3.59 (d, 2H, J = 13.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.9 (d, $J_{p\text{-}c}$ = 3.2 Hz), 132.1 (d, $J_{p\text{-}c}$ = 98.8 Hz), 132.0 (d, $J_{p\text{-}c}$ = 2.3 Hz), 131.5 (d, $J_{p\text{-}c}$ = 5.2 Hz), 131.2 (d, $J_{p\text{-}c}$ = 9.3Hz), 129.8 (d, $J_{p\text{-}c}$ = 8.2 Hz), 128.7, 128.6, 37.6 (d, $J_{p\text{-}c}$ = 65.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7. This compound is known.[30b]



2-1d

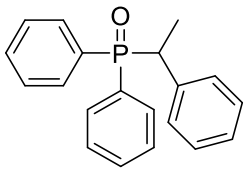
(4-Bromobenzyl)diphenylphosphine oxide **(2-1d)**. White solid: 67.3 mg, 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.65 (m, 4H), 7.53–7.49 (m, 2H), 7.46–7.41 (m, 4H), 7.29 (d, 2H, J = 8.4 Hz), 6.98–6.96 (m, 2H). 3.58 (d, 2H, J = 13.6 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.1 (d, $J_{p\text{-}c}$ = 100.7 Hz), 132.0 (d, $J_{p\text{-}c}$ = 2.3 Hz), 131.8 (d, $J_{p\text{-}c}$ = 5.3 Hz), 131.6 (d, $J_{p\text{-}c}$ = 2.0 Hz), 131.2 (d, $J_{p\text{-}c}$ = 9.0 Hz), 130.3 (d, $J_{p\text{-}c}$ = 8.0 Hz), 128.7, 128.6, 37.6 (d, $J_{p\text{-}c}$ = 65.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.6. This compound is known.[30c]



2-1e

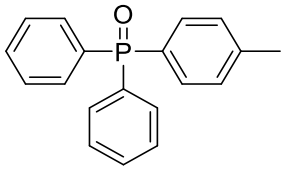
Isopropyldiphenylphosphine oxide **(2-1e)**. White solid: 29.3 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ

7.80–7.75 (m, 4H), 7.50–7.43 (m, 6H), 2.56–2.47 (m, 1H), 1.17 (dd, 6H, J_1 = 16.4 Hz, J_2 = 7.2 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 132.4 (d, $J_{p\text{-}c}$ = 94.1 Hz), 131.6 (d, $J_{p\text{-}c}$ = 2.0 Hz), 131.1 (d, $J_{p\text{-}c}$ = 8.5 Hz), 128.6 (d, $J_{p\text{-}c}$ = 11.0 Hz), 27.2 (d, $J_{p\text{-}c}$ = 72.4 Hz), 15.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 37.6. This compound is known.[10]



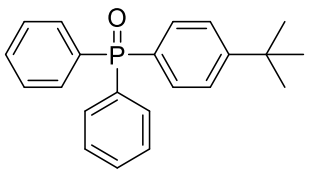
2-1f

Diphenyl(1-phenylethyl)phosphine oxide **(2-1f)**. White solid: 50.2 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.86 (m, 2H), 7.54–7.46 (m, 3H), 7.44–7.41 (m, 2H), 7.35–7.31 (m, 1H), 7.26–7.12 (m, 7H), 3.63–3.55 (m, 1H), 1.57 (dd, 3H, J_1 = 16.0 Hz, J_2 = 7.2 Hz). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 138.0 (d, $J_{p\text{-}c}$ = 5.3 Hz), 132.5 (d, J = 13.7 Hz), 131.8 (d, $J_{p\text{-}c}$ = 2.1 Hz), 131.6 (d, $J_{p\text{-}c}$ = 9.9 Hz), 131.5 (d, $J_{p\text{-}c}$ = 8.4 Hz), 131.4 (d, $J_{p\text{-}c}$ = 2.5 Hz), 131.2 (d, $J_{p\text{-}c}$ = 8.8 Hz), 129.3 (d, $J_{p\text{-}c}$ = 5.5 Hz), 128.7 (d, $J_{p\text{-}c}$ = 11.1 Hz), 128.3 (d, $J_{p\text{-}c}$ = 1.3 Hz), 128.1 (d, $J_{p\text{-}c}$ = 11.4 Hz),127.0 (d, $J_{p\text{-}c}$ = 1.8 Hz), 41.0 (d, $J_{p\text{-}c}$ = 66.8 Hz), 15.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 34.1. This compound is known.[30a]



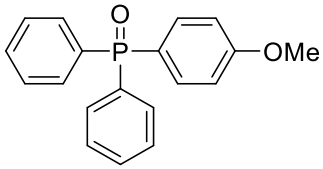
2-2a

Diphenyl(p-tolyl)phosphine oxide **(2-2a)**. White solid: 49.7 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.61 (m, 4H), 7.55–7.48 (m, 4H), 7.44–7.39 (m, 4H), 7.25–7.22 (m, 2H), 2.37 (s, 3H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 142.6 (d, $J_{p\text{-}c}$ = 2.6 Hz), 132.8 (d, $J_{p\text{-}c}$ = 103.7 Hz), 132.2 (d, $J_{p\text{-}c}$ = 9.7 Hz), 132.1 (d, $J_{p\text{-}c}$ = 9.7 Hz), 132.0 (d, $J_{p\text{-}c}$ = 2.4 Hz), 129.6, 129.4 (d, $J_{p\text{-}c}$ = 12.5 Hz), 128.5 (d, $J_{p\text{-}c}$ = 11.9 Hz), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.1. This compound is known.[31a]



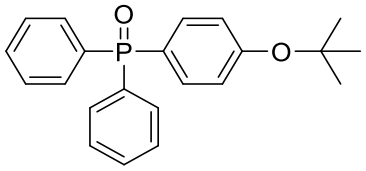
2-2b

(4-(Tert-butyl)phenyl)diphenylphosphine oxide **(2-2b)**. White solid: 52.8 mg, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.64 (m, 4H), 7.60–7.52 (m, 4H), 7.48–7.42 (m, 6H), 1.31 (s, 9H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 155.5 (d, $J_{p\text{-}c}$ = 2.8 Hz), 132.9 (d, $J_{p\text{-}c}$ = 103.6 Hz), 132.2 (d, $J_{p\text{-}c}$ = 10.0 Hz), 132.1 (d, $J_{p\text{-}c}$ = 10.8 Hz), 131.9 (d, $J_{p\text{-}c}$ = 2.1 Hz), 129.2 (d, $J_{p\text{-}c}$ = 105.9 Hz), 128.5 (d, $J_{p\text{-}c}$ = 12.0 Hz), 125.6 (d, $J_{p\text{-}c}$ = 12.1 Hz), 35.1, 31.2. ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.6. This compound is known.[31b]



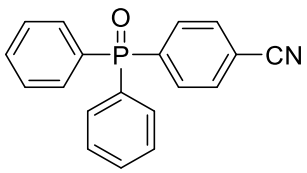
2-2c

(4-Methoxyphenyl)diphenylphosphine oxide **(2-2c)**. White solid: 46.8 mg, 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.60 (m, 4H), 7.58–7.52 (m, 2H), 7.51–7.46 (m, 2H), 7.43–7.38 (m, 4H), 6.94–6.91 (m, 2H), 3.79 (s, 3H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 162.6 (d, $J_{p\text{-}c}$ = 2.6 Hz), 134.0 (d, $J_{p\text{-}c}$ = 11.3 Hz), 133.0 (d, $J_{p\text{-}c}$ = 103.9 Hz), 132.1 (d, $J_{p\text{-}c}$ = 9.7 Hz), 131.9 (d, $J_{p\text{-}c}$ = 2.1 Hz), 128.5 (d, $J_{p\text{-}c}$ = 12.2 Hz), 123.6 (d, $J_{p\text{-}c}$ = 109.8 Hz), 114.2 (d, $J_{p\text{-}c}$ = 13.1 Hz), 55.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7. This compound is known.[31a]



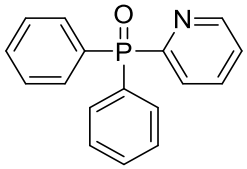
2-2d

(4-(Tert-butoxy)phenyl)diphenylphosphine oxide **(2-2d)**. White solid: 57.4 mg, 82% yield. mp 135–141 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.63 (m, 4H), 7.55–7.50 (m, 4H), 7.46–7.42 (m, 4H), 7.05–7.02 (m, 2H), 1.38 (s, 9H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 159.3 (d, $J_{p\text{-}c}$ = 2.6 Hz), 133.4 (d, $J_{p\text{-}c}$ = 10.8 Hz), 132.3 (d, $J_{p\text{-}c}$ = 20.4 Hz), 132.2 (d, $J_{p\text{-}c}$ = 9.7 Hz), 131.9 (d, $J_{p\text{-}c}$ = 2.3 Hz), 128.5 (d, $J_{p\text{-}c}$ = 12.1 Hz), 125.9 (d, $J_{p\text{-}c}$ = 108.0 Hz), 122.9 (d, $J_{p\text{-}c}$ = 13.0 Hz), 79.6, 29.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.8. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{22}H_{23}NaO_2P$ 373.1333, Found 373.1335.



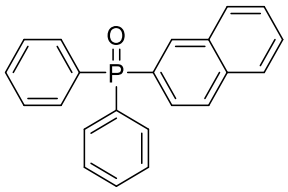
2-2e

4-(diphenylphosphoryl)benzonitrile **(2-2e)**. White solid: 29.1 mg, 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80–7.71 (m, 4H), 7.65–7.54 (m, 6H), 7.49–7.45 (m, 4H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 138.6 (d, J_{p-c} = 98.5 Hz), 132.7 (d, J_{p-c} = 10.9 Hz), 132.6 (d, J_{p-c} = 3.1 Hz), 132.1 (d, J_{p-c} = 10.5 Hz), 131.3 (d, J_{p-c} = 104.9 Hz), 128.9 (d, J_{p-c} = 12.3 Hz), 128.6 (d, J_{p-c} = 12.1 Hz), 117.9, 115.7 (d, J_{p-c} = 3.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.3. This compound is known.[31c]



2-2f

Diphenyl(pyridin-2-yl)phosphine oxide **(2-2f)**. White solid: 25.2 mg, 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, 1H, J = 4.8 Hz), 8.29 (t, 1H, J = 4.8 Hz), 7.90–7.80 (m, 5H), 7.52–7.47 (m, 2H), 7.45–7.41 (m, 4H), 7.38–7.35 (m, 1H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 156.5 (d, J_{p-c} = 131.2 Hz), 150.2 (d, J_{p-c} = 19.1 Hz), 136.3 (d, J_{p-c} = 9.1 Hz), 132.3 (d, J_{p-c} = 103.7 Hz), 132.0 (d, J_{p-c} = 2.4 Hz), 131.2 (d, J_{p-c} = 9.4 Hz), 128.6 (d, J_{p-c} = 9.3 Hz), 128.4 (d, J_{p-c} = 12.2 Hz), 125.3 (d, J_{p-c} = 2.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 21.4. This compound is known.[31d]



2-2g

Naphthalen-2-yldiphenylphosphine oxide **(2-2g)**. White solid: 59.0 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, 1H, J = 14.0 Hz), 7.89–7.83 (m, 3H), 7.72–7.68 (m, 4H), 7.65–7.60 (m, 1H), 7.56–7.49 (m, 4H), 7.46–7.42 (m, 4H). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 134.8 (d, J_{p-c} = 1.6 Hz), 134.1 (d, J_{p-c} = 9.3 Hz), 132.6 (d, J_{p-c} = 103.8 Hz), 132.5 (d, J_{p-c} = 13.0 Hz), 132.2 (d, J_{p-c} = 9.8 Hz), 132.1 (d, J_{p-c} = 2.2 Hz), 129.7 (d, J_{p-c} = 103.7 Hz), 129.1, 128.7 (d, J_{p-c} = 12.0 Hz),128.5, 128.4, 127.9, 127.1, 126.9 (d, J_{p-c} = 10.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.9. This compound is known.[31a]

3.5 References

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[22] It should be noted that the product PhBnP(O)*n*-Bu **1g-2** *via P-Ph bond's cleavage* was not detected under the current conditions (1,4-dioxane, 100 °C). And $Ph_2P(O)CH(Ph)$*n*-Bu **1g-3** *via benzylic C-H bond's cleavage* by BnNa was also isolated in 43% yield.

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Chapter 4 Reductive Conversion of Phosphoryl P(O) Compounds to Trivalent Organophosphines R_3P

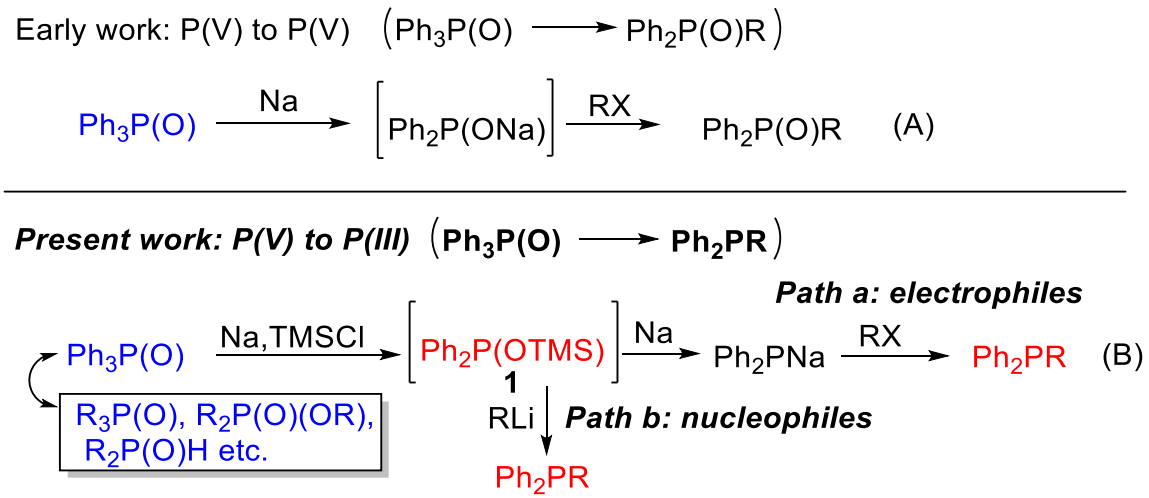
Abstract

By introducing trimethylsilyl chloride (TMSCl), the pentavalent phosphoryl P(V) compounds such as triphenylphosphine oxides, secondary phosphine oxides etc., were readily converted to the corresponding R2P(OTMS) intermediates, that can further react efficiently with an electrophile R'X or with a nucleophile R'Li to produce the corresponding trivalent phosphines R_2PR'. Chiral phosphines could also be obtained stereospecifically by this strategy.

4.1 Introduction

Triphenylphosphine oxide $Ph_3P(O)$ is a well-known chemical waste generated from the Wittig reactions etc. that are widely used in organic synthesis and industry for the preparation of highly valuable compounds such as Vitamin A.[1] Tens of thousands tons of $Ph_3P(O)$ are generated every year, and a large portion of them have to be discarded as useless chemical waste because of the limited utilities.[2] This situation has been a big concern for more than half a century. To solve this problem, extensive studies on $Ph_3P(O)$ are carried out world widely.[3]

Scheme 4.1 Conversion of $Ph_3P(O)$ to $Ph_2P(O)R$ and Ph_2PR. (A): P(V) to P(V); (B): P(V) to P(III).



