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## ARTICLE

## Direct synthesis of phosphorothioites and phosphorothioates from white phosphorus and thiols

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White phosphorus (P<sub>4</sub>) is still the major commercial P-atom source for the production of organophosphorus compounds. Conventionally, C–S–P bonds were constructed from environmentally questionable P(O)X directly or indirectly. From the green chemistry point of view, formation of C–S–P bonds in an easy-to-operate and atom-economical fashion from inorganic molecule P<sub>4</sub> is essential because it will avoid the hazardous chlorination process. Only five methods for the formation of C–S–P bonds from P<sub>4</sub> have been developed over the past 70 years. Here, the first general and high-yielding synthesis of P(SR)<sub>3</sub> and P(O)(SR)<sub>3</sub> involving P<sub>4</sub> and thiols is presented. With the use of KOH or K<sub>2</sub>CO<sub>3</sub> as base, DMSO-toluene as solvent, both arylthiols and alkylthiols are tolerant in this transformation. The reaction is characterized by a complete conversion of white phosphorus. This operationally simple and environmentally sound reaction shows broad scope of substrates and good functional group tolerance. Moreover, this method can be easily adapted to large-scale preparation.

## Introduction

The chemistry of activation of small molecules continues to fascinate researchers worldwide. Neutral white phosphorus (P<sub>4</sub>), prepared by the industrial reduction of phosphate rocks, is still the major commercial P-atom source for the production of organophosphorus compounds (OPCs).<sup>1</sup> However, multistep and environmentally toxic processes are usually involved to make OPCs from white phosphorus via chlorinated or oxygenated products (such as PCl<sub>3</sub>, PCl<sub>5</sub>, POCl<sub>3</sub>, P<sub>4</sub>O<sub>6</sub>, or P<sub>4</sub>O<sub>10</sub>). This represents a general problem for its industrial use, since large amounts of HCl or metal halide are produced during the following industrial processes to obtain the desired OPCs.<sup>2</sup> The highly toxic and pyrophoric phosphine (PH<sub>3</sub>) gas is also used to prepare various OPCs.<sup>3</sup> As such, the activation of white phosphorus remains a popular and competitive area of research to avoid the environmentally questionable P–Cl compounds in organophosphorus chemistry.<sup>4–7</sup> Although the activation of P<sub>4</sub> by main group elements,<sup>8–12</sup> transition-metal complexes<sup>13–18</sup> and rare-earth-metals<sup>19</sup> started and is still being well developed, the synthesis of organophosphorus compounds with high yields via a combination of white phosphorus with organic substrates is still a main challenge in this area.<sup>20,21</sup>

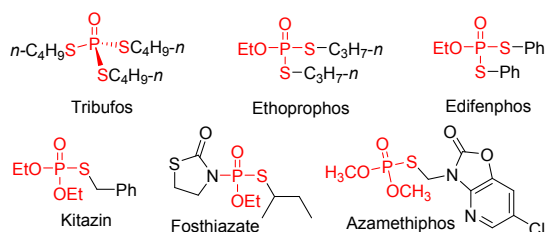
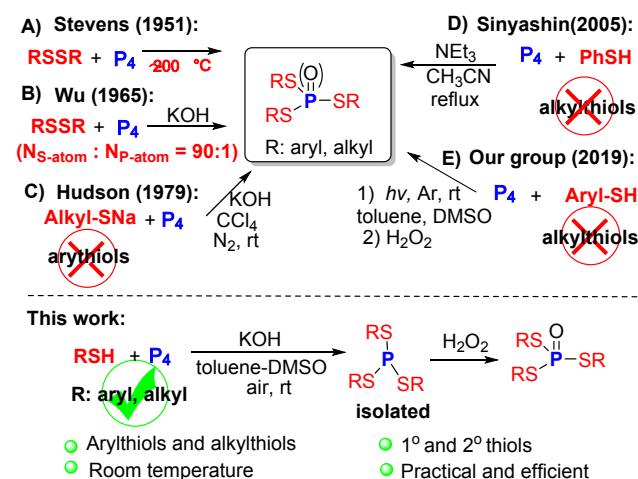


Fig. 1 Selected agrochemicals of phosphorothioates.

