

## Cs<sub>2</sub>CO<sub>3</sub>-Mediated synthetic strategy for iprobenfos derivatives *via* thiophilic addition of *H*-phosphites on *in situ* generated thioaldehydes

Rekha Bai,<sup>a</sup> Ke-Chien Liu,<sup>a</sup> Ze-Wei Chen,<sup>a</sup> Asha Gurjar,<sup>d</sup> Satpal Singh Badsara,<sup>d</sup> and Chin-Fa Lee\*<sup>a-c</sup>

<sup>a</sup>Department of Chemistry, National Chung Hsing University, Taichung, Taiwan 402, R.O.C.

<sup>b</sup>i-Center for Advanced Science and Technology (iCAST), National Chung Hsing University, Taichung City 402, Taiwan, R.O.C.

<sup>c</sup>Innovation and Development Center of Sustainable Agriculture (IDCSA), National Chung Hsing University, Taichung City 402, Taiwan, R.O.C.

<sup>d</sup>MFOS Laboratory, Department of Chemistry, University of Rajasthan, Jaipur, Rajasthan 302004, India  
E-mail: [cfalee@dragon.nchu.edu.tw](mailto:cfalee@dragon.nchu.edu.tw)

This article is dedicated to Prof. Tien-Yau Luh on the occasion of his 76th birthday

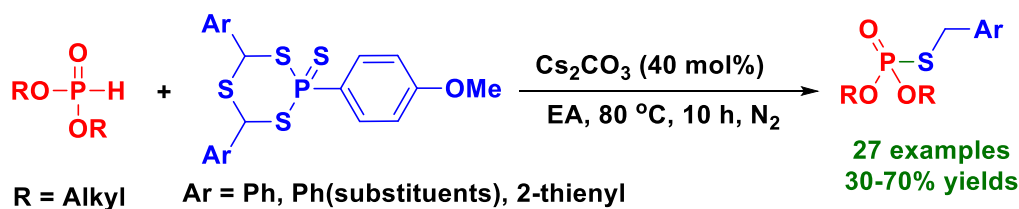
Received 07-17-2023

Accepted Manuscript 01-15-2024

Published on line 01-29-2024

### Abstract

The cesium carbonate-mediated synthetic approach for the synthesis of thiophosphates derivatives under mild conditions is reported. A variety of *H*-phosphonate successfully reacted with trithiaphosphinane sulfide derivatives possessing EWGs and EDGs. This method provides the synthetic platform for a broad spectrum of aryl sulfur surrogate to afford the desired products in 30-70% yields. In addition to practical utility, this protocol is feasible for the straightforward one-step synthesis of value-added agrochemical Iprobenfos derivatives in good yields.

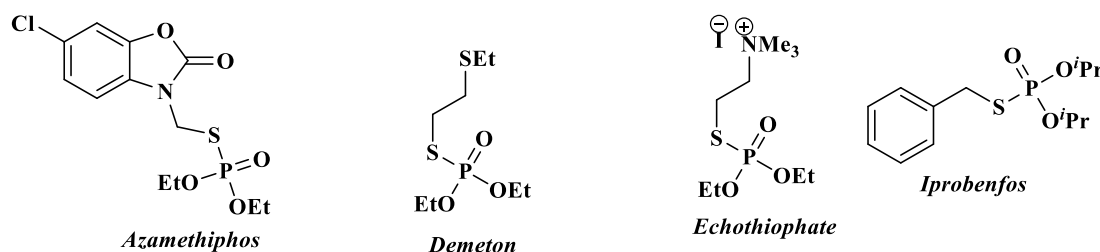


- \* Base mediated catalysis
- \* Transition-metal and Oxidant free
- \* wide functional group tolerances
- \* Gram-scale synthesis