I have recently reported that, sodium is superior to lithium and potassium, that can efficiently convert $Ph_3P(O)$ and related organophosphorus compounds easily and efficiently, by cleaving a Ph-P bond, to other phosphoryl P(O) compounds $Ph_2P(O)R$ etc. (R = H, alkyl and aryl groups), providing a new general and

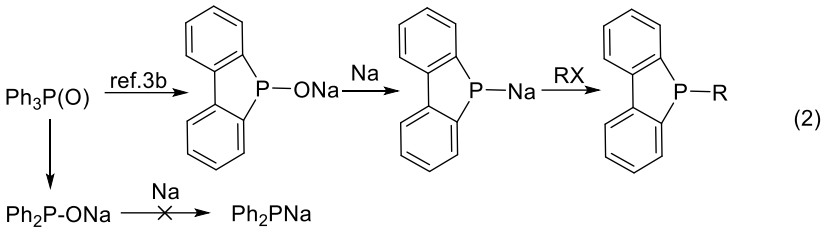
economic way for transforming P(V) compounds to other P(V) compounds (Scheme 4.1A).[3b,4] During these investigations, I also noted that, occasionally, a small amount of trivalent phosphine Ph_2PR could be also observed as a side product. This phenomenon greatly attracted our attention because it unusually indicates that, *from this disposed waste $Ph_3P(O)$, I can not only produce the pentavalent phosphoryl compounds $Ph_2P(O)R$, but may also produce the more valuable trivalent phosphine Ph_2PR* that possesses a central position in organic synthesis and organometallic chemistry.[5] Of course, in the laboratory, Ph_2R may be produced from Ph_2PCl and RM (M = Li, MgX) (eq 1). However, chlorophosphines are expensive and difficult to handle. Beyond the economic advantage, this shows a new way for converting $R_3P(O)$ compounds to trivalent phosphines R_3P, as the known conventional methods predominantly use a hydride reducing reagent such as $LiAlH_4$ etc. in order to remove the oxygen on P(O) (eq 1).[3,6]

$$Ph_2PCl \xrightarrow[M = Li, MgX]{RM} Ph_2PR \xleftarrow{LiAlH_4,\ HSiR_3\ etc.} Ph_2P(O)R \quad (1)$$

Herein, I communicate that by introducing TMSCl to the $Ph_3P(O)$/Na reaction system, diphenyl(trimethylsiloxy)phosphine $Ph_2P(OTMS)$ can be generated that react efficiently further with an electrophile (path a) or with a nucleophile (path b) to produce the desired Ph_2PR (Scheme 4.1B). The reaction can be carried out one-pot by sequentially adding the required chemicals starting from $Ph_3P(O)$, thus providing a convenient way for directly converting $Ph_3P(O)$ to Ph_2PR. This strategy can be applied to a variety of phosphoryl compounds, showing this is a general way for reductively converting a pentavalent P(V) phosphoryl compound to the corresponding trivalent P(III) organophosphines R_3P. It was noted that, to the best of our knowledge, the present strategies are surprisingly totally unprecedented to date.[7]

4.2 Results and discussion

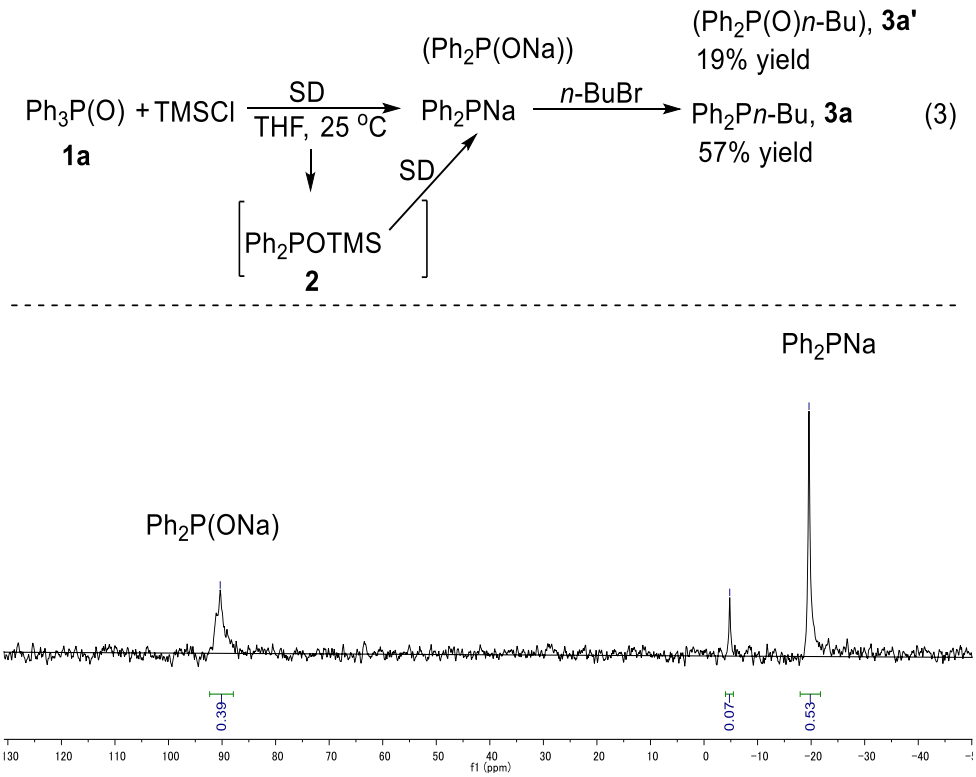
I have found that the trivalent dibenzophospholes can be generated by a mild reduction with sodium via sequential reactions starting from $Ph_3P(O)$ (eq 2).[3b] Therefore, I initially thought that Ph_2PONa might also be similarly reduced to Ph_2PNa by sodium (SD: sodium dispersed in paraffin with μm-scale particles). However, disappointedly, contrary to our expectation, I found that Ph_2PONa could hardly be reduced to Ph_2PNa even under heating at an elevated temperature for a long time in the presence of a large excess amount of SD, the reason was present in scheme 3.4 in chapter 3.



(2)

Since Na alone is not able to reduce Ph_2PONa to Ph_2PNa, I then added an additive to the reaction system that might act as an "activator" to "activate" Ph_2PONa so that it could be reduced to Ph_2PNa. Many such "activators" were then tested, and finally I noted that when TMSCl was introduced to the reaction system, the corresponding Ph_2Pn-Bu was detected (eq 3). Thus, to a mixture of $Ph_3P(O)$ (0.25 mmol) and TMSCl (0.50 mmol) in THF (2 mL) was added SD (0.50 mmol) at room temperature. The color of the solution gradually changed from grey to black and then orange, after stirring the mixture for 4 h. The precipitates were removed by centrifugation and ^{31}P NMR spectroscopy showed that Ph_2PNa (d_p = -19.6 ppm) was generated (Scheme 4.2).

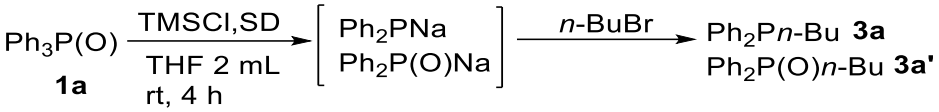
Scheme 4.2 Reduction of $Ph_3P(O)$ to Ph_2PNa



Then *n*-BuBr (0.5 mmol) was added to the transparent solution and Ph_2Pn-Bu (d_p = -15.8 ppm) was obtained in 57% yield based on $Ph_3P(O)$ used as estimated by ^{31}P NMR spectra. The product $Ph_2P(O)n$-Bu (d_p = 28.7

ppm) *via* $Ph_2P(ONa)$ (d_p = 90.3 ppm) was also generated in 19% yield. Then, efforts were devoted to improving the yield of Ph_2Pn-Bu (Table 4.1). However, only 72% yield of **3a** could be achieved (run 1).

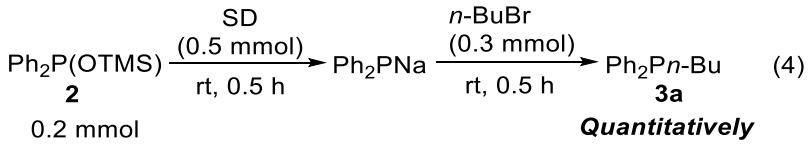
Table 4.1 Reaction conditions optimization[a]



run	SD	TMSCl	Yield of **3a**/**3a'**
1	4 equiv	2 equiv	72%/22%
2	6 equiv	2 equiv	62%/17%
3	8 equiv	2 equiv	69%/15%
4	4 equiv	1 equiv	33%/67%
5	4 equiv	3 equiv	42%/39%

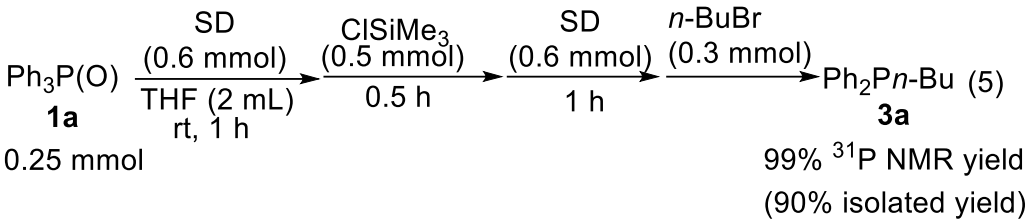
[a]Reaction condition: $Ph_3P(O)$ **1a**, (0.25 mmol), THF (2.0 mL), TMSCl (0.25-0.75 mmol), SD (1.0-2.0 mmol), rt, 4 h. After filtration, *n*-BuBr (0.5 mmol), rt, 0.5 h. Yields refer to ^{31}P NMR yields based on **1a** used.

Carefully analyzing the reaction paths for the formation of Ph_2PNa in eq 3, I realized that Ph_2POTMS perhaps was the reactive intermediate because $Ph_2P(ONa)$ generated from $Ph_3P(O)$ with sodium could be readily trapped by TMSCl. This speculation was correct as confirmed by a separate experiment by employing the isolated $Ph_2P(OTMS)$, and Ph_2Pn-Bu could be obtained in a quantitative yield (eq 4).



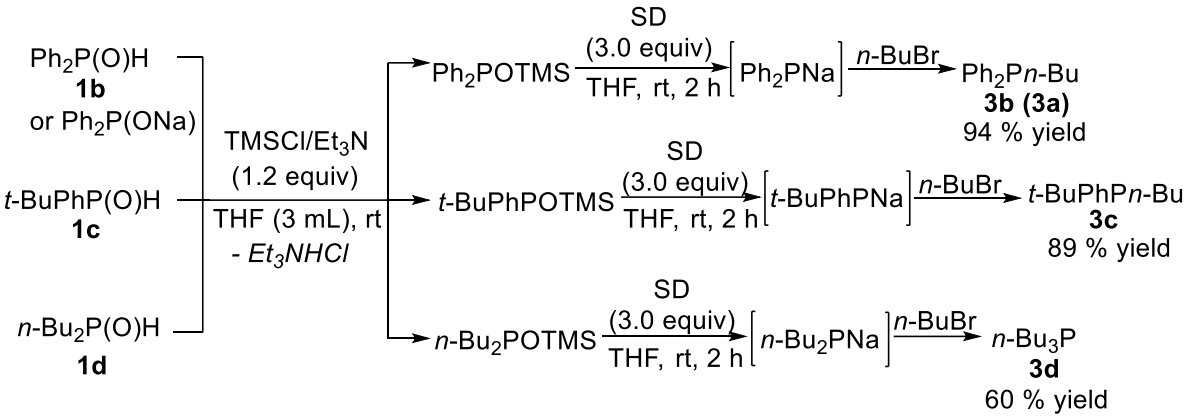
(4)

Having verified that $Ph_2P(OTMS)$ was the real active intermediate for the conversion of $Ph_3P(O)$ to Ph_2Pn-Bu, I can conduct a one-pot reaction starting from $Ph_3P(O)$ more efficiently without isolating $Ph_2P(OTMS)$. Thus, as shown in eq 5, $Ph_3P(O)$ reacted with sodium to generate $Ph_2P(ONa)$ first. To this mixture was then added TMSCl to in situ give $Ph_2P(OTMS)$. Sodium was then added to generate Ph_2PNa which was trapped by *n*-BuBr to give Ph_2Pn-Bu in 90% yield!



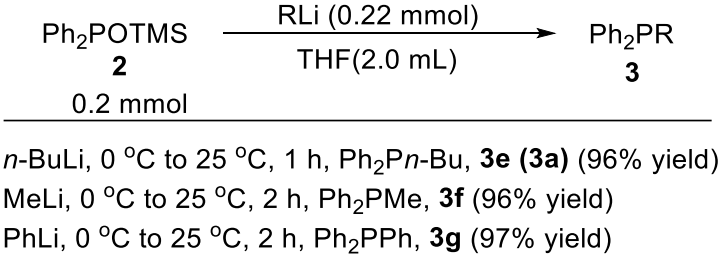
As could be readily expected, by using this strategy, other secondary phosphine oxides $R_2P(O)H$ could be also readily reductively converted to the corresponding trivalent phosphines (Scheme 4.3).

Scheme 4.3. Efficient P-OTMS bond cleavage of $R_2P(OTMS)$ by sodium generating R_2PNa.



A further study on the reactivity of $Ph_2P(OTMS)$ fantastically revealed that the OTMS unit can be replaced easily by RLi via a nucleophilic substitution reaction, remarkably demonstrating that $Ph_2P(OTMS)$ can act like "an ambiguous reagent" that both an electrophile and an nucleophile can be used for converting $Ph_2P(OTMS)$ to Ph_2PR (Scheme 1). For example, $Ph_2P(OTMS)$ in THF rapidly reacted with *n*-BuLi at 0 °C to produce Ph_2Pn-Bu in 96% yield (Scheme 4.4). In addition, MeLi and PhLi could also be used as efficient nucleophiles to react with $Ph_2P(OTMS)$, to give the substitution product Ph_2PMe and Ph_3P in 96% and 97% yield, respectively.

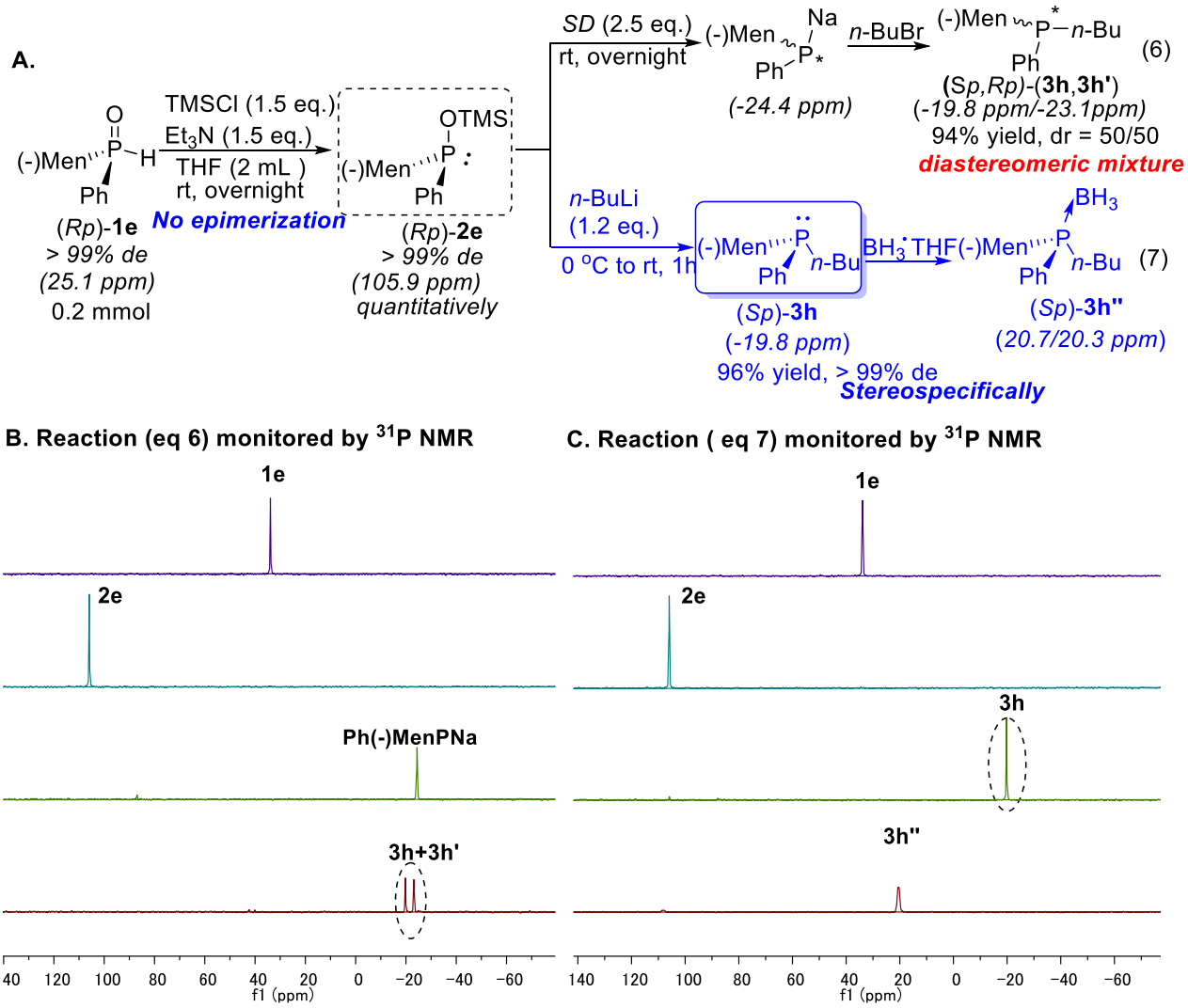
Scheme 4.4. Efficient substitution reactions of $Ph_2P(OTMS)$ with RLi generating Ph_2PR.