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Sulfur-containing organophosphorus compounds (C–S–P bonds) provide important utilities in the fields of medicinal chemistry and agrochemistry.<sup>22–25</sup> In particular, some simple phosphorothioates such as tribufos, ethoprophos, edifenphos, kitazin, fosthiazate, and azamethiphos have been found to be very effective pesticides and insecticides (Figure 1).<sup>25</sup> In fact, at least 60 molecules containing C–S–P bonds were used as pesticides.<sup>25</sup>

Several elegant strategies for the construction of C–S–P bonds have been developed:<sup>26</sup> a) nucleophilic substitution of the moisture sensitive S–X directly or indirectly;<sup>27,28</sup> b) condensation reaction between phosphorylation reagents and thiols;<sup>29</sup> c) dehydrogenative coupling of P(O)H groups with thiols;<sup>30–32</sup> d) multicomponent reactions of diaryl disulfide, alkyl halides, arylboronic acids, diazonium, or iodonium salts using elemental sulfur and R<sub>2</sub>P(O)H compounds.<sup>33–36</sup> Surprisingly, only a small effort has been devoted to the preparation of these substances from elemental phosphorus.

Scheme 1. C–S–P(O) bond formations from P<sub>4</sub>.

Only five methods for the preparation of C–S–P bonds from P<sub>4</sub> are known. In 1951, interaction of dialkyl disulfides and P<sub>4</sub> at 170–210 °C was reported by Stevens and coworkers (Scheme 1A).<sup>37</sup> In 1965, Wu developed the KOH-mediated reactions of white phosphorus with a large excess of dialkyl (diaryl) disulfides (90 equivalents of sulfur atom per phosphorus atom) in dipolar aprotic solvents leading to trialkyl phosphorotrithioite [P(III)] (Scheme 1B).<sup>38</sup> Because white phosphorus and thiols are easily oxidized by stoichiometric oxidants, Hudson and coworkers investigated the sulfenylation of white phosphorus with sodium alkanethiolates under a nitrogen atmosphere in 1979. Moreover, this approach is only suitable for highly active alkyl thiols, and fails for the synthesis of triaryl phosphorotrithioites (Scheme 1C).<sup>39,40</sup> In 2005, Sinyashin group reported the reactions of thiophenol with white phosphorus at an elevated temperature leading to *S,S,S*-triphenyl phosphorotrithioate in moderate yield; however, alkylthiols didn't complete this kind of conversion (Scheme 1D).<sup>41–43</sup> In 2019, our group developed a light-promoted phosphorylation of arylthiols from white phosphorus (Scheme 1E).<sup>44</sup> In light of the significance of these reports, in the present work, we sought to develop a general method for the synthesis of P(SR)<sub>3</sub> and P(O)(SR)<sub>3</sub> with a broad substrate scope, a good atom economy, and an environmentally friendly strategy (Scheme 1).

## Results and discussion

A preliminary optimization of the reaction conditions was carried out with *n*-C<sub>10</sub>H<sub>21</sub>SH and P<sub>4</sub> as reaction partners (Table 1). Inspired by Sinyashin's significant work,<sup>41</sup> triethylamine was investigated in this reaction, but it failed to complete the process (entries 1 and 2). In the presence of KOH, toluene and CH<sub>3</sub>CN afforded product (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P (**3a**) with very low yield and the remaining P<sub>4</sub> was stable at room temperature (entries 3 and 4). When the reaction was conducted under reflux conditions for 4 h, no desired product **3a** or (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P(O) **4w** was obtained and P<sub>4</sub> was decomposed completely (entries 3 and 4). In order to improve the conversion of P<sub>4</sub> to C–S–P bonds, a further reaction was conducted under oxygen at room temperature, giving a 100% conversion of white phosphorus but a low yield of **3a** (entry 5). When DMSO was used as the solvent, white phosphorus was disappeared completely after 2 hours, but only trace amount of **3a** was obtained (entry 6). Pleasingly, the targeted product **3a** was detected in 45% yield in the mixed solvent of toluene (0.9 mL) and DMSO (0.1 mL) at room temperature for 4 h (entry 7). The amount of DMSO seemed to significantly affect the reaction (entries 7–10). Increasing the amount of DMSO from 20% (entry 8) to 50% (entry 9) resulted in a higher yield of the transformation. When the amount of DMSO was further increased to 70%, the reaction afforded **3a** with a slightly lower yield (entry 10). The amount of KOH was also crucial to this reaction (entries 10–13). Interestingly, the use of 130 mol% of KOH afforded product **3a** in 78% yield (entry 11). Addition of 200 mol% of KOH produced **3a** in 65% yield (entry 12). The yield of **3a** was further increased to 84% by using 6 equivalents of *n*-C<sub>10</sub>H<sub>21</sub>SH (entry 14) along with producing **4w** in 8% yield. The reaction performed under an argon atmosphere led to a 9% yield (entry 15). The reaction of *n*-