**Keywords:** Thiophilic addition; iprobenfos derivatives; phosphorothioates

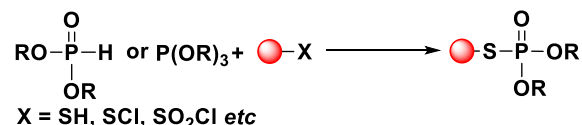
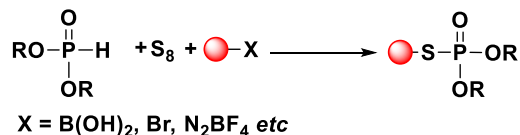
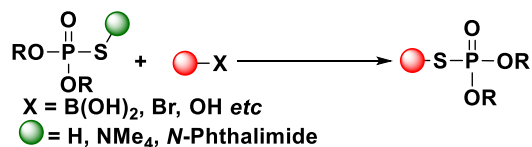
## Introduction

Phosphorothioates having the phosphorus-sulfur bond are among the important scaffolds that exist in many bioactive molecules, drugs, and functional materials. The pharmaceutically privileged molecules containing the phosphorothioates skeleton exhibit significant biological activities such as anti-viral, anti-bacterial, anti-cancer agents, anti-fungal, and anti-inflammatory.<sup>1-3</sup> Phosphorothioates molecules such as demeton-S are used as insecticides whereas omethoate is used in the agrochemical industry.<sup>4-6</sup> Phosphorothioate molecule echothiophate (AChE inhibitor) is used in cardioprotective therapeutics (Figure 1).<sup>7-8</sup> Furthermore, phosphorothioates are also used as a key intermediate for synthesizing value-added complex molecules.<sup>9-10</sup> Therefore, the chemistry of phosphorus-sulfur compounds has become an interesting area of research for the scientific community. The related preceding research work such as the nucleophilic substitution reaction of dialkyl chlorophosphate with thiols, disulfides or sulfonyl halides and the Michaelis-Arbuzov-type reaction have been associated with some drawbacks and limitations such as the requirement of high temperature, and of hazardous and moisture-sensitive sulfur reagents, as well as with environmental pollution.<sup>11-17</sup>

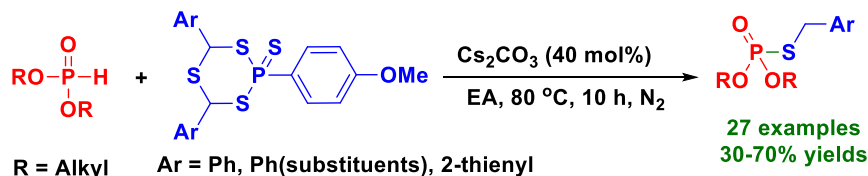


**Figure 1.** Pharmaceutically privileged molecules containing phosphorothioates system.

Numerous organic sulfide surrogates which either not easily available or in unpleasant nature as disulfides, sulfonyl chlorides, sulfonyl hydrazides, and sulfenyl cyanides have been employed as coupling partners in the phosphorothiolation processes (Scheme 1a).<sup>18-23</sup> Tang and co-workers reported a Cu-catalyzed multicomponent reaction (MCR) using aryl boronic acids, elemental sulfur, and P(O)H compounds.<sup>24</sup> Later on, the Tang group successfully achieved direct C(sp<sup>2</sup>)-H and C(sp<sup>3</sup>)-H phosphorothiolation *via* a multi-component composition strategy as shown in Scheme 1b.<sup>25-26</sup> The development of phosphorothiolic acids, phosphorothiolate salts, *O, O*-dialkyl-*S*-(*N*-phthalimido)-phosphorothioate, and dialkyl (2-cyanoethyl)-phosphonate has been achieved by phosphorothiolation process employing with alkyl halides, arylboronic acids, and arenediazonium salts, *etc* (Scheme 1c).<sup>27-30</sup> Despite the significant value of these methods for *S*-alkyl thiophosphates, the mostly substrates are pre-synthesized organic sulfides. Hence, a sustainable synthetic procedure which easily feasible with simple readily available and low-toxic reagents is still a desired place of research for phosphorothiolation reactions. Herein, we report a base-mediated novel, regioselective, and efficient synthetic approach for the synthesis of iprobenfos derivatives under mild reaction conditions (Scheme 1d).