Very importantly, this substitution reaction can be used for the preparation of the highly valuable chiral phosphines that are quite difficult to prepare by other methods despite its high value. I have developed an

efficient way for the preparation of chiral-P(O) compounds.[9] As demonstrated in Scheme 4.5, I first confirmed that a chiral-P(O)H compound (*Rp*)-**1e** (s, δ_p = 25.1 ppm) can readily be changed to the corresponding POTMS (*Rp*)-**2e** (s, δ_p = 105.9 ppm) (B). No epimerization took place at all, and the stereochemistry retained at the phosphorus center. Treatment of the POTMS **2e** with 2.5 equivalents of SD at room temperature and subsequent quenching with *n*-BuBr resulted in the diastereomeric mixture of (*Sp*,*Rp*)-(-)MenPhP*n*-Bu (**3h**/**3h'**) (d, δ_p = -19.8/-23.1 ppm), albeit with high yield (eq 6). Secondly, and excitingly, the substitution with RLi took place stereospecifically. Thus, to the POTMS solution was dropwise added 1.2

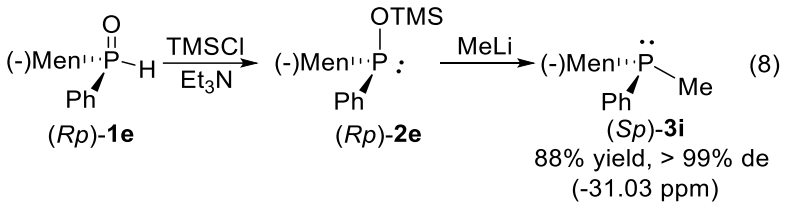
Scheme 4.5. Preparation of chiral-phosphines via the reaction of (*Rp*)-(-)MenPhP(O)H with SD or *n*-BuLi monitored by ^{31}P NMR.



equivalents of *n*-BuLi at 0 °C and stirring for 1 hour, only one signal appeared at -19.8 ppm as confirmed by ^{31}P NMR, indicating that (*Sp*)-(-)MenPhP*n*-Bu **3h** was generated stereospecifically in a high yield (eq 7).

Protection with BH_3·THF afforded the air-stable P-B compound **3h''** (d, δ_p = 20.5 ppm, $J_{B\text{-}P}$ = 64.8 Hz) that was characterized by ^1H and ^{13}C NMR. [10a]

Using the same strategy, MeLi could also efficiently react with (*Rp*)-**2e** with inversion of configurations at phosphorus to give the stereospecific product (*Sp*)(-)MenPhPMe in 88% yield (eq 8).[10b]



4.3 Conclusion

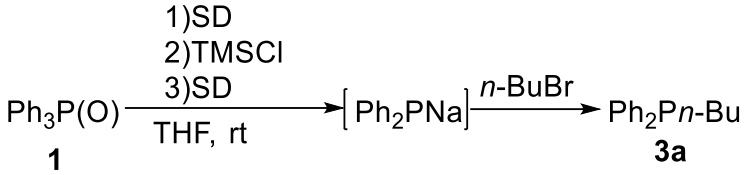
In summary, I have developed a TMSCl/SD reduction strategy for the conversion of pentavalent phosphoryl compounds to trivalent phosphines. This method completed our on-going studies on the utilization of $Ph_3P(O)$, showing that from $Ph_3P(O)$ not only $Ph_2P(O)R$ but also Ph_2PR could be produced via the key $Ph_2P(OTMS)$ intermediate. In addition, the highly valuable chiral-phosphines can also be easily generated stereospecifically from the corresponding phosphine oxide by using this new strategy.

4.4 Experimental Section

4.4.1 General Information

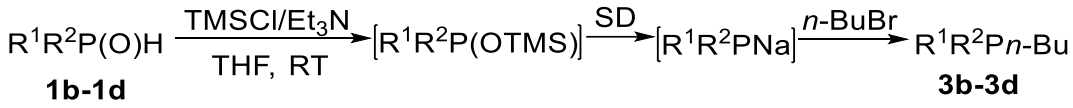
The reactions were carried out in oven-dried Schlenk tubes under an argon atmosphere. The sodium I used was dispersed in paraffin oil with an average particle size smaller than10 μm and a concentration of ~10.0mol/L. All the solvents and reagents were purified and dried by standard methods. Column chromatography was performed using Silica Gel 60 N (TCI, spherical, neutral). Purification of the oil products by a bulb to bulb distillation was conducted on SIBATA Glass Tube Oven, GTO-350RD. ^1H, ^{13}C, and ^{31}P NMR were recorded on a JEOL JNM-ECS400 (400 MHz for ^1H NMR, 100 MHz for ^{13}C NMR, and 162 MHz for ^{31}P NMR spectroscopy). Chemical shifts for ^1H NMR are referred to internal Me_4Si (0 ppm) and reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. Chemical shifts for ^{31}P NMR were relative to H_3PO_4 (85% solution in D_2O, 0 ppm).

4.4.2 Typical procedure for the synthesis of Ph_2Pn-Bu 3a from $Ph_3P(O)$.



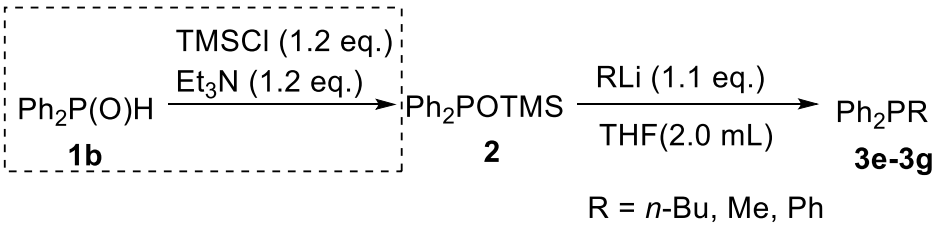
Under argon atmosphere, to a stirring solution of $Ph_3P(O)$ (0.25 mmol, 69.5 mg, 1 equiv) and THF (2.0 mL) was added SD (0.6 mmol, 60 μL, 2.4 equiv) via a syringe. The mixture was stirred at room temperature for 1 h, resulting in a deep brown solution. Then TMSCl (0.5 mmol, 63 μL, 2 equiv) was added and continued the reaction for 0.5 h. Next, SD (0.6 mmol, 60 μL, 2.4 equiv) was again added and stirring the mixture for another 1 h. After filtration of excessive Na by syringe filter, *n*-BuBr (0.3 mmol, 32 μL) was added and stirring the mixture for 0.5 h. The resulting mixture was filtered and concentrated under vacuum, then the crude residue was purified by a bulb to bulb distillation (100 °C, 60 Pa) to give Ph_2P*n*-Bu (54.5 mg, 0.225 mmol, 90% yield).

4.4.3 General procedure for the synthesis of phosphines 3b-3d from R2P(O)H.



Under argon atmosphere, to a stirring solution of $R^1R^2P(O)H$ (0.3 mmol) and THF (2.0 mL) was added TMSCl (0.4 mmol, 1.33 equiv, 51 μL) and Et_3N (0.4 mmol, 56 μL). And the mixture was stirred at room temperature overnight. After filtering the Et_3NHCl and evaporation of the excessive TMSCl, Et_3N and solvent, the residue was dissolved in THF (2.0 mL) and then SD (1.0 mmol, 100 μL, 3.3 equiv) was added via a syringe. Further stirring the mixture for 2 h, after removal of the excessive Na by filtration, *n*-BuBr (0.4 mmol, 1.33equiv, 56 μL) was added, and stirring the mixture for 1 h. After filtering NaBr and evaporation of solvent, distillation of the obtained residue afforded pure R^1R^2P*n*-Bu.

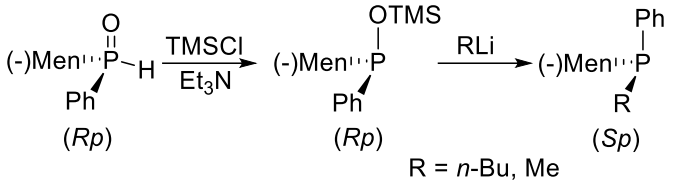
4.4.4 General procedure for the synthesis of phosphines 3e-3g from Ph2POTMS and RLi



Under argon atmosphere, to a stirring solution of Ph_2POTMS (0.2 mmol, 55 mg) (prepared from $Ph_2P(O)H$ with TMSCl/Et_3N) and THF (2.0 mL) was added RLi (0.22 mmol) solution in dropwise at 0 °C, and

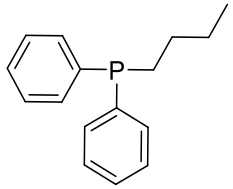
then the mixture was stirred for 2 h. After that, 2 mL of degassed H_2O was added, the resulting mixture was extracted with hexane (2 mL *3), and then the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum. For **3e** and **3f**, the obtained residue was distilled to afford pure Ph_2P*n*-Bu (46.5 mg, 96% yield) and Ph_2PMe (38.6 mg, 96% yield), respectively. For **3g**, the obtained residue was eluted with hexane via a silica gel column to give pure Ph_3P (50.8 mg, 97% yield).

4.4.5 Procedure for the synthesis of chiral phosphines (-)MenPhPn-Bu 3h and (-)MenPhPMe 3i



Under argon atmosphere, to a stirring solution of (*Rp*)-(-)MenPhP(O)H (0.2 mmol, 52.8 mg, 1 equiv) and THF (2 mL) was added TMSCl (0.3 mmol, 38 μL, 1.5 equiv) and Et_3N (0.3 mmol, 42 μL, 1.5 equiv) at room temperature, and then the mixture was stirred overnight. After filtering the Et_3NHCl and evaporation of the excessive TMSCl, Et_3N and solvent, the residue was dissolved in THF (2.0 mL), then RLi (1.2 equiv) was added in dropwise at 0°C and continued to stir the mixture for 1 h. After that, 2 mL of degassed H_2O was added, the resulting mixture was extracted with hexane (2 mL *3), and then the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum. For (*Sp*)-(-)MenPhP*n*-Bu **3h**, BH_3-THF solution was added to afford the P-B crude product, extraction with hexane and then recrystallization in hexane give pure **3h''** (61.0mg, 96% yield)**.** For (*Sp*)-(-)MenPhPMe **3i**, the obtained residue was distilled (120 °C, 60 Pa) to afford pure **3i** (46.2 mg, 88% yield).

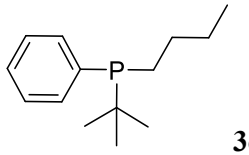
4.4.6 ^{1}H, ^{13}C and ^{31}P NMR Spectral Data of the Products



3a (3b, 3e)

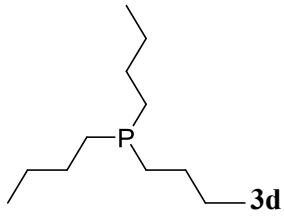
Diphenyl(*n*-butyl)phosphine (3a, 3b, 3e).[11] Preparation by Procedure 2.1 (**3a**, 54.5 mg, 90% yield), 2.2 (**3b**, 68.0 mg, 94% yield), 2.3 (**3e**, 46.3 mg, 96% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.44 (m, 4H), 7.37–7.34 (m, 6H), 2.10–2.06 (m, 2H), 1.50–1.43 (m, 4H), 0.93 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 139.2 (d, $J_{P\text{-}C}$ = 12.9 Hz), 132.8 (d, $J_{P\text{-}C}$ = 18.2 Hz), 128.53 (d, $J_{P\text{-}C}$ = 2.9 Hz), 128.45, 28.3 (d, $J_{P\text{-}C}$ = 15.6 Hz), 27.9 (d, $J_{P\text{-}C}$ = 11.1 Hz), 24.5 (d, $J_{P\text{-}C}$ = 13.2 Hz), 13.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ -15.4.



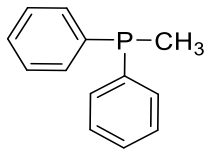
3c

Tert-butyl (*n*-butyl)phenylphosphine (3c). Preparation by Procedure 2.2 (59.2mg, 89% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.46 (m, 2H), 7.35–7.33 (m, 3H), 2.02–1.93 (m, 1H), 1.62–1.55 (m, 1H), 1.47–1.35 (m, 4H), 0.96 (d, 9H, J = 12.0 Hz), 0.88 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.5 (d, $J_{P\text{-}C}$ = 19.0 Hz), 134.3 (d, $J_{P\text{-}C}$ = 19.0 Hz), 128.84, 127.8 (d, $J_{P\text{-}C}$ = 7.0 Hz), 28.8 (d, $J_{P\text{-}C}$ = 16.6 Hz), 28.8 (d, $J_{P\text{-}C}$ = 11.7 Hz), 27.5 (d, $J_{P\text{-}C}$ = 13.0 Hz), 24.7 (d, $J_{P\text{-}C}$ = 12.7 Hz), 20.2 (d, $J_{P\text{-}C}$ = 14.7 Hz), 13.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ 4.27.



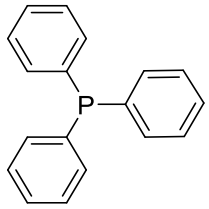
3d

Tri(*n*-butyl)phosphine (3d).[12] Preparation by Procedure 2.2 (36.3mg, 60% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39–1.30 (m, 18H), 0.87 (t, 9H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.2 (d, $J_{P\text{-}C}$ = 12.3 Hz), 26.9 (d, $J_{P\text{-}C}$ = 11.5 Hz), 24.6 (d, $J_{P\text{-}C}$ = 10.7 Hz), 13.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ -30.0.



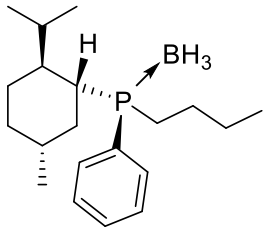
3f

Diphenyl(methyl)phosphine (3f).[13] Preparation by Procedure 2.3 (38.6 mg, 96% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.41 (m, 4H), 7.37–7.32 (m, 6H), 1.65 (d, 3H, J = 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3 (d, $J_{P\text{-}C}$ = 12.0 Hz), 132.2 (d, $J_{P\text{-}C}$ = 18.3 Hz), 128.53 (d, $J_{P\text{-}C}$ = 4.0 Hz), 128.48, 12.7 (d, $J_{P\text{-}C}$ = 13.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ -26.2.



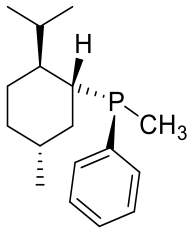
3g

Triphenylphosphine (3g).[13] Preparation by Procedure 2.3 (50.7 mg, 97% yield), white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.31 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.3 (d, $J_{P\text{-}C}$ = 10.6 Hz), 133.9 (d, $J_{P\text{-}C}$ = 19.5 Hz), 128.8, 128.6 (d, $J_{P\text{-}C}$ = 6.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -4.8.



3h"

(*Sp*)-(-)Menthyl(phenyl)(*n*-butyl)phosphine borane (3h).[14] Preparation by Procedure 2.4, (61.0mg, 96% yield), oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.70 (m, 2H), 7.44–7.39 (m, 3H), 2.14–2.07 (m, 1H), 1.83–1.59 (m, 7H), 1.46–1.33 (m, 2H), 1.32–1.16 (m, 6H), 0.94 (d, 3H, J = 6.8 Hz), 0.78 (t, 3H, J = 7.2 Hz), 0.73 (d, 3H, J = 6.8 Hz), 0.05 (d, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.3 (d, $J_{P\text{-}C}$ = 8.2 Hz), 131.1 (d, $J_{P\text{-}C}$ = 49.0 Hz), 130.7 (d, $J_{P\text{-}C}$ = 1.6 Hz), 128.6 (d, $J_{P\text{-}C}$ = 9.3 Hz), 44.4, 36.9 (d, $J_{P\text{-}C}$ = 32.1 Hz), 35.7, 34.3, 33.7 (d, $J_{P\text{-}C}$ = 10.3 Hz), 29.8, 28.0 (d, $J_{P\text{-}C}$ = 4.1 Hz), 24.9, 24.7 (d, $J_{P\text{-}C}$ = 45.0 Hz), 24.4 (d, $J_{P\text{-}C}$ = 13.6 Hz), 22.7, 21.2, 14.1 (d, $J_{P\text{-}C}$ = 98.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 20.5 (d, $J_{B\text{-}P}$ = 64.5 Hz).



3i

(*Sp*)-(-)Menthyl(phenyl)(methyl)phosphine (3i).[15] Preparation by Procedure 2.4, (46.2 mg, 88% yield). colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.23 (m, 5H), 2.59–2.51 (m, 1H), 1.74–1.60 (m, 3H), 1.42–1.25 (m, 2H), 1.21 (d, 3H, J = 4.0 Hz), 1.17–1.14 (m, 2H), 1.10 –0.96 (m, 2H), 0.93 (d, 3H, J = 6.8 Hz), 0.81 (d, 3H, J = 7.2 Hz), 0.74 (d, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4 (d, $J_{P\text{-}C}$ = 14.9 Hz), 131.3

(d, $J_{P\text{-}C}$ = 17.0 Hz), 128.2 (d, $J_{P\text{-}C}$ = 5.4 Hz), 127.4, 45.2 (d, $J_{P\text{-}C}$ = 9.3 Hz), 39.4 (d, $J_{P\text{-}C}$ = 15.6 Hz), 35.3, 34.8 (d, $J_{P\text{-}C}$ = 4.3 Hz), 33.6, 28.0 (d, $J_{P\text{-}C}$ = 20.2 Hz), 25.5 (d, $J_{P\text{-}C}$ = 7.6 Hz), 22.6, 21.7, 15.2; ^{31}P NMR (162 MHz, $CDCl_3$): δ -30.3.