C<sub>10</sub>H<sub>21</sub>SH with P<sub>4</sub> under oxygen in toluene-DMSO gave both the normal coupling product (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P **3a** and (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P(O) **4w** in 55% and 28% yields, respectively (entry 15). The reaction was carried out under air, in an open flask with a calcium chloride drying tube, leading to **3a** and **4w** in 60% and 25% yields, respectively (entry 15). *t*-BuOK was also a suitable base, affording the product **3a** in 80% yield (entry 16). Other alkali-metal salts (K<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>) and organic bases (pyridine, DBU and NEt<sub>3</sub>) could not promote this process (entry 17). In the presence of 130 mol% of *t*-BuOK or KOH, other solvents such as toluene-DMF, -CH<sub>3</sub>CN, -THF, -EtOH, -1,4-dioxane were less effective, indicating that DMSO was vital in the transformation (entries 18 and 19).

**Table 1.** Synthesis of (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P (**3a**) from *n* decane-1-thiol and 0.25P<sub>4</sub> under air <sup>a</sup>

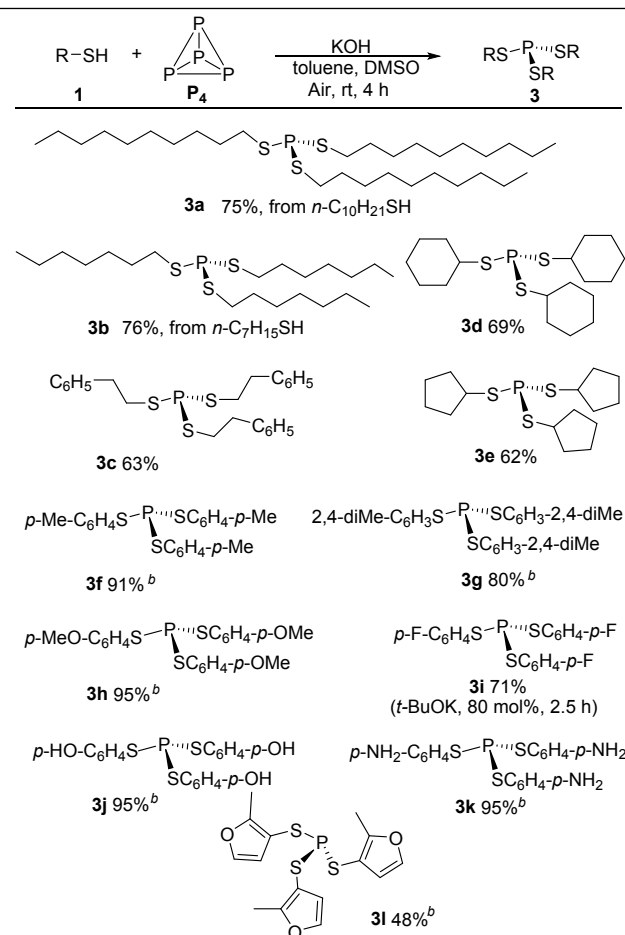
Entry	n <sup>b</sup>	Base <sup>c</sup>	Solvent (mL)	Yield <sup>d</sup>
1 <sup>e</sup>	3.6	(Et) <sub>3</sub> N (300%)	CH <sub>3</sub> CN	<10
2 <sup>e</sup>	3.6	(Et) <sub>3</sub> N (300%)	PhMe	<10
3 <sup>e</sup>	3.6	KOH (100%)	PhMe	<18
4 <sup>e</sup>	3.6	KOH (100%)	CH <sub>3</sub> CN	<10
5	3.6	KOH (100%)	PhMe (O <sub>2</sub> balloon)	<10
6	3.6	KOH (100%)	DMSO	<10
7	3.6	KOH (100%)	PhMe(0.9)+DMSO(0.1)	45
8	3.6	KOH (100%)	PhMe(0.8)+DMSO(0.2)	60
9	3.6	KOH (100%)	PhMe(0.5)+DMSO(0.5)	74
10	3.6	KOH (100%)	PhMe(0.3)+DMSO(0.7)	71
11	3.6	KOH (130%)	PhMe(0.5)+DMSO(0.5)	78
12	3.6	KOH (200%)	PhMe(0.5)+DMSO(0.5)	65
13	3.6	KOH (80%)	PhMe(0.5)+DMSO(0.5)	70
14	6	KOH (130%)	PhMe(0.5)+DMSO(0.5)	84
15	6	KOH (130%)	PhMe(0.5)+DMSO(0.5)	5–60 <sup>f</sup>
16	6	<i>t</i> -BuOK(130%)	PhMe(0.5)+DMSO(0.5)	80
17	6	Base <sup>g</sup>	PhMe(0.5)+DMSO(0.5)	0–20
18	6	<i>t</i> -BuOK (130%)	PhMe(0.5)+DMF(0.5)	36
19	6	KOH (130%)	PhMe(0.5)+Solvent(0.5) <sup>h</sup>	<15