1a) Organic sulfides as sulfur source<sup>18-23</sup>1b) Inorganic sulfides as sulfur source<sup>24-26</sup>1c) New phosphorothiolation reagents<sup>27-30</sup>

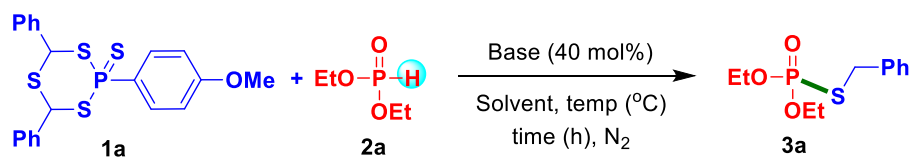
## 1d) This work:Thialdehyde as sulfur source



Scheme 1. Synthetic strategies for P-S bond formation.

## Results and Discussion

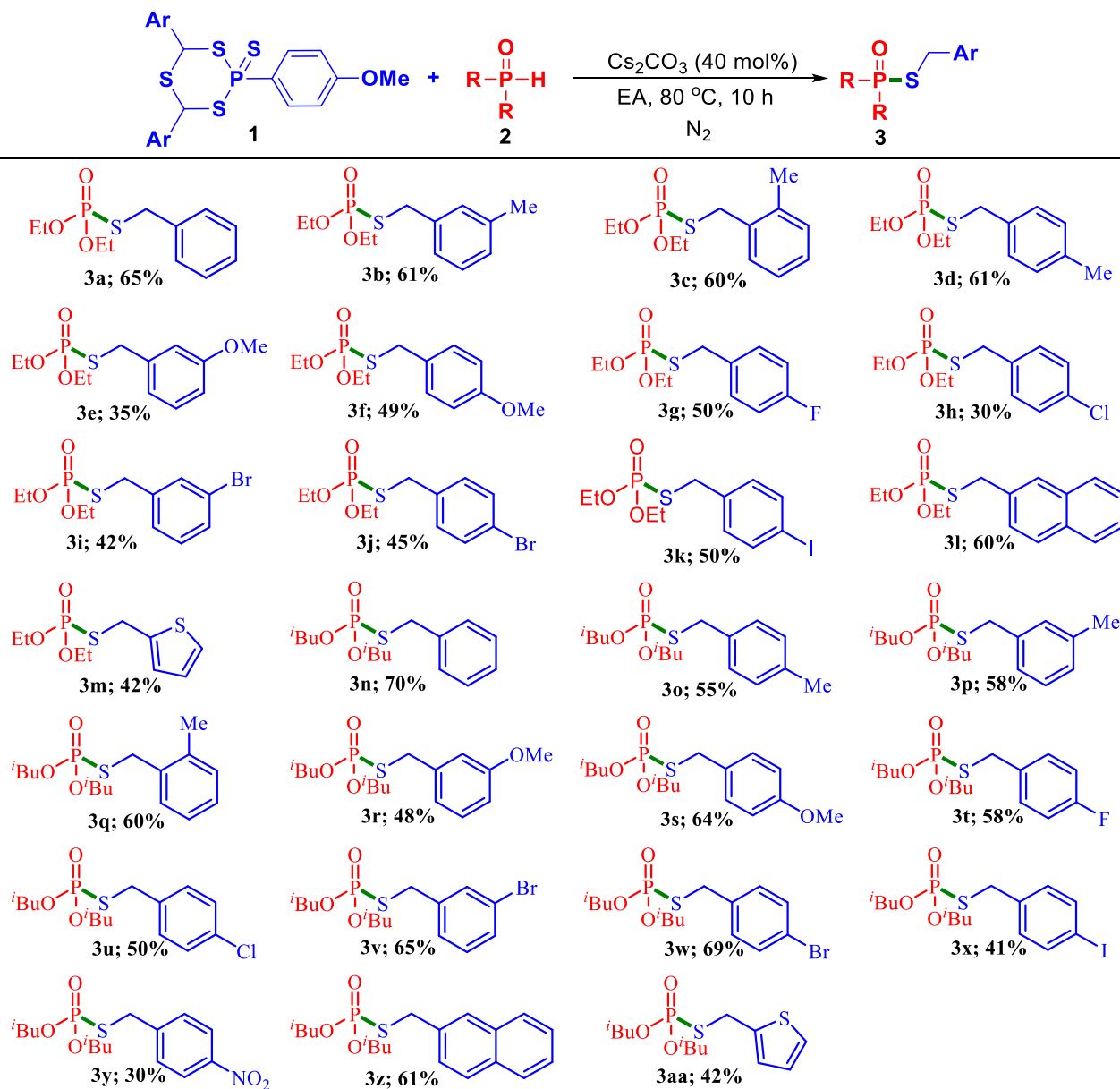
To achieve the base-catalyzed P-S bond formation strategy, we chose trithiaphosphinane sulfide derivative **1a** and diethyl phosphites (**2a**) as model substrates. Initially, a reaction was carried out with the substrate **1a** and **2a** in the presence of potassium carbonate (40 mol %) in ethyl acetate at 80 °C for 10 hours under nitrogen atmosphere. Fascinatingly, the desired product **3a** was obtained in 25% yield (Table 1, entry 1). To further optimize the reaction conditions, we screened a variety of bases and specifically K<sub>2</sub>CO<sub>3</sub>, NEt<sub>3</sub>, DBU, CsF, <sup>t</sup>BuOK, NaOH, pyridine, and Cs<sub>2</sub>CO<sub>3</sub>. Among them, Cs<sub>2</sub>CO<sub>3</sub> was found to be the most effective base that provided the compound **3a** in 65% yield (entries 2-8). Subsequently, solvent systems such as ethanol (EtOH), dimethyl sulfoxide (DMSO), 1,4-dioxane *N,N*-dimethylformamide (DMF), tetrahydrofuran (THF), and 1,2-dichloroethane (DCE) were screened. However, none of them was found to be superior to ethyl acetate (entries 9-14). A detrimental impact was observed on increasing the reaction temperature up to 100 °C (entry 15). Lower yields of **3a** were observed, in reducing and prolonging the reaction time (entries 16-18). Based on the above discussed results Cs<sub>2</sub>CO<sub>3</sub> (40 mol %), and ethyl acetate at 80 °C for 10 hours were identified as the optimal reaction conditions that gave the optimal yield of 65% of **3a** (entry 8).