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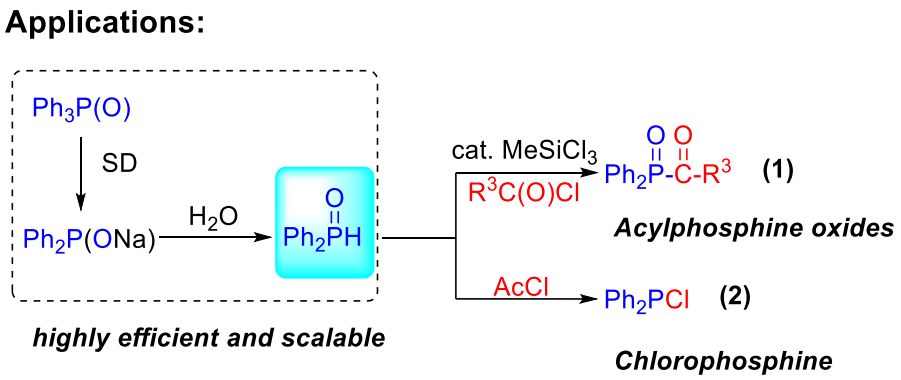
Chapter 5 Applications: Synthesis of Acylphosphine Oxides and Chlorophosphines

Abstract

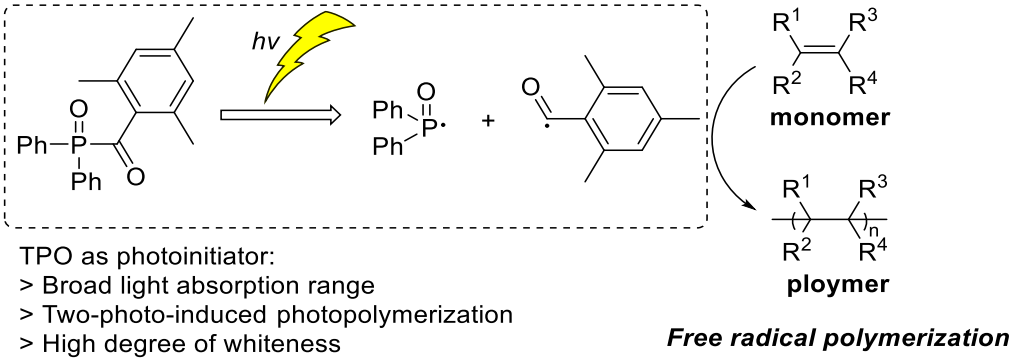
Regarding to the moderate efficiency of producing diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO) from Ph_2PONa with mesitoyl chloride (MesC(O)Cl) (Scheme 2.8, **B**) as well as the high efficiency of obtaining $Ph_2P(O)H$ via hydrolysis of Ph_2PONa in situ generated from $Ph_3P(O)$ (Scheme 2.12), in this study, direct synthesis of TPO from $Ph_2P(O)H$ and MesC(O)Cl mediated or catalyzed by chlorosilane has been developed. In the meantime, I accidently found that a byproduct Ph_2PCl appeared after the reaction of $Ph_2P(O)H$ and MesC(O)Cl, and finally fixed the optimal conditions for converting $Ph_2P(O)H$ to Ph_2PCl by treating with a readily available and cheap AcCl in THF.



5.1 Introduction

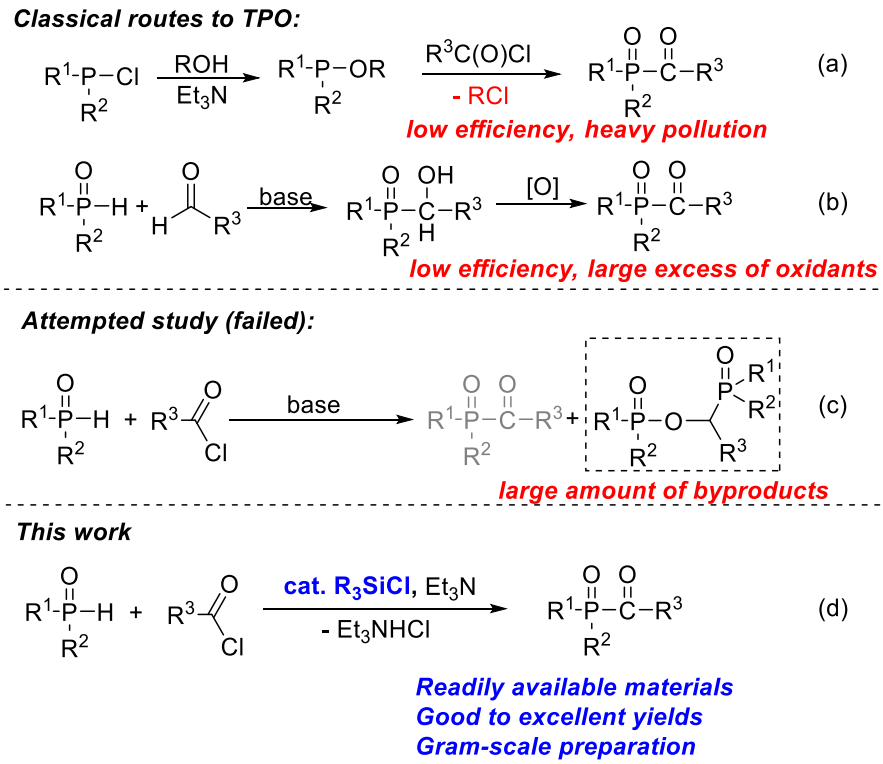
Acylphosphine oxides $R_2P(O)C(O)R'$ exhibit broad light absorption range and can decompose on exposing to light. Therefore, these compounds have broad applications as efficient radical photoinitiators for photopolymerization such as surface coatings, finishes, and printing inks.[1] Recently, they are also found unique applications in organic synthesis.[2] Among them, diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO) is a successfully commercialized photoinitiator in the industry. Photolysis of TPO yields phosphinoyl and acyl radicals (Scheme 5.1).[3] Because both radicals are able to initiate the polymerization, fast polymerization rates and high curing efficacy can be achieved. The high degree of whiteness is another outstanding feature of TPO since the current aromatic-ketones-type photoinitiators usually suffer from undesirable yellowing.[4]

Scheme 5.1 Photolysis and Application of TPO



Currently, acylphosphine oxides were synthesized by the Arbuzov-type reactions from acyl chlorides (RCOCl) with the air and moisture-sensitive alkoxylphosphines (R_2POR) prepared by chlorophosphines (R_2PCl) with low-boiling point-alcohols (Scheme 5.2a).[5] However, R_2PCl is not a readily available compound and the industrial preparation of R_2PCl is a heavy-pollution process.[6] In addition, during the preparation of TPO, one equivalent of the toxic low boiling point chloroalkanes (RCl) such as EtCl are inevitably released as volatile organic compounds (VOCs) that are hard to handle and environment-harmful.[7] To find more efficient alternative ways for the preparation of $R_2P(O)C(O)R'$, the oxidation of α- hydroxyphosphine oxide prepared

Scheme 5.2 Preparations of Acylphosphine Oxides



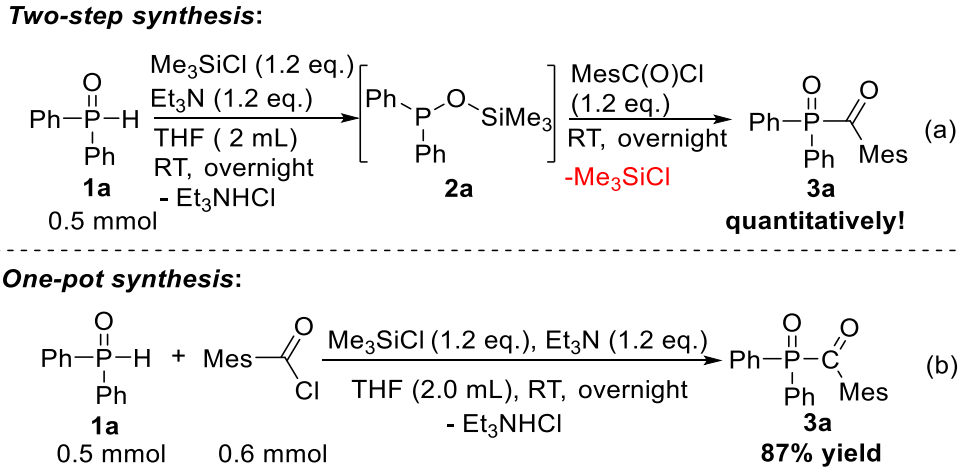
via the addition of secondary phosphine oxides to aldehydes was extensively studied in recent years (Scheme 5.2b).[8] However, the oxidation efficiency was low and usually a large amount of oxidants have to be used in order to get good yields of the desired products. For example, up to 20 equivalents of MnO_2 was required in the oxidizing process.[1e] The direct coupling of hydrophosphoryl compounds $R^1R^2P(O)H$ with acyl chlorides R^3COCl is a straightforward strategy (Schemes 5.2c and 5.2d) that can solve the problems for the preparation of TPO etc. as mentioned above. However, previous literatures indicated that it was hard to efficiently obtain such acylphosphorus compounds directly from R^3COCl and $R^1R^2P(O)H$ (Scheme 5.2c),[2b] since a large amount of an undesired byproducts were generated.

Herein I report our study that by using chlorosilanes, I have successfully overcome the obstacles and a variety of acylphosphine oxide compounds $R_2P(O)C(O)R'$ can be efficiently generated by the coupling of $R^1R^2P(O)H$ with acyl chlorides R^3COCl. Furthermore, I successfully found that chlorosilanes can be used as catalysts for these coupling reactions (Scheme 5.2d). To the best of our knowledge, this is the first chlorosilane-catalyzed coupling reactions of $R^1R^2P(O)H$ with acyl chlorides R^3COCl generating $R^1R^2P(O)C(O)R^3$.

5.2 Results and Discussion

Preliminary studies were commenced by mixing 0.5 mmol of diphenylphosphine oxide ($Ph_2P(O)H$) **1a** with 0.6 mmol of chlorotrimethylsilane (Me_3SiCl) in the presence of 0.6 mmol of triethylamine (Et_3N) in 2 mL THF at room temperature (Scheme 5.3a). After an overnight-stirring, ^{31}P NMR showed that Ph_2P-O-$SiMe_3$ **2a** was

Scheme 5.3 Preparation of TPO using Me_3SiCl

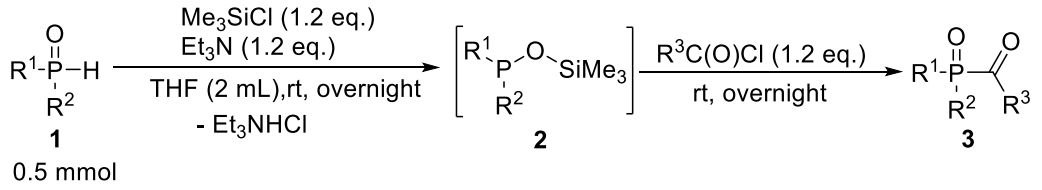


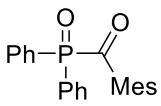
observed at 96.3 ppm, and generated quantitatively. To our delight, subsequent addition of 0.6 mmol of

mesitoyl chloride (MesCOCl) yielded the expected product TPO **3a** in a quantitative yield. More conveniently, as shown in Scheme 3b, the reaction could be simply carried out in one-pot affording TPO in 87% yield.[9]

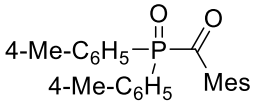
This method is applicable to the preparation of a variety of $R^1R^2P(O)C(O)R^3$. As shown in Table 5.1, three kinds of P(O)−H compounds, i.e., secondary phosphine oxides, H-phosphonate, and H-phosphinate were all compatible for this transformation. For example, diarylphosphine oxides with methyl, trifluoromethyl as well as chloro groups on the phenyl rings all could produce the corresponding acyl phosphine oxides with high yields (**3b**–**3d**). It seems that phosphine oxides having an electron-withdrawing group like $(p\text{-}CF_3C_6H_4)_2P(O)H$ **1c** and $(p\text{-}ClC_6H_4)_2P(O)H$ **1d** reacted with Me_3SiCl faster than $Ph_2P(O)H$ **1a**. However, the consequent second step reactions with MesC(O)Cl to give acylphosphine oxides proceeded slower because a long-time heating (70 °C, 24 h) were required. On the other hand, the reaction of $(p\text{-}MeC_6H_4)_2P(O)H$ **1b** affording the P-O-Si

Table 5.1. Synthesis of Acylphosphine Oxides Using Me_3SiCl.[a]

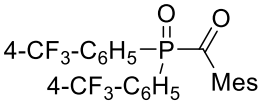




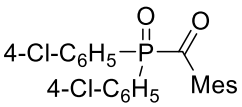
3a, 95%



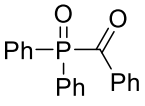
3b, 97%[b]



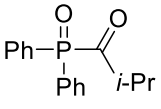
3c, 93%[c,d]



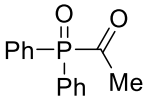
3d, 88%[c,d]



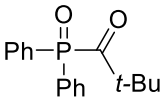
3e, 99%[e]



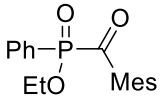
3f, 96%[e,f]



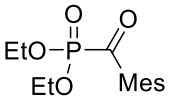
3g, 69%[e,f]



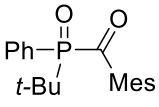
3h, 98%



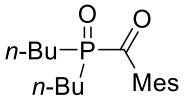
3i, 90%[b]



3j, 85%[g]



3k, 67%[g]



3l, 91%[h]

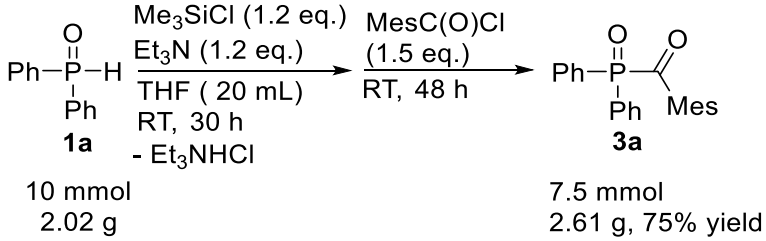
[a]Reaction conditions: Step 1: $R^1R^2P(O)H$ (0.5 mmol), THF (2.0 mL), Me_3SiCl (0.6 mmol), Et_3N (0.6 mmol), 25 °C, overnight. Step 2: Acyl chloride RCOCl (0.6 mmol), 25 °C, overnight. Isolated yield. [b]60 °C for step 1. [c]2 h for step 1. [d]70 °C, 24 h for step 2. [e]^{31}P NMR yield based on **1a** used. [f]0 °C, 2 h for step 2. [g]100 °C, overnight for step 2. [h]2 h for step 2.

intermediate required heating at 60 °C. However, the subsequent reaction with MesC(O)Cl took place smoothly

at room temperature. As shown in the table, ethyl phenylphosphinate Ph(EtO)P(O)H **1i**, diethyl phosphonate $(EtO)_2P(O)H$ **1j** as well as phenyl(*tert*-butyl)phosphine oxide Ph*t*-BuP(O)H **1k** and dibutylphosphine oxide *n*-$Bu_2P(O)H$ **1l** all served well to afford the desired products in satisfactory yields under similar reaction conditions (**3i**–**3l**). As to acyl chlorides, other substrates such as PhCOCl, *i*-PrCOCl and MeCOCl could also be used as the substrates. High yields of the products from these substrates were also formed as confirmed by ^{31}P NMR spectroscopies. These compounds (**3e**–**3g**) readily decompose in moisture atmosphere, and are difficult to prepare by the old conventional methods. To date, bulky acylphosphine oxides are the isolable and easily handled compounds, as the C=O group of the acylphosphine oxides is easily attacked by nucleophiles.[10,11] By using the sterically hindered *t*-BuCOCl, the stable aliphatic acylphosphine oxide **3h** could be obtained in 98% isolated yield.