<sup>a</sup> Reaction conditions: (1) *n*-C<sub>10</sub>H<sub>21</sub>SH (n eq.), P<sub>4</sub> (6.2 mg, 0.050 mmol of P<sub>4</sub>, 0.2 mmol of P atom, a 0.10 M solution of P<sub>4</sub> in toluene, 0.5 mL), and base in solvent (1 mL) were stirred at room temperature for 4 h under aerobic conditions. <sup>b</sup> Equivalents of thiol per P-atom. <sup>c</sup> mol% per P-atom. <sup>d</sup> Yield of **3a**, determined by <sup>31</sup>P NMR analysis of the crude reaction mixture using (C<sub>6</sub>H<sub>5</sub>O)<sub>3</sub>P(O) as an internal standard. <sup>e</sup> The reactions were conducted both at room temperature and under reflux conditions. <sup>f</sup> Atmosphere: Ar (4–24 h, <9%); O<sub>2</sub> balloon (**3a**, 55%; **4w**, 28%); Open to air (**3a**, 60%; **4w**, 25%). <sup>g</sup> Base: K<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, pyridine, DBU or (Et)<sub>3</sub>N as a base. <sup>h</sup> Solvent: CH<sub>3</sub>CN, THF, EtOH, 1,4-dioxane.

We then evaluated the reaction of white phosphorus and thiols **1** in the presence of KOH at room temperature under air (Table 2). It is worth noting that relatively hindered primary thiols (*n*-C<sub>10</sub>H<sub>21</sub>SH, *n*-C<sub>7</sub>H<sub>15</sub>SH, 2-phenylethane-1-thiol) were efficiently phosphorylated with our method to afford the phosphorotrithioites [P(III)] **3a–3c** in 75%, 76% and 63% yields, respectively. When secondary thiols such as cyclohexanethiol and cyclopentanethiol were employed for the transformation, the corresponding products **3d** and **3e** were obtained in 69% and 62% yields. Moreover, this method provided a direct approach to *S,S,S*-triaryl phosphorotrithioites. Aromatic thiols

bearing Me, MeO, or F groups furnished the desired phosphorotrithioates (P(III)) in high yields (**3f-3i**). Notably, free amine and hydroxy groups, which hardly survive in traditional approaches, were tolerated under these conditions to afford the corresponding products **3j** and **3k** in high yields. Furthermore, 5-methylfuran-2-thiol containing a reactive furan ring was competent to do this transformation, affording the product **3l** in 48% yield. A small amount of phosphorotrithioates [P(V), <10%] were detected by <sup>31</sup>P NMR analysis of the crude reaction mixture in all the above-mentioned reactions.