**Table 1.** Optimization of the Reaction conditions<sup>a</sup>

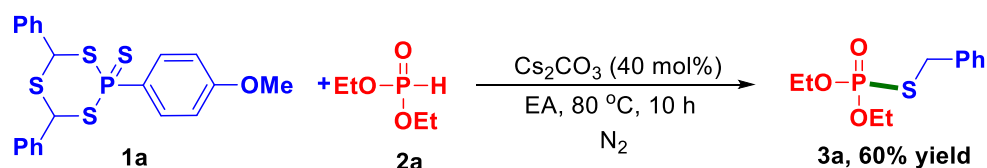
Entry	Base	Solvent (2 mL)	Temp (°C)	Time (h)	Yield (3a) <sup>b</sup>
1	K <sub>2</sub> CO <sub>3</sub>	EA	80	10	25
2	NEt <sub>3</sub>	EA	80	10	15
3	DBU	EA	80	10	trace
4	CsF	EA	80	10	trace
5	<sup>t</sup> BuOK	EA	80	10	NR
6	NaOH	EA	80	10	trace
7	Pyridine	EA	80	10	NR
8	Cs <sub>2</sub> CO <sub>3</sub>	EA	80	10	65
9	Cs <sub>2</sub> CO <sub>3</sub>	EtOH	80	10	NR