To further demonstrate the usefulness of the current method for the preparation of acylphosphine oxides, a gram-scale reaction was conducted. As shown in Scheme 5.4, 2.02g of $Ph_2P(O)H$ was treated with 1.2 equivalents of Me_3SiCl in the presence of Et_3N followed by adding MesCOCl at room temperature. After filtration removing the amine salt Et_3NHCl, followed by removing the volatiles under a reduced pressure, the residue was purified by chromatography on silica gel using ethyl acetate/n-hexane as an eluent. The desired product TPO was obtained in 75% isolated yield.

Scheme 5.4 Gram-Scale preparation of TPO



As shown in Scheme 5.3, since Me_3SiCl was regenerated during the synthesis of acylphosphine oxides, I considered that a catalytic synthesis of $R^1R^2P(O)C(O)R^3$ should be operable in the presence of a catalytic amount of chlorosilanes. Thus, it is expected that, as illustrated in Scheme 5.5, Me_3SiCl firstly reacts with $R_2P(O)H$ to form the P-O-Si intermediate in the presence of Et_3N.[12] Subsequent reaction of the P-O-Si species with MesC(O)Cl produces the target TPO and regenerates Me_3SiCl that reacts with $R_2P(O)H$ again to start

another cycle of the reaction.

Scheme 5.5 Generation of TPO Catalyzed by TMSCl

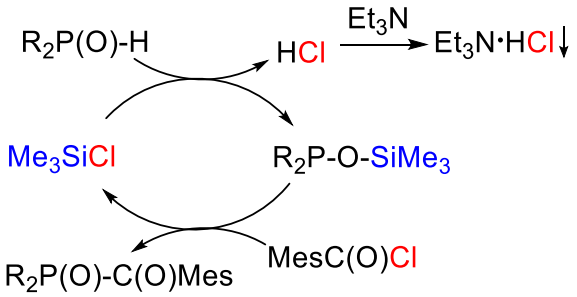
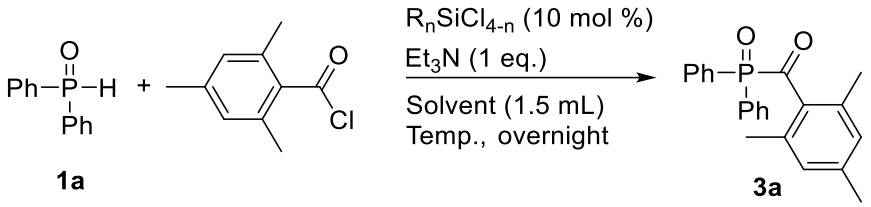


Table 5.2 Reaction Condition Optimization.[a]



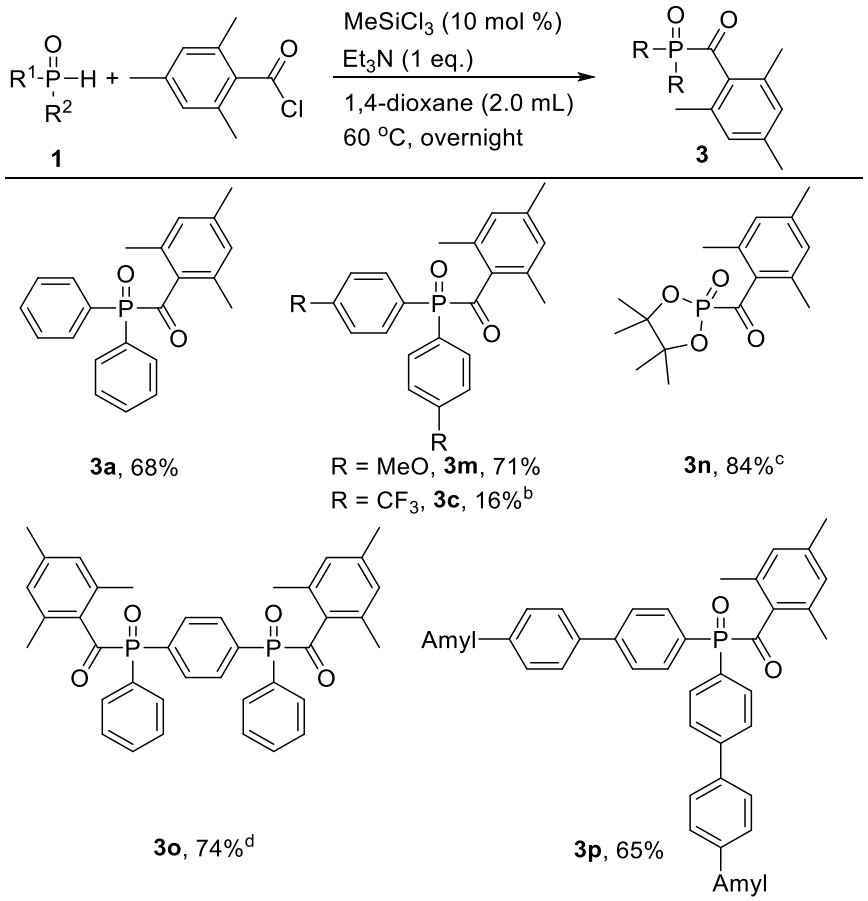
entry	R_nSiX_{4-n}	solvent	Temp. (°C)	yield (%)[b]
1	Me_3SiCl	THF	60	37
2	Me_3SiCl	THF	60	trace
3	Me_3SiOTf	THF	60	n.d.
4	Me_3SiI	THF	60	4
5	Me_2SiCl_2	THF	60	50
6	$MeSiCl_3$	THF	60	62
7	$SiCl_4$	THF	60	13
8[c]	$PhSiCl_3$	THF	60	30
9	Ph_2SiHCl	THF	60	19
10	-	THF	60	trace
11	$MeSiCl_3$	THF	70	64
12	$MeSiCl_3$	THF	90	64
13	$MeSiCl_3$	THF	50	60
14[d]	$MeSiCl_3$	toluene	60	65
15[e]	**$MeSiCl_3$**	**1.4-dioxane**	**60**	**70**
16	$MeSiCl_3$	MeCN	60	5
17	$MeSiCl_3$	DMF	60	N.D.
18	$MeSiCl_3$	benzene	60	72

[a]Reaction conditions: under argon atmosphere, $Ph_2P(O)H$ **1a** (0.6 mmol), R_nSiX_{4-n} (10 mol %), Et_3N (0.6 mmol), MesCOCl (0.9 mmol), solvent (1.5 mL), 60 °C, overnight. [b]Yield determined by ^{31}P-NMR based on **1a** used. [c]Without Et_3N.

Indeed, it was the case. As shown in Table 5.2, I investigated the catalytic synthesis of TPO by examining the reactivity of $Ph_2P(O)H$ **1a** with 1.5 equivlents of MesCOCl in the presence of 10 mol % of Me_3SiCl and 1 equivlent of Et_3N at 60 °C. The desired product TPO **3a** could be obtained in 37% yield (entry 1). As expected,

the use of triethylamine was crucial to this transformation as only a trace amount of the desired product was obtained in the absence of Et_3N (entry 2). In order to find a better catalyst, the reactivity of other silylating agents were screened. Unfortunately, the results showed that the expected more active trimethylsilyl triflate or iodide hardly worked for this transformation (entries 3–4). However, among other silyl chlorides reagents, I was pleased to find that trichloro(methyl)silane ($MeSiCl_3$) was proved to be the best catalyst that can produces TPO in 62% yield (entries 5–9). Blank experiments showed that the target product could be scarcely formed in the absence of a silyl chloride (entry 10). Additionally, conducting the reaction at an elevated or decreased temperature could not improve the reaction`s efficiency (entries 11–13). Finally, the effect of solvents was investigated (entries 14–18). 1,4-dioxane, benzene and toluene could also be used as the solvents. However, the reaction hardly proceeded in DMF and MeCN.

Table 5.3 $MeSiCl_3$-catalyzed synthesis of TPO and its analogues.[a]



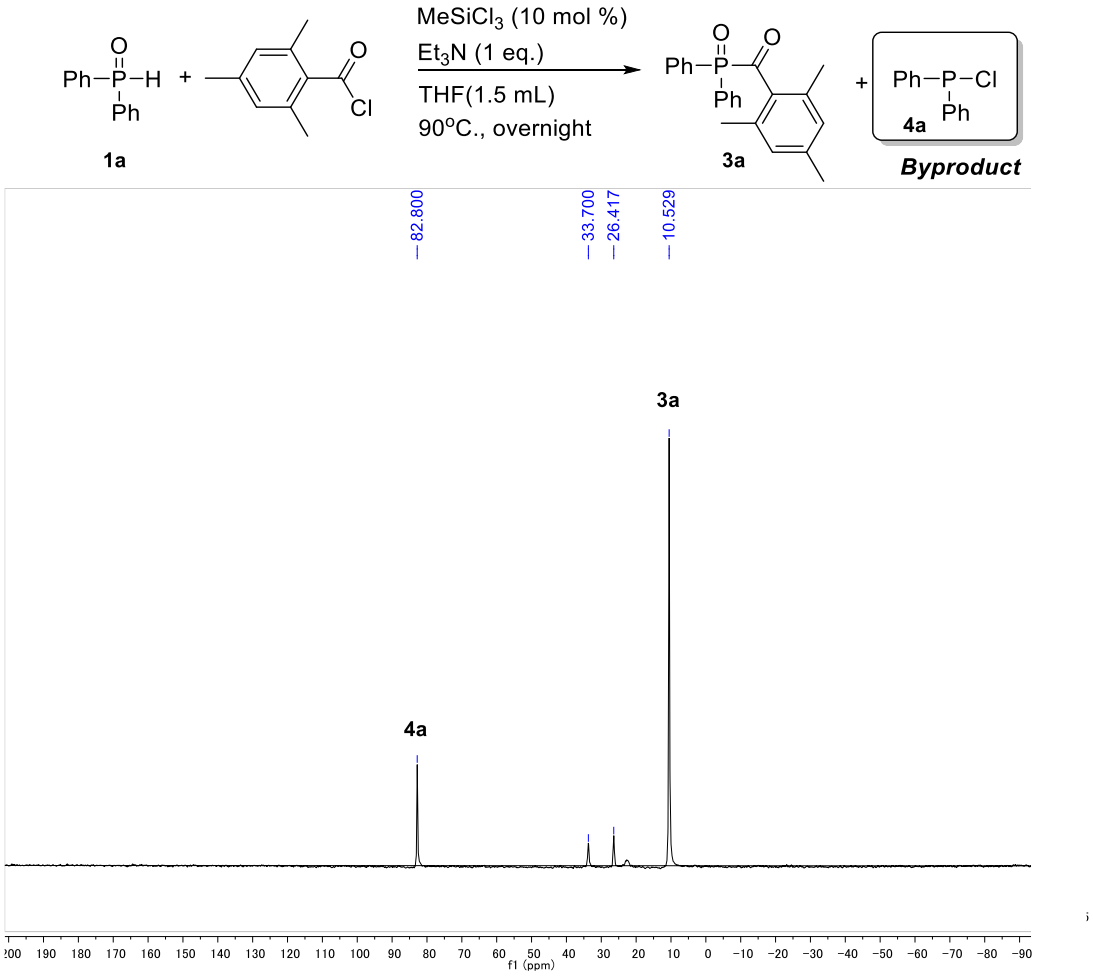
[a]Reaction conditions: under argon atmosphere, $R^1R^2P(O)H$ (0.6 mmol), MesCOCl (0.9 mmol), $MeSiCl_3$ (0.06 mmol), Et_3N (0.6 mmol) and 1,4-dioxane (1.5 mL), 60 °C, overnight. Isolated yield. [b]Yield determined by ^{31}P-NMR based on **1c** used. [c]20 mol % of $MeSiCl_3$ and Et_3N (1.2 equiv.) were used, 120 °C. [d]20 mol % of $MeSiCl_3$ and MesCOCl (3 equiv.) were used.

This catalytic reaction is applicable to the synthesis of other TPO analogues, as illustrated in Table 5.3. For example, (p-$MeOC_6H_4)_2P(O)H$ could couple with MesC(O)Cl giving 71% yield of the product **3m**. In addition, 1,4-phenylene-bis(phenylphosphine oxide) **1o**, equipped with two P(O)-H moieties, was smoothly acylated to furnish diacylphosphoryl product **3o** in 74% yield. Furthermore, a more conjugated di([1,1'-bi(p-amylphenyl]-4-yl)phosphine oxide **1p** could also underwent the catalytic reaction with MesCOCl efficiently, affording a good yield of product **3p**. Last, five-membered cyclic hydrogen phosphonate **1n** was successfully introduced into the acylphosphoryl skeleton **3n** in a high yield.

5.3 Accident discovery: synthesis of R^1R^2PCl form $R^1R^2P(O)H$

During the condition optimization of the above catalytical reaction, I accidently found when the temperature was elevated to 90 °C, a byproduct with a single peak at 82.80 ppm appeared, which seemed to be

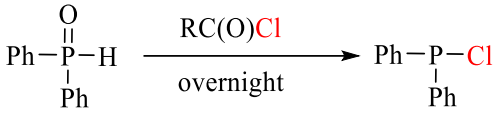
Scheme 5.6 Discovery of the byproduct Ph_2PCl



diphenylphosphine chloride Ph_2PCl **4a** (Scheme 5.6). As we know that Ph_2PCl is a key reagent for the

introduction of Ph_2P motif to other molecules, especially the phosphine ligands.[13] Therefore, to further find out the optimal conditions for converting $Ph_2P(O)H$ to Ph_2PCl is desirable (Table 5.4). Initially, a mixture of diphenylphosphine oxide **1a** (0.05 mmol) and mesityl chloride MesC(O)Cl (0.6 mmol) in THF (0.5 mL) in a sealed NMR tube was heated at 100 °C overnight. As indicated by ^{31}P NMR spectroscopy, the signal at 82.8 ppm assignable to Ph_2PCl was observed obviously and 85% yield of Ph_2PCl was generated via integral calculation (run 1). Under similar conditions, when I increased the amount of mesityl chloride to 1.2 mmol (2.0 equivalent to **1a**) (runs 2 and 3), the yield of Ph_2PCl was obtained in 94% yield. Under lower temperatures,

Table 5.4. Reaction condition optimization.



1a **4a**

Run	R	RC(O)Cl (equiv.)	Solvent	Tempt./°C	Yield/%
1	Mes	1.2	THF	100	85
2	Mes	1.6	THF	100	87
3	Mes	2.0	THF	100	94
4	Mes	2.0	THF	80	73
5	Mes	2.0	THF	70	48
6	Mes	2.0	THF	60	30
7	Mes	2.0	THF	50	8
8	Ph	2.0	THF	100	25
9	^{i}Pr	2.0	THF	100	90
10	Me	2.0	THF	100	97
11	Me	2.0	Dioxane	100	99
12	Me	2.0	Toluene	100	92
13	Me	2.0	CH_2Cl_2	100	77
14	Me	2.0	Dioxane	25	95
15	**Me**	**2.0**	**THF**	25	**95**
16	Me	1.5	THF	25	82(95)[b]
17	Me	1.2	THF	25	81(94)[b]
18	Me	1.0	THF	25	66(92)[b]

[a]Reaction conditions: under argon atmosphere, $Ph_2P(O)H$ **1a** (0.05 mmol) was dissolved in 0.5 mL solvent in an NMR tube. RC(O)Cl was added and the mixture was heated overnight at the temperature indicated. Yield refres to ^{31}P-NMR yield based on **1a** used (Mes: mesityl or 1,3,5-trimethylphenyl). [b]The reaction was conducted at 50 °C.