**Table 2.** Synthesis of phosphorotrithioates [P(III)]<sup>a</sup>

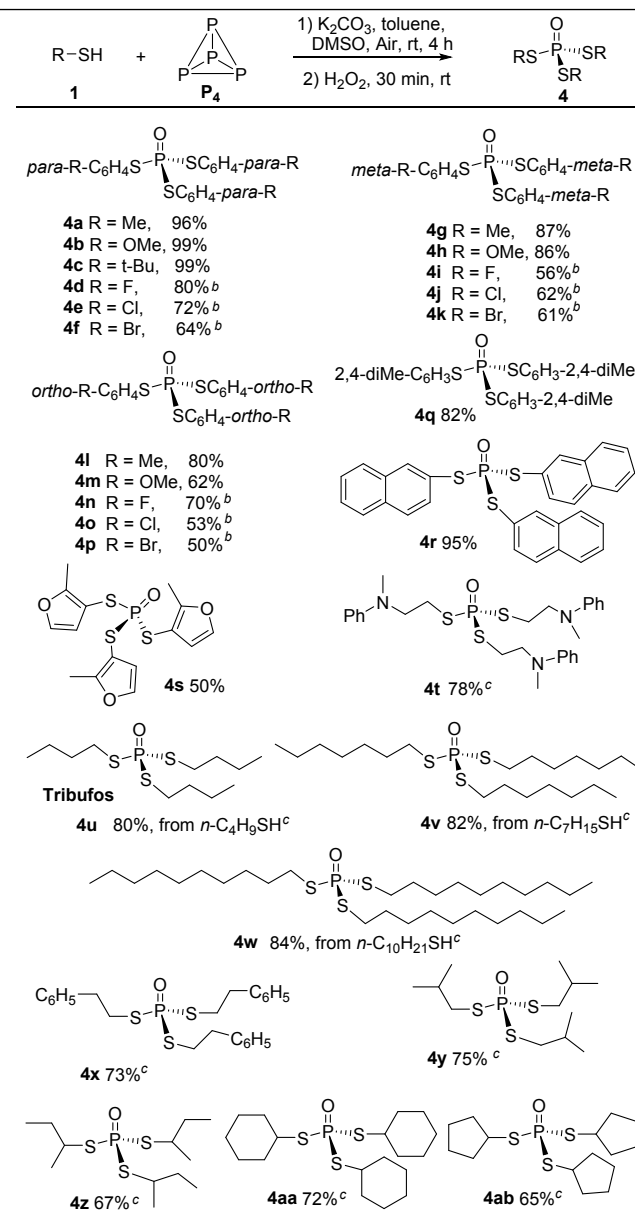


<sup>a</sup> Thiol **1** (1.2 mmol, 6 equivalents per phosphorus atom), P<sub>4</sub>-toluene solution (6.2 mg total P<sub>4</sub>, 0.050 mmol, a 0.10 M solution of P<sub>4</sub> in toluene, 0.5 mL), DMSO (0.5 mL), KOH (0.26 mmol, 16 mg), room temperature, under air, 4 h. Yields of isolated products. <sup>b</sup> K<sub>2</sub>CO<sub>3</sub> (0.2 mmol, 28 mg), 4 h.

Encouraged by the above results, we decided to further explore the synthesis of phosphorotrithioates [P(V), Table 3]. Aromatic thiols **1** with different *para*, *meta*, and *ortho* substituents all gave the corresponding products in good yields (**4a-4p**). Steric effect played a key role in the synthesis of phosphorotrithioates from white phosphorus. For example, the *para*-methyl, *para*-methoxyl, *para*-tertbutyl substituted aryl thiols reacted with P<sub>4</sub> efficiently and gave the desired products **4a-c** in almost quantitative yields. Benzenethiols with *ortho*-methyl (**4l**) and *ortho*-methoxyl (**4m**) substituents on the aromatic ring afforded the desired products in

low yields under the standard conditions (**4a** and **4b** vs **4l** and **4m**). Halogen atoms such as fluoro, chloro, and bromo on the aromatic ring were unaffected under the present reaction conditions to afford the corresponding products **4d-4f**, **4i-4k**, and **4n-4p** in moderate to good yields, which could allow for further synthetic transformations. Furthermore, both bulky 2,4-dimethylbenzenethiol and naphthalene-2-thiol gave the corresponding products **4q** and **4r** in satisfied yields. Significantly, the reaction proceeds well in the presence of a reactive furan ring, giving the product **4s** in 50% yield.

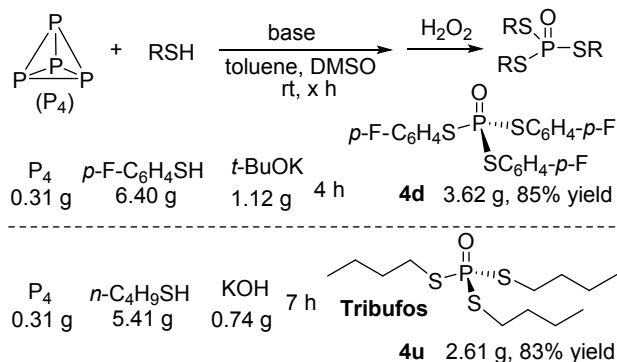
**Table 3.** Synthesis of phosphorotrithioates [P(V)]<sup>a</sup>



<sup>a</sup> 1) Thiol **1** (1.0 mmol, 5 equivalents per phosphorus atom), P<sub>4</sub>-toluene solution (6.2 mg total P<sub>4</sub>, 0.050 mmol, a 0.10 M solution of P<sub>4</sub> in toluene, 0.5 mL), DMSO (0.5 mL), K<sub>2</sub>CO<sub>3</sub> (0.2 mmol, 28 mg), room temperature, under air, 4 h. 2) 30% H<sub>2</sub>O<sub>2</sub> (1 mL), 30 min, rt. Yields of isolated products. <sup>b</sup> t-BuOK (0.2 mmol), 2.5 h. <sup>c</sup> Thiol **1** (1.2 mmol), KOH (0.26 mmol, 16 mg).

Aside from aromatic thiols, aliphatic thiols could react well with white phosphorus to produce **4t–4ab** in good yields (Table 3). It is noteworthy that tribufos (**4u**), a famous plant growth regulator, was obtained in 80% yield. When other aliphatic primary thiols such as heptane-1-thiol, decane-1-thiol, 2-phenylethane-1-thiol and 2-methylpropane-1-thiol could be transformed into their corresponding *S,S,S*-trialkyl phosphorothioates **4v–4y** in good yields. In addition, aliphatic secondary thiols such as butane-2-thiol, cyclohexanethiol and cyclopentanethiol could be easily coupled with  $P_4$ , producing the products **4z–4ab** in 67%, 72% and 65% yields, respectively.

In order to demonstrate the application potential of this method, the 10.0 mmol scale (P atom) reactions of  $P_4$  with 4-fluorobenzenethiol and  $P_4$  with 1-butanethiol were employed and delivered **4d** and **4u** in 85% and 83% yields, respectively (Scheme 2).



**Scheme 2.** Gram-scale preparation of **4d** and **4u**.

To understand the underlying mechanism, further experiments were conducted (Scheme 3). When 12 equivalents of 1,1-diphenylethylene, norbornene, or 2,2,6,6-Tetramethyl-1-piperidinyloxy (tempo) was added into the reaction mixture under the standard conditions, the desired product **3a** was obtained in slightly lower yield, which suggested that radical transformation may be involved, but not the main process (Scheme 3-1). Carrying out the reaction of disulfide (**5**, 3 eq) and  $P_4$  generated ( $n-C_{10}H_{21}S$ )<sub>3</sub>P (**3a**) in 20% yield (Scheme 3-2). The combination of  $n-C_{10}H_{21}SH$  (**1a**, 3eq) and disulfide (**5**, 1.5 eq) produced **3a** with almost quantitative yield either in air or in an argon atmosphere, while  $n-C_{10}H_{21}SH$  (**1a**, 6 eq.) alone only gave **3a** in 9% yield under argon (Scheme 3-3 and table 1, entry 14). These results suggest that both disulfides and thiols were essential to this transformation, and oxidation of these thiolates to form thiyl species and therefore the formation of necessary disulfides should be one of the main process.