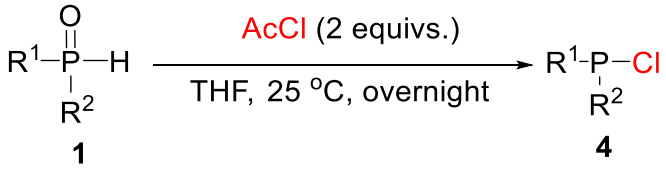
however, only low yields of the product were obtained (runs 4-7), it should be noted that the reactivity of

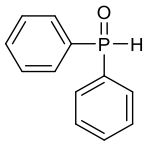
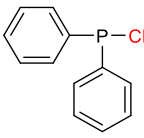
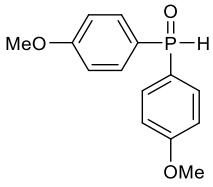
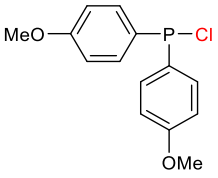
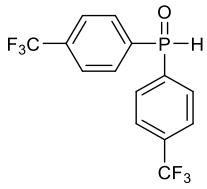
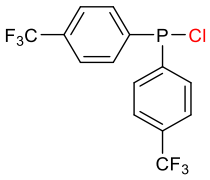
$Ph_2P(O)H$ with MesC(O)Cl is relatively low that required heating and higher energy barrier, maybe the critical point of temperature is at 50-60ºC, so when temperature was down from 60 to 50 ºC, the reaction speed was slow down dramatically. Next, I decided to investigate the reactivity of other acyl chlorides (runs 8-10), and found that the simplest acetyl chloride MeC(O)Cl showed highest reactivity for this reductive chlorination reaction (run 10), since the electronegativity of methyl group (Me) is stronger than Aryl group, so the inductive effect of Me is stronger, the carbon atom of C=O of acetyl chloride is more cationic, facilitating the nucleophilic attack of $Ph_2P(O)H$ to RC(O)Cl. The effect of solvent was also investigated (runs 11–13). Solvent like 1,4-dioxane and toluene could also be used in this transformation. Dichloromethane gave 77% yield of the product under similar conditions (run 13). In consideration of the safety problem at high temperature, I then tried to conduct the above reaction again under mild conditions. To our surprise, such a reductive transformation smoothly proceeded even at room temperature by using acetyl chloride MeC(O)Cl (runs 14–15). The reaction could also take place smoothly with less loadings of acetyl chloride (runs 16-18) under room temperature. However, in order to obtain a high yield (over 90%) of the desired product Ph_2PCl, the use of a slightly higher temperature 50 °C was preferred. Therefore, after the above comprehensive evaluation on the reaction conditions, the reaction conditions by using THF as solvent and 2.0 equivalents of acetyl chloride were chosen as the optimized parameters for this reaction.

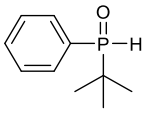
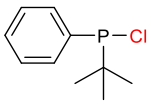
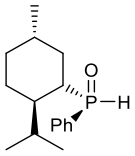
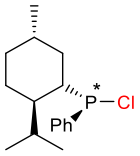
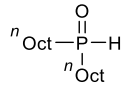
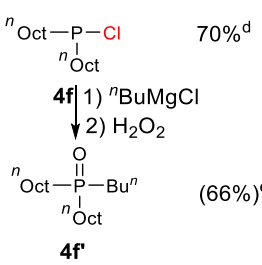
As shown in Table 5.5, to explore its generality, a varies of representative secondary phosphine oxides (SPOs) were used as the reagents for this transformation. Both aromatic and aliphatic SPOs were all readily reduced to the corresponding phosphine chlorides with excellent yields under similar reactions. For example, in addition to $Ph_2P(O)H$ **1a** (Table 5.5, run 1**)**, SPO bearing an electron-denoting group (p-MeO-$C_6H_4)_2P(O)H$ **1b** and an electron-withdrawing group (p-CF_3-$C_6H_4)_2P(O)H$ **1c**, all were reduced to the corresponding phosphine chlorides in high yields (Table 5.5, runs 2-3). The conversion of an arylalkylphosphine oxide like Ph*t*-BuP(O)H **1d** and the chiral (R_P)-PhMenP(O)H **1e** also could proceed smoothly to produce the corresponding P-Cl products in nearly quantitative yields (Table 5.5, runs 4-5**)**. Moreover, dioctyl phosphine oxide n-$Oct_2P(O)H$ also reacted with MeC(O)Cl quickly to give n-Oct_2PCl (Table 5.5, run 6). Since the high reactivity of n-Oct_2PCl, the confirmation of its formation was carried out by quenching the reaction mixture

using *n*-BuMgCl following oxidation with hydrogen peroxide to produce the corresponding stable butyldioctylphosphine oxide **2f** (66% isolated yield). However, diethyl phosphite $(EtO)_2P(O)H$ and ethyl phenylphosphinate Ph(EtO)P(O)H sluggishly reacted with AcCl even at a higher temperature (120°C).

Table 5.5. Ready conversion of secondary phosphine oxides by acetyl chloride to chlorophosphines.[a]



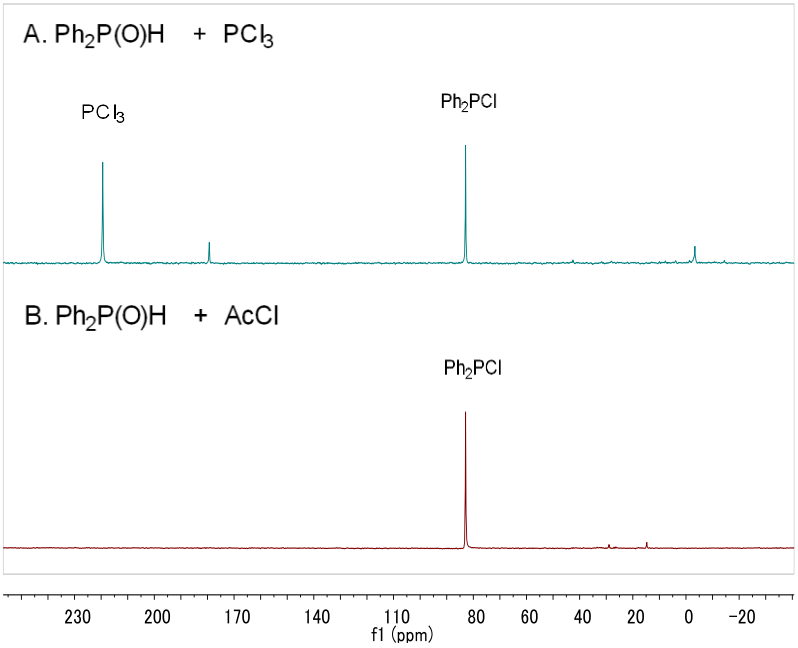
Run	$R^1R^2P(O)H$ (**1**)	R^1R^2PCl (**2**)	Yield
1	 **1a**	 **4a**	95%(93%)
2	 **1b'**	 **4b**	90%(87%)
3	 **1c'**	 **4c**	99%(96%)[b]

Run	$R^1R^2P(O)H$ (**1**)	R^1R^2PCl (**2**)	Yield
4	 **1d'**	 **4d**	98%(94%)
5	 **1e'**	 **4e**	> 99% (98%) (*dr* ratio 74/26)[c]
6	 **1f'**	 **4f** 1) ^{n}BuMgCl 2) H_2O_2 **4f'**	70%[d] (66%)[e]

[a]Reaction conditions: under argon atmosphere, $R^1R^2P(O)H$ **1** (1.0 mmol) was dissolved in 2.0 mL THF, and then MeC(O)Cl (2.0 mmol) was added to the solution. The mixture was stirred at room temperature overnight. Yields were determined by ^{31}P-NMR spectra based on **1** used, and the isolated yield was shown in parentheses. [b]50 °C. [c]Reaction time was 1 hour. [d]At 0°C for 1h. ^{31}P-NMR yield. [e]Isolated as **3f** by treating **2f** with ^{n}BuMgCl and then H_2O_2.

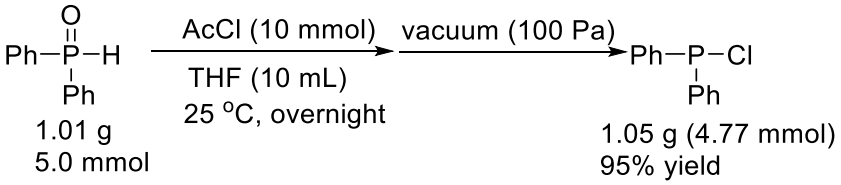
Although treating $Ph_2P(O)H$ with 2 equivalents of either PCl_3[14] or AcCl in THF can lead to the generation of Ph_2PCl (Scheme 5.7), the reaction with AcCl is cleaner than that of PCl_3 which was accompanied by the formation of a few phosphorus by-products. In addition, the by-product AcOH from the AcCl system, if necessary, can be easily pumped off from the chlorophosphines under vacuum to give highly pure chlorophosphines.

Scheme 5.7. ^{31}P NMR spectroscopies of the reaction mixture of $Ph_2P(O)H$ with PCl_3 (**A**) or AcCl (**B**)



To further demonstrate the practical application, as shown in Scheme 5.8, a gram-scale transformation of $Ph_2P(O)H$ to Ph_2PCl was conducted by stirring 1.01 g $Ph_2P(O)H$ with 2 equivalent of AcCl in 10 mL THF at room temperature overnight. After the reaction, volatiles were removed under a reduced pressure (less than 100 Pa) to afforded pure Ph_2PCl in 95% yield.

Scheme 5.8. Gram-scale preparation of Ph_2PCl from $Ph_2P(O)H$ by AcCl



5.4 Conclusion

In summary, in this chapter, I have disclosed a novel protocol for the synthesis of acylphosphine oxides from hydrophosphoryl compounds and acyl chlorides by using the readily available chlorosilanes. Three kinds of P(O)H compounds including secondary phosphine oxides $R^1R^2P(O)H$, H-phosphinate $R^1(R^2O)P(O)H$ and H-phosphonate $(RO)_2P(O)H$ were all efficiently transformed into the corresponding acylphosphine oxides in good yields. More importantly, a catalytic amount of chlorosilane could also work well for the couplings. Compared to the conventional routes, chemicals used in this new method are readily available. Moreover, the new method prohibits the emission of the volatile chloroalkanes and the use of oxidants providing a greener

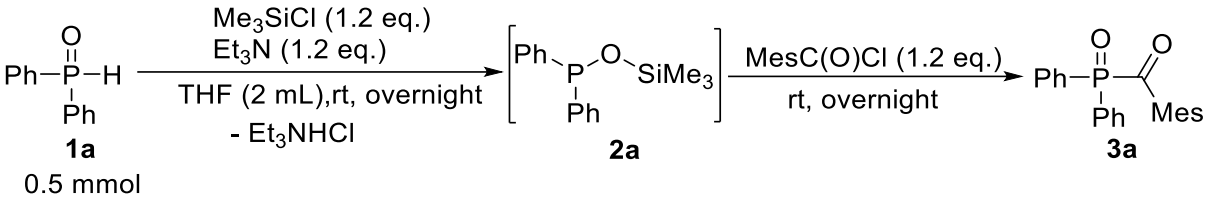
and safer approach to a wide range of acylphosphine oxides that are useful as photoinitiators. On the other hand, I subsequently disclosed a convenient new method for the synthesis of phosphines chlorides from secondary phosphine oxides by using acetyl chloride under mild conditions. Various secondary phosphine oxides, diarylphosphine oxides, alkyl(aryl)phosphine oxides and dialkylphosphine oxides, all could be used as the substrates, and were reduced readily to the corresponding phosphine chlorides in high yields. And simple removal of THF, the remained AcCl and AcOH under vacuum after the reactions can afford the target R_2PCl in quite pure form.

5.5 Experimental Section

5.5.1 General Information

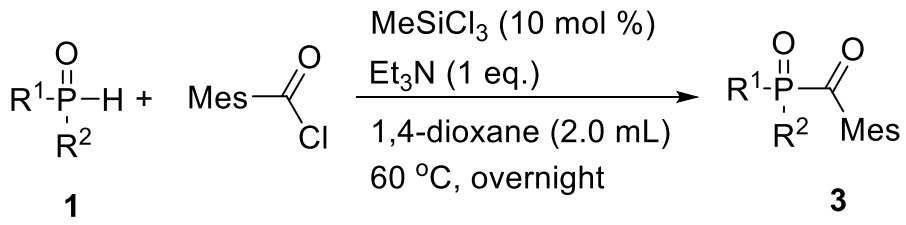
All reactions were carried out in oven dried Schlenk tubes under argon atmosphere, and the reactions require heating were conducted on a SIBATA Chemi Chemi-200 heating machine equipped with digital-temperature-controlled aluminum heating blocks and magnetic stirrers. Commercially available materials were purchased and used without further purification unless otherwise noted. The secondary phosphine oxides were prepared according to the previous reported methods. Column chromatography was performed using Silica Gel 60 N (spherical, neutral). HPLC (recycle GPC) method for isolation was performed on *J*APAN ANALYTICAL INDUSTRY LC-908. The HPLC was a recycling preparative HPLC (Gel permeation chromatography) with two columns (20 mm I.D. -600 mm L; JAIGEL-1H and JAIGEL-2H). All the products isolated by GPC were purified by the same conditions: $CHCl_3$ as eluent, flow rate: 4.0 mL/min, and the spectra was recorded at a moving paper in the speed of 60 mm/h. ^{1}H NMR spectra were recorded on *J*EOL *J*NM-ECS400 (400 MHz) FT NMR in $CDCl_3$ with Me_4Si as an internal standard. ^{13}C NMR spectra were taken on *J*EOL *J*NM-ECS400 (100 MHz) FT NMR system in $CDCl_3$. ^{31}P NMR spectra were taken on *J*EOL *J*NM-ECX400 (162 MHz) FT NMR system in $CDCl_3$ with 85% H_3PO_4 solution as an external standard. The High-resolution ESI mass spectra were obtained on Bruker micrOTOF II.

5.5.2 Typical Procedure A for the Two-step Preparation of Acylphosphine Oxides 3a



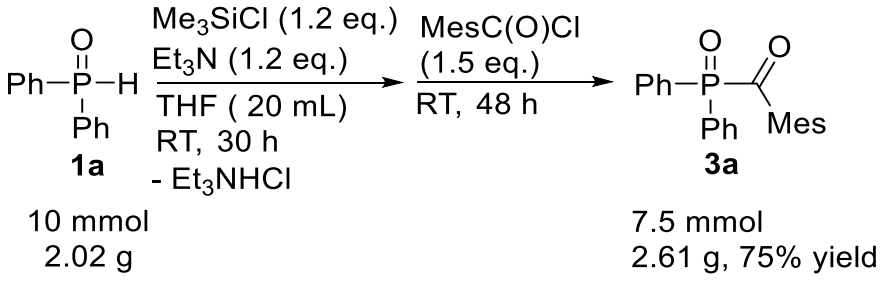
Under the argon atmosphere, to a solution of $Ph_2P(O)H$ **1a** (0.5 mmol) in THF (2.0 ml) was added Et_3N (0.6 mmol, 1.2 equiv.) and Me_3SiCl (0.6 mmol, 1.2 equiv.), after stirring the mixture at 25 °C for overnight, MesCOCl (0.6 mmol, 1.2 equiv.) was added and stirring the mixture at 25 °C for overnight. After that, the mixture was filtered and concentrated under vacuum. The obtained residue was eluted by EtOAc via a silica gel column to give the crude product, which was then diluted in $CHCl_3$ and purified by GPC to afford pure product **3a** (165.2 mg, 0.474 mmol, 95% yield).

5.5.3 General Procedure B for the $MeSiCl_3$-catalyzed Synthesis of Acylphosphine Oxides 3



Under the argon atmosphere, to a solution of $R^1R^2P(O)H$ **1** (0.6 mmol) in 1,4-dioxane (1.5 mL) was sequentially added Et_3N (0.6 mmol,1.0 equiv.), $MeSiCl_3$ (0.06 mmol, 10 mol %) and MesCOCl (0.9 mmol, 1.5 equiv.). The mixture was heated at 60 °C for overnight. After that, the mixture was filtered and concentrated under vacuum, the obtained residue was eluted by EtOAc via a silica gel column to give the crude product, which was then diluted in $CHCl_3$ and purified by GPC to afford the pure products **3**.

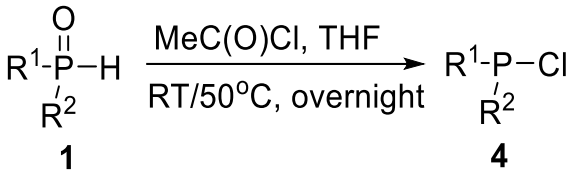
5.5.4 Procedure for the Gram-Scale Preparation of Diphenyl(mesitoyl)phosphine Oxides (TPO)



Under the argon atmosphere, to a solution of $Ph_2P(O)H$ **1a** (10 mmol, 2.02 g) in THF (20 mL) was added

Et_3N (12.0 mmol, 1.66 mL) and Me_3SiCl (12.0 mmol, 1.39 mL), after stirring the mixture at 25 °C for 30 h, MesCOCl (15.0 mmol, 2.5 mL) was added and stirring the mixture at 25 °C for 48 h. After that, the mixture was filtered and concentrated under vacuum. The obtained residue was eluted by EtOAc/Hexane (1/3) *via* a silica gel column to give the pure product TPO (2.61 g, 0.75 mmol, 75% yield).

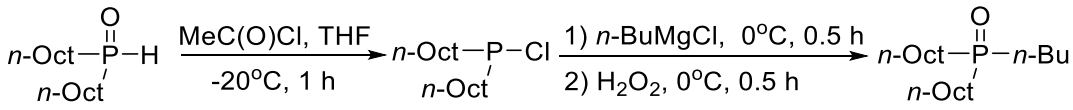
5.5.5 General procedure C for the synthesis of chlorophosphines 4a to 4e



1 **4**

To an 10mL oven-dried Schlenk tube under argon atmosphere were added $R_1R_2P(O)H$ (1.0 mmol) and THF (2.0 mL), stirring the solution until all the solid was totally dissolved, and then MeC(O)Cl (2.0 mmol) was added to the solution and the mixture was stirred at room temperature or 50°C for overnight. After reaction, the excessive MeC(O)Cl, byproduct AcOH and solvent THF were removed under ultra-high vacuum to afford pure R^1R^2PCl.

5.5.6 Procedure D for the synthesis of *n*-Oct_2PCl and its derivative *n*-$Oct_2P(O)$*n*-Bu

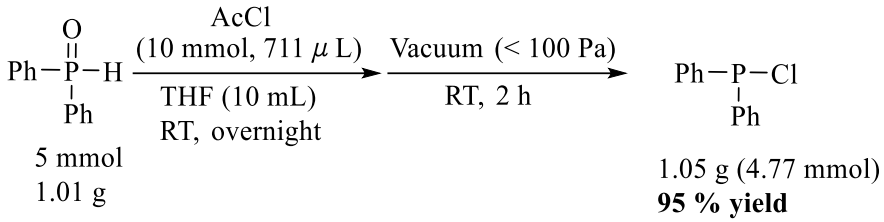


1f' **4f** **4f'**

To an 20 mL oven-dried Schlenk tube under argon atmosphere were added *n*-$Oct_2P(O)H$ (1.0 mmol, 1 equiv.) and THF (4.0 mL), stirring the solution until all the solid was totally dissolved, and then MeC(O)Cl (2.0 mmol, 2 equiv.) was added to the solution and the mixture was stirred under -20°C for 1 h to afford crude *n*-Oct_2PCl **4f** solution with a signal at 114.86 ppm detected by ^{31}P NMR. Next, *n*-BuMgCl (THF solution, 1M, 4mL, 4 equiv.) was added in dropwise and the mixture was stirred for 0.5 h, and then quenched by 5.0 mL of saturated aqueous NH_4Cl solution, after extracted with CH_2Cl_2 (5 mL×3), the combined organic layer was evaporated and then diluted in 2 mL CH_2Cl_2 at 0°C, then 0.5 mL 30% H_2O_2 was added in dropwise and the mixture was stirred for 0.5 h. At last, the crude solution was dried over anhydrous Na_2SO_4, then filtered and evaporated. The final residues were diluted in $CHCl_3$ and isolated by HPLC (Conditions: polystyrene-based

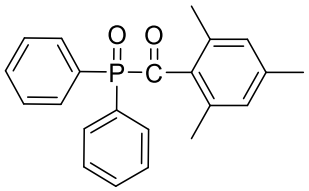
column, $CHCl_3$ as eluent, flow rate = 4.0 mL/min, the spectra was recorded at a moving paper in the speed of 60 mm/h.) to afford analytically pure **4f'**.

5.5.7 Scale-up synthesis of Ph_2PCl from $Ph_2P(O)H$



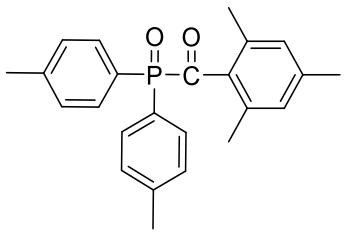
To a 50 mL oven-dried Schlenk tube under argon atmosphere were added $Ph_2P(O)H$ (5.0 mmol, 1 equiv.) and THF (10.0 mL), stirring the solution until all the solid was totally dissolved, and then MeC(O)Cl (10.0 mmol, 2 equiv.) was added to the solution and the mixture was stirred at room temperature for overnight. After reaction, the excessive MeC(O)Cl, byproduct AcOH and solvent THF were removed under high vacuum (< 100 Pa) to afford pure product Ph_2PCl in 95% yield.

5.5.8 Characterization and analytical data of products



3a

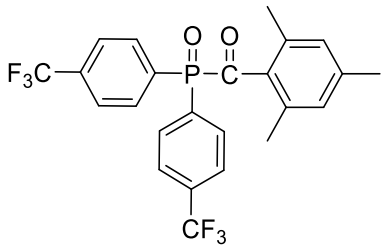
(2,4,6-trimethylbenzoyl)diphenylphosphine oxide (3a). Prepared by procedure A (Step 1: 25 °C and overnight; Step 2: 25 °C and overnight); pale yellow solid (165.2 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.96 (m, 4H), 7.57–7.47 (m, 6H), 6.80 (s, 2H), 2.25 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.2 (d, $J_{P\text{-}C}$ = 71.8 Hz), 140.7, 136.4 (d, $J_{P\text{-}C}$ = 39.5 Hz), 135.0, 132.5 (d, $J_{P\text{-}C}$ = 2.5 Hz), 132.0 (d, $J_{P\text{-}C}$ = 8.7 Hz), 129.9 (d, $J_{P\text{-}C}$ = 93.1 Hz), 129.0, 128.8 (d, $J_{P\text{-}C}$ = 11.6 Hz), 21.1, 19.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 13.8.



3b

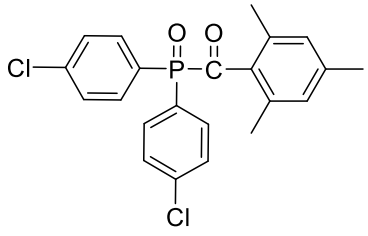
(2,4,6-trimethylbenzoyl)di(p-tolyl)phosphine oxide (3b). Prepared by procedure A (Step 1: 60 °C and

overnight; Step 2: 25 °C and overnight); white solid (182.5 mg, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.83 (m, 4H), 6.99–6.96 (m, 4H), 6.77 (s, 2H), 3.79 (s, 6H), 2.22 (s, 3H), 1.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.5 (d, $J_{P\text{-}C}$ = 74.5 Hz), 163.0 (d, $J_{P\text{-}C}$ = 2.7 Hz), 140.4, 136.5 (d, $J_{P\text{-}C}$ = 39.4 Hz), 134.9, 133.9 (d, $J_{P\text{-}C}$ = 10.2 Hz), 128.9, 120.5 (d, $J_{P\text{-}C}$ = 100.4 Hz), 114.5 (d, $J_{P\text{-}C}$ = 12.7 Hz), 55.4, 21.3, 19.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 15.4.



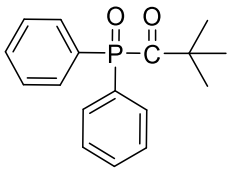
3c

(2,4,6-trimethylbenzoyl)di(p-trifluoromethylphenyl)phosphine oxide (3c). Prepared by procedure A (Step 1: 25 °C and 2 h; Step 2: 70 °C and 24 h); white solid (225.1 mg, 93% yield). mp 144–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20–8.15 (m, 4H), 7.80–7.78 (m, 4H), 6.85 (s, 2H), 2.28 (s, 3H), 2.05 (s, 6H),; ^{13}C NMR (100 MHz, $CDCl_3$): δ 218.0 (d, $J_{P\text{-}C}$ = 72.6 Hz), 173.9, 141.6, 139.5, 135.4 (d, $J_{P\text{-}C}$ = 47.1 Hz), 132.3 (d, $J_{P\text{-}C}$ = 8.9 Hz), 128.8 (d, $J_{P\text{-}C}$ = 58.9 Hz), 125.8 (dd, $J_{P\text{-}C}$ = 7.8 Hz, $J_{F\text{-}C}$ = 3.4 Hz), 125.7, 21.1 (d, $J_{F\text{-}C}$ = 14.9 Hz), 19.9 (d, $J_{F\text{-}C}$ = 25.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.43. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{24}H_{19}F_6O_2PNa$ 507.0925, Found 507.0920.



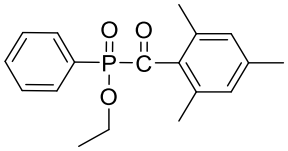
3d

(2,4,6-trimethylbenzoyl)di(p-chlorophenyl)phosphine oxide (3d). Prepared by procedure A (Step 1: 25 °C and 2 h; Step 2: 70 °C and 24 h); white solid (183.0 mg, 88% yield). mp 133–137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.89 (m, 4H), 7.48–7.45 (m, 4H), 6.80 (s, 2H), 2.23 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 219.4 (d, $J_{P\text{-}C}$ = 73.0 Hz), 141.2, 139.5 (d, $J_{P\text{-}C}$ = 3.5 Hz), 135.8 (d, $J_{P\text{-}C}$ = 40.2 Hz), 133.2 (d, $J_{P\text{-}C}$ = 9.5 Hz), 129.4 ($J_{P\text{-}C}$ = 12.1 Hz), 129.1, 128.1 ($J_{P\text{-}C}$ = 93.9 Hz), 21.3, 19.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ 12.0. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{22}H_{19}Cl_2O_2PNa$ 439.0397, Found 439.0391.



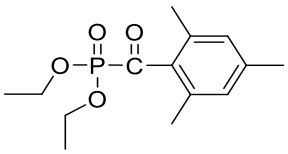
3h

(pivaloyl)diphenylphosphine oxide (3h). Prepared by procedure A (Step 1: 25 °C and overnight; Step 2: 25 °C and overnight); white solid (141.0 mg, 98% yield). mp 80–84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.77 (m, 4H), 7.53–7.42 (m, 6H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.9 (d, $J_{P\text{-}C}$ = 60.4 Hz), 132.2 (d, $J_{P\text{-}C}$ = 2.5 Hz), 131.6 (d, $J_{P\text{-}C}$ = 9.2 Hz), 130.8 (d, $J_{P\text{-}C}$ = 93.3 Hz), 128.7 (d, $J_{P\text{-}C}$ = 11.7 Hz), 49.2 (d, $J_{P\text{-}C}$ = 38.6 Hz), 24.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 19.2.



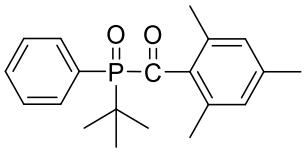
3i

(2,4,6-trimethylbenzoyl)ethylphenylphosphinate (3i). Prepared by procedure A (Step 1: 60 °C and overnight; Step 2: 25 °C and overnight); colorless oil (142.3 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.80 (m, 2H), 7.60–7.56 (m, 1H), 7.49–7.44 (m, 2H), 6.79 (s, 2H), 4.18–4.11 (m, 2H), 2.25 (s, 3H), 2.13 (s, 6H), 13.2 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.6 (d, $J_{P\text{-}C}$ = 112.3 Hz), 140.0, 136.7 (d, $J_{P\text{-}C}$ = 46.2 Hz), 134.5, 133.3 (d, $J_{P\text{-}C}$ = 2.6 Hz), 133.0 (d, $J_{P\text{-}C}$ = 9.9 Hz), 128.7, 128.7 (d, $J_{P\text{-}C}$ = 12.5 Hz), 127.4 (d, $J_{P\text{-}C}$ = 123.7 Hz), 62.5 (d, $J_{P\text{-}C}$ = 7.5 Hz), 21.3, 19.5, 16.6 (d, $J_{P\text{-}C}$ = 5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.1.



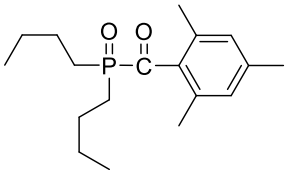
3j

(2,4,6-trimethylbenzoyl)diethylphosphinate (3j). Prepared by procedure A (Step 1: 25 °C and overnight; Step 2: 100 °C and overnight); colorless oil (120.7 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.788 (s, 2H), 4.21–4.04 (m, 4H), 2.22 (s, 3H), 2.20 (s, 6H), 1.24 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.4 (d, $J_{P\text{-}C}$ = 170.6 Hz), 139.9, 137.0 (d, $J_{P\text{-}C}$ = 55.2 Hz), 134.3, 128.7, 64.1 (d, $J_{P\text{-}C}$ = 7.3 Hz), 21.2, 19.3, 16.4 (d, $J_{P\text{-}C}$ = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -3.2.



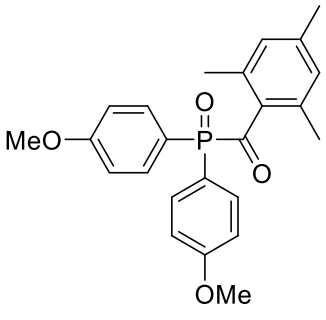
3k

(2,4,6-trimethylbenzoyl)phenyl(t-butyl)phosphine oxide (3k). Prepared by procedure A (Step 1: 25 °C and overnight; Step 2: 100 °C and overnight); white solid (109.8 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.90 (m, 2H), 7.53–7.44 (m, 3H), 6.75 (s, 2H), 2.21 (s, 3H), 2.12 (s, 6H), 1.29 (d, 9H, J = 15.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.7 (d, $J_{P\text{-}C}$ = 60.2 Hz), 140.6, 137.0 (d, $J_{P\text{-}C}$ = 36.9 Hz), 135.5, 132.5 (d, $J_{P\text{-}C}$ = 7.5 Hz), 132.1 (d, $J_{P\text{-}C}$ = 2.3 Hz), 129.2, 128.3 (d, $J_{P\text{-}C}$ = 10.5 Hz), 127.6 (d, $J_{P\text{-}C}$ = 76.2 Hz), 35.5 (d, $J_{P\text{-}C}$ = 61.2 Hz), 25.3, 21.2, 20.2; ^{31}P NMR (162 MHz, $CDCl_3$): δ 32.1.



3l

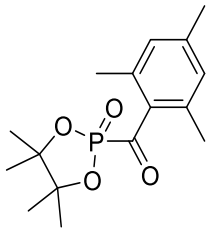
(2,4,6-trimethylbenzoyl)di(n-butyl)phosphine oxide (3l). Prepared by procedure A (Step 1: 25 °C and overnight; Step 2: 25 °C and overnight); white solid (140.5 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.79 (s, 2H), 2.24 (s, 6H), 2.20 (s, 3H), 1.94–1.74 (m, 4H), 1.61–1.45 (m, 4H), 1.40–1.31 (m, 4H), 0.85 (t, 6H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.9 (d, $J_{P\text{-}C}$ = 63.7 Hz), 140.6, 136.5 (d, $J_{P\text{-}C}$ = 37.1 Hz), 134.9, 129.2, 26.8 (d, $J_{P\text{-}C}$ = 59.9 Hz), 24.3 (d, $J_{P\text{-}C}$ = 14.1 Hz), 23.5 (d, $J_{P\text{-}C}$ = 4.0 Hz), 21.2, 19.9, 13.6 ; ^{31}P NMR (162 MHz, $CDCl_3$): δ 42.6.



3m

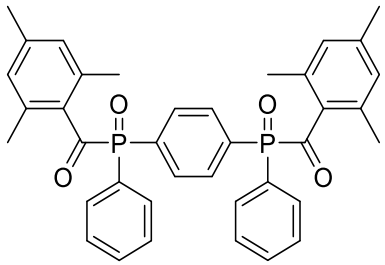
(2,4,6-trimethylbenzoyl)di(p-methoxylphenyl)phosphine oxide (3m). Prepared by the general procedure B; white solid (173.8 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.77 (m, 4H), 6.93–6.90 (m, 4H), 6.71 (s, 2H), 3.76 (s, 6H), 2.17 (s, 3H), 1.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.7 (d, $J_{P\text{-}C}$ = 74.5 Hz), 163.0 (d, $J_{P\text{-}C}$ = 2.6 Hz), 140. 4, 136.5 (d, $J_{P\text{-}C}$ = 39.4 Hz), 134.9, 133.9 (d, $J_{P\text{-}C}$ = 10.3 Hz), 128.9, 120.7 (d, $J_{P\text{-}C}$ =

100.3 Hz), 114.5 (d, J_{P-C} = 12.8 Hz), 55.4, 21.3, 19.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 15.4.



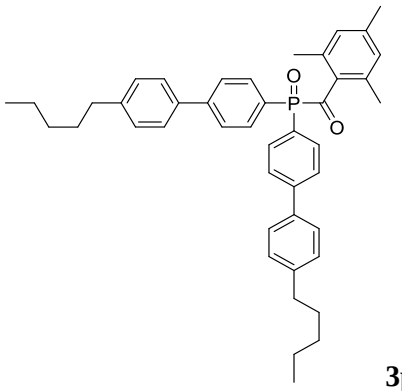
3n

(2,4,6-trimethylbenzoyl)(4,4,5,5-tetramethyl-1,3,2-dioxaphosphinate (3n). Prepared by the general procedure B (20 mol % of $MeSiCl_3$ and 1.2 equiv. Et_3N, 120 °C); brown oil (156.3 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.83 (s, 2H), 2.27 (s, 6H), 2.26 (s, 3H), 1.52 (s, 6H), 1.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.2 (d, J_{P-C} = 157.6 Hz), 140.5, 136.6 (d, J_{P-C} = 58.3 Hz), 134.9, 129.0, 90.1, 25.1 (d, J_{P-C} = 3.3 Hz), 24.1 (d, J_{P-C} = 5.1 Hz), 21.3, 19.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.7. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{16}H_{23}O_4PNa$ 333.1232, Found 333.1241.