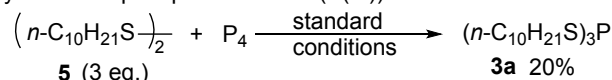
To classify the function of DMSO, further experiments were conducted (Scheme 3-4). When the reaction was conducted for 4 h under argon, the desired product **3a** was obtained in 9% yield (Table 1, entry 14). The control experiments using tetrahydrothiophene 1-oxide and *n*-butyl sulfoxide instead of DMSO were conducted, which gave **3a** in 68% and 62% yields, respectively, and the corresponding thioethers were not detected by HRMS (Scheme 3-4). Under the standard conditions without the addition of  $P_4$ ,  $n-C_{10}H_{21}SH$  (**1a**) was converted into disulfide **5** in 85% yield (Scheme 3-5).<sup>47</sup> Without DMSO, KOH or air, only a trace amount of disulfide

**5** was obtained (Scheme 3-5). These results suggest that DMSO mainly acts as a good solvent to promote the transformation.

### 1) Radical trapping experiments

$n-C_{10}H_{21}SH$	$P_4$	radical scavenger	standard conditions	<b>3a</b>
<b>1a</b>				
6 eq	1 eq	12 eq		84%
(based on P-atom)	no			
		1,1-diphenylethylene		58%
		norbornene		80%
		tempo		70%

### 2) Synthesis of phosphorotrithioite (P(III)) from disulfide



### 3) The combination of disulfide and thiol

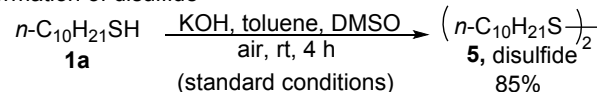
<b>1a</b>	<b>5</b>	$P_4$	standard conditions	<b>3a</b>
(3 eq.)	(1.5 eq.)		air	> 90%
			Ar	> 90%

### 4) Function of sulfoxide

<b>1a</b>	$P_4$	standard conditions	<b>3a</b>	thioether
		solvent: toluene + DMSO	84%	$\begin{matrix} S \\ \diagup \quad \diagdown \\ \text{---} \end{matrix}$ n.d.
		toluene + $\begin{matrix} S=O \\   \\ \text{---} \end{matrix}$	68%	tetrahydrothiophene n.d.
		toluene + $\begin{matrix} S=O \\   \\ \text{---} \end{matrix}$	62%	dibutylsulfane n.d.

n.d.: not detected by HRMS

### 5) Formation of disulfide

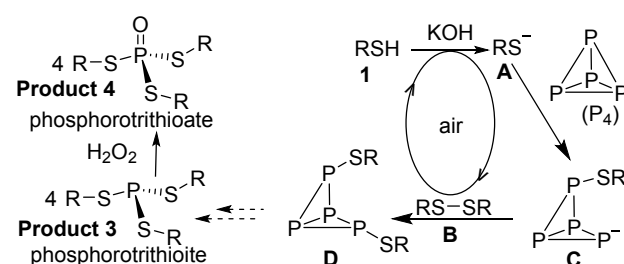


Deviation from standard conditions	without DMSO	without KOH	Argon atmosphere
	15%	trace	trace

### 6) Stability of $P_4$ in the presence of KOH

$P_4$	standard conditions	$P_4$
6.2 mg	KOH	Undestroyed
	0 mg, 0 mol%	90%
	16 mg, 130 mol%	70%
	34 mg, 300 mol%	54%
	(based on P atom)	