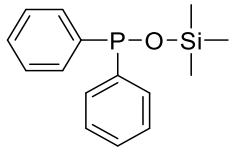
3o

1,4-phenylenebis(2,4,6-trimethylbenzoyl(phenyl)phosphine oxide) (3o). Prepared by the general procedure B (3 equivalents of MesCOCl was used); white solid (274.0 mg, 74% yield). mp 238–240 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08–8.04 (m, 4H), 7.94–7.89 (m, 4H), 7.53–7.42 (m, 6H), 6.74 (s, 4H), 2.19 (s, 6H), 1.94 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 218.2 (d, J_{P-C} = 72.3 Hz), 139.9, 134.8 (d, J_{P-C} = 40.6 Hz), 134.2 (d, J_{P-C} = 2.7 Hz), 133.9, 133.3 (d, J_{P-C} = 2.6 Hz), 131.3 (d, J_{P-C} = 76.5 Hz), 130.8 (d, J_{P-C} = 9.6 Hz), 128.0, 127.9, 127.8 (d, J_{P-C} = 92.8 Hz), 20.2, 18.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 12.0. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{38}H_{36}O_4P_2Na$ 641.1987, Found 641.2018.



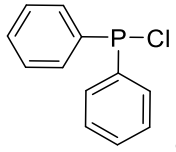
3p

(2,4,6-trimethylbenzoyl)di(4'-n-amyl-[1,1'-biphenyl]-4-yl)phoshine oxide (3p). Prepared by the general procedure B; white solid (249.6 mg, 65% yield). mp 144–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09–8.04 (m, 4H), 7.75–7.72 (m, 4H), 7.54 (d, 4H, J = 8.0 Hz), 7.27 (t, 4H, J = 8.0 Hz), 6.83 (s, 2H), 2.65 (t, 4H, J = 6.8 Hz), 2.27 (s, 3H), 2.08 (s, 6H), 1.69–1.63 (m, 4H), 1.36–1.33 (m, 8H), 0.90 (t, 6H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.4 (d, $J_{P\text{-}C}$ = 72.7 Hz), 145.2 (d, $J_{P\text{-}C}$ = 1.8 Hz), 143.5, 140.7, 137.1, 135.1, 132.5 (d, $J_{P\text{-}C}$ = 8.5 Hz), 129.2, 129.0, 127.9 (d, $J_{P\text{-}C}$ = 94.7 Hz), 127.3, 127.2, 35.7, 31.6, 31.2, 22.7, 21.3, 19.9, 14.1; ^{31}P NMR (162 MHz, $CDCl_3$): δ 15.0. HRMS (ESI-TOF): m/z: ($[M+Na]^+$) Calcd. for $C_{44}H_{49}O_2PNa$ 663.3368, Found 663.3372.



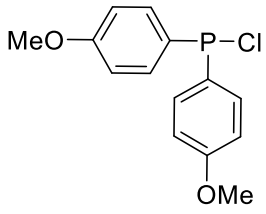
2a

diphenyl((trimethylsilyl)oxy)phosphine (2a). Under argon atmosphere, to a dry Schleck tube was in sequence added $Ph_2P(O)H$ (1 mmol), THF (5 mL), TMSCl (1.2 mmol) and Et_3N (1.2 mmol), then the mixture was stirred at 25 °C for overnight. After the reaction, the mixture was filtered and washed with hexane under argon atmosphere, and then removal all the volatile compounds afforded a pure colorless oil (274 mg, 99% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, 4H, J = 7.2 Hz), 7.42–7.33 (m, 6H), 0.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6 (d, $J_{P\text{-}C}$ = 20.1 Hz), 129.6 (d, $J_{P\text{-}C}$ = 22.4 Hz), 129.1, 128.4 (d, $J_{P\text{-}C}$ = 7.0 Hz), 1.2 (d, $J_{P\text{-}C}$ = 2.9 Hz),; ^{31}P NMR (162 MHz, $CDCl_3$): δ 95.3.



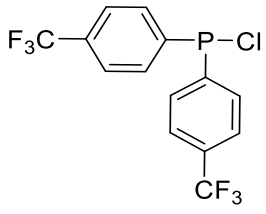
4a

Chlorodiphenylphosphine (4a). Preparation by procedure C with 205 mg, 93% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.59 (m, 4H), 7.43–7.41 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.94 (d, $J_{P\text{-}C}$ = 32.4 Hz), 131.87 (d, $J_{P\text{-}C}$ = 24.2 Hz), 130.48, 128.75 (d, $J_{P\text{-}C}$ = 7.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 82.42.



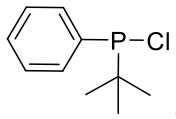
4b

Chlorobis(4-methoxyphenyl)phosphine (4b). Preparation by Procedure C with 243 mg, 87% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (t, 4H, J = 8.0 Hz), 6.92 (d, 4H, J = 8.8 Hz), 3.81 (s, 3H); ^{31}P NMR (162 MHz, $CDCl_3$): δ 84.82.



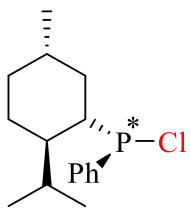
4c

Chlorobis(4-trifluoromethylphenyl)phosphine (4c). Preparation by Procedure C (50 ^{o}C, overnight) with 342 mg, 96% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72–7.66 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.73 (d, $J_{P\text{-}C}$ = 34.9 Hz), 132.69 (d, $J_{P\text{-}C}$ = 32.6 Hz) 132.02 (d, $J_{P\text{-}C}$ = 24.3 Hz),125.70 (b), 123.72 (d, $J_{F\text{-}C}$ = 271.2 Hz);^{31}P NMR (162 MHz, $CDCl_3$): δ 75.58.



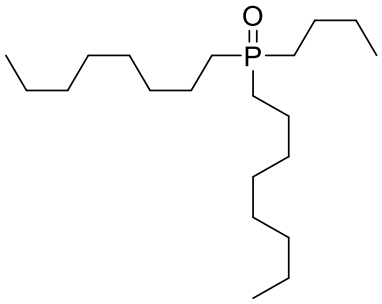
4d

tert-butylchloro(phenyl)phosphine (4d). Preparation by Procedure C with 188 mg, 94% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65–7.60 (m, 2H), 7.43–7.39 (m, 3H), 1.05 (d, 9H, J = 13.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.65 (d, $J_{P\text{-}C}$ = 39.9 Hz), 131.93 (d, $J_{P\text{-}C}$ = 25.2 Hz), 130.20, 127.96 (d, $J_{P\text{-}C}$ = 8.1 Hz);^{31}P NMR (162 MHz, $CDCl_3$): δ 108.22.



4e

Chloro((1R,2R,5S)-2-isopropyl-5-methylcyclohexyl)(phenyl)phosphine (4e). Preparation by Procedure C (r.t., 1h) with 276 mg, 98% yield, *dr* ratio = 74/26, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (t, 2H, *J* = 7.2 Hz), 7.44–7.35 (m, 3H), 2.68–2.63 (m, 1H), 1.73–1.67 (m, 3H), 1.44–1.18 (m, 3H), 1.13–1.02 (m, 2H), 0.98 (d, 3H, *J* = 6.8 Hz), 0.89 (d, 3H, *J* = 6.8 Hz), 0.77 (d, 3H, *J* = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 105.75 (74%), 101.45 (26%).



4f'

Butyldioctylphosphine oxide (4f'). Preparation by procedure D with 218 mg, 66% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.80 (b, 4H), 1.55 (b, 5H), 1.37 (b, 7H), 1.25–1.24 (m, 18H), 0.91 (d, 3H, *J* = 6.0 Hz), 0.85 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.87, 31.43, 29.214, 29.141, 24.53, 24.01, 22.70, 21.93, 14.15, 13.75; ^{31}P NMR (162 MHz, $CDCl_3$): δ 51.31. MS (ESI) m/z: ([M]+) Calcd for $C_{20}H_{43}OP$ 330, found 330.

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[9] The slightly lower yield of TPO prepared by one-pot was attributed to side reactions of $Ph_2P(O)H$ and MesCOCl generating Ph_2PCl. See: Zhang, J.-Q., Yang, S., Han, L.-B. *Tetrahedron Lett.* **2020**, *61*,151556.

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[11] In industrial applications, the most significant acylphosphine oxide photoinitiators are diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO), ethyl(2,4,6-trimethylbenzoyl) phenylphosphinate (TPO-L) and phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (BAPO). See: Introduction of acylphosphine oxide photoinitiator. http://www.sellchems.com/acylphosphine-oxide-photoinitiator/

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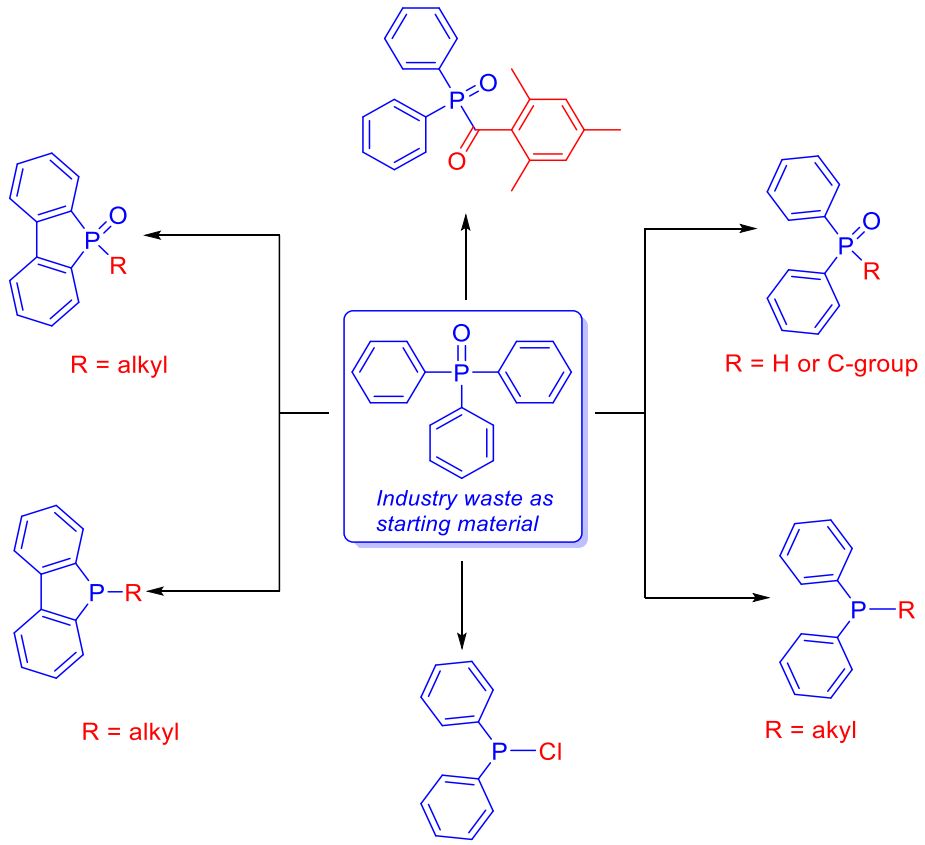
Chapter 6 Conclusions

The studies on the efficient utilization of an industry waste-triphenylphosphine oxide had been comprehensively carried out (Scheme 6.1). By using the triphenylphosphine oxide as starting material, a series of valuable organophosphorus compounds including those pentavalent phosphorus such as diphenylphosphine oxide, diphenyl(alkyl)phosphine oxides, diphenyl(aryl)phosphine oxides, dibenzophosphole oxides as well as the trivalent phosphorus like diphenyl(alkyl)phosphines, diphenyl chloride and dibenzophospholes, were efficiently and selectively synthesized. This systematical study not only solve the long-time waste problem of triphenylphosphine oxide, but also provide a series of new approaches toward organophosphorus compounds that are tediously accessed by the classical methods.

Scheme 6.1. Utilization of triphenylphosphine oxide: from a waste to valuables



List of Publications

1. **Zhang, J.-Q**.; Ye, J.; Huang, T.; Shinohara, H.; Fujino, H.; Han, L.-B.* Conversion of triphenylphosphine oxide to organophosphorus via selective cleavage of C-P, O-P, and C-H bonds with sodium. *Commun. Chem.* **2020**, *3*, 1−9. (Chapter 2)

2. **Zhang, J.-Q.**; Ikawa, E.; Fujino, H.; Naganawa, Y.; Nakajima, Y.; Han, L.-B.* Selective C-P(O) Bond Cleavage of Organophosphine Oxides by Sodium. *J. Org. Chem*. **2020**, *85*, 14166–14173. (Chapter 3)

3. **Zhang, J.-Q.**; Han, L.-B.* Chlorosilane-Catalyzed Coupling of Hydrogen Phosphine Oxides with Acyl Chlorides Generating Acylphosphine Oxides. *Org. Lett*. **2020**, *22*, 4633−4637. (Chapter 5)

4. **Zhang, J.-Q**.; Yang, S.; Han, L.-B.* Facial Conversion of Secondary Phosphine Oxides $R^1R^2P(O)H$ to Chlorophosphines R^1R^2PCl by Acetyl Chloride. *Tetrahedron Lett*. **2020**, *61*, 151556. (Chapter 5)

5. **Zhang, J.-Q.**; Han, L.-B.* Reductive conversion of phosphoryl P(O) compounds to trivalent organophosphines R_3P. *Tetrahedron. Lett*. **2021**, *67*, 152870. (Chapter 4)

6. **Zhang J.-Q.**; Zhao, J.; Li, C.; Ye, J.; Han, L.-B.* Conversion of *a*-hydroxy(2,4,6-trimethylbenzyl)diphenyl phosphine oxide to TPO: oxidation *vs* decomposition. *Phosphorus Sulfur Silicon Relat. Elem.* **2021**, *196*, 207–210.

7. **Zhang, J.-Q.**; Ye, J.-J.; Han, L.-B.* Selective C-P bond cleavage of tertiary phosphine boranes by sodium. *Phosphorus Sulfur Silicon Relat. Elem.* **2021**, DOI: 10.1080/10426507.2021.1948851.

8. Ye, J.; **Zhang, J.-Q.**; Saga, Y.; Onozawa, S.Y.; Kobayashi, S.; Sato, K.; Fukaya, N.; Han, L.-B.* Ready Approach to Organophosphines from ArCl via Selective Cleavage of C–P Bonds by Sodium. *Organometallics* **2020**, *39*, 2682−2694.

9. Li, C.; Wang, Q.; **Zhang, J.-Q.**; Ye, J.; Xie, J.; Xu, Q.*; Han, L.-B.* Water determines the products: An unexpected Brønsted acid-catalyzed PO–R cleavage of P (III) esters selectively producing P (O)–H and P (O)–R compounds. *Green Chem.* **2019**, *21*, 2916−2922.

Acknowledgements

First of all, I very much thank my supervisor Prof. Li-Biao Han for his initial acceptance that provides such a precious opportunity for me to pursuit the Ph. D degree of Chemistry in University of Tsukuba and to experience a three-year unforgettable life in Japan. During the course and research in the last few years, Prof. Han guided me with tremendous patience and encouragements on how to establish good scientific literacy, conduct the chemical experiments efficiently as well as to prepare manuscripts. His extensive and profound knowledge in organic chemistry is what I admire, his pragmatic spirits of focusing on the practical and useful research as well as his perseverance of concentrating on the field of phosphorous chemistry for several decades of years inspired me a lot. It was a great pleasure to learn from him in my lifetime.

I would also like to express my appreciations to the lab mates in AIST. Thank Dr. Chunya Li, Dr. Jingjing Ye, Ms. Jingzhuo Zhao, Dr Jing Xiao, Dr. Zhiping Yang and the secret Ms. Tanaka for their kind help and assistance on my study and life. Working with them in the same lab is full of enjoyment. So much gratitude also must be given to everyone who I've met in Japan during the past 3 years, including Dr Yazhou Chen (NIMS), Dr Ningjie Fang (AIST), Dr Xiao Zheng (NIMS), Dr Yaping Hu (University of Tsukuba), etc.

On the other hand, I shall give my thanks to my best friends Dr. Peiming Liu, Xinwei Zhu and Dong Xia, they are the soulmates who always support me at any time, keep in close touch with me to relieve my anxiety and accompany me by chatting on the internet, even we are so far away from each other.

I also appreciate the financial support sponsored by China Scholarship Council (CSC).

Finally, I'd like to convert my deepest gratitude to my mother Mrs. Xingui Wen and my grandmother Mrs Xuejiao Hu for bringing me up and their selfless encouragement and support on my road to exploring the scientifical world.

July 2021, Tsukuba, Japan

Jian-Qiu Zhang