**Scheme 3.** Investigation for reaction mechanism.



**Scheme 4.** Tentative mechanistic pathway.

To understand why moderate yields were obtained in some transformations but along with the high conversion of P<sub>4</sub>, the stability of white phosphorus was monitored. It was found that the proportion of undestroyed P<sub>4</sub> became lower and lower with the increase of amount of KOH (Scheme 3-6). Attack by hydroxide ion on the P<sub>4</sub> tetrahedron cleaves the first phosphorus-phosphorus bond, giving the phosphide anion. Repetition of this step breaks all P-P bonds in P<sub>4</sub> under air conditions, leading to the side product potassium phosphate.<sup>48</sup>

Based on the above experiments and previous reports,<sup>46-48</sup> a possible reaction mechanism is depicted in Scheme 4. Initially, thiol **1** affords RSK **A** in the presence of KOH. Meanwhile, the oxidative coupling of thiol **1** affords disulfide **B** in the presence of KOH and air. Subsequent RSK **A** attack at a phosphorus atom with concomitant breakage of one P-P bond results in the opening of the white phosphorus tetrahedron and formation of a phosphorus-based anion **C**. The nucleophilic attack of anion **C** to disulfide **B** affords intermediate **D** along with the regeneration of RSK **A**. Further repetition of these steps results in the formation of phosphorotrithioite **3**. A final oxidation of phosphorotrithioite **3** gives phosphorotrithioate **4**.

## Conclusions

In summary, we have successfully developed the first general and high yielding synthesis of pharmacologically- and synthetically-important P(SR)<sub>3</sub> and P(O)(SR)<sub>3</sub> involving P<sub>4</sub>, arylthiols and alkylthiols. The use of KOH or K<sub>2</sub>CO<sub>3</sub> as base, DMSO-toluene as solvent, makes this transformation practical and green. The operationally simple and mild oxidative reaction shows a broad scope of substrates and a good functional group tolerance. Moreover, this method can be easily adapted to large-scale preparation.

## Experimental

**Safety note for white phosphorus (P<sub>4</sub>):** White phosphorus is spontaneously flammable; it should be stored in water or glove box. On the other hand, white phosphorus is very soluble in toluene.

### Synthesis of (*n*-C<sub>10</sub>H<sub>21</sub>S)<sub>3</sub>P(O) (**4w**) from 1-decanethiol and white phosphorus (P<sub>4</sub>)

KOH (0.26 mmol, 16 mg), *n*-C<sub>10</sub>H<sub>21</sub>SH (210 mg, 1.2 mmol), and DMSO (0.5 mL) were put into a Schlenk tube with a magnetic stirrer under air conditions. Then white phosphorus-toluene solution (6.2 mg total P<sub>4</sub>, 0.5 mL, 0.1 mol/L) was added. The tube was sealed and the reaction mixture was stirred for 4 hours at room temperature. After completion, H<sub>2</sub>O<sub>2</sub> (0.5 mL) was added slowly, and the mixture was stirred at room temperature for another 30 min. The mixture was extracted by EtOAc (3×10.0 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by flash chromatography using petroleum-AcOEt [from 50:1 to 10:1 (v/v)] as the eluent to give the product **4w** (95 mg, 84%).

### Gram-scale synthesis of (*n*-C<sub>4</sub>H<sub>9</sub>S)<sub>3</sub>P(O) (**4u**) from *n*-C<sub>4</sub>H<sub>9</sub>SH and white phosphorus (P<sub>4</sub>)

KOH (0.74 g), *n*-C<sub>4</sub>H<sub>9</sub>SH (5.41 g), and DMSO (25 mL) were put into a 100 mL-round bottomed flask with a magnetic stirrer under air conditions. Then white phosphorus-toluene solution (25 mL, 310 mg total P<sub>4</sub>, 0.1 mol/L) was added under air conditions. The flask was stoppered with a glass stopper and the reaction mixture was stirred for 7 hours at room temperature. After completion, H<sub>2</sub>O<sub>2</sub> (15 mL) was added slowly within 10 min, and the mixture was stirred at room temperature for another 2 hours. Saturated brine (30 mL) was added into the above reaction mixture. The mixture was extracted by EtOAc (3×20.0 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by flash chromatography using petroleum-AcOEt [from 50:1 to 10:1 (v/v)] as the eluent to give the product **4u** (2.61 g, 83%).

## Conflicts of interest

There are no conflicts to declare.

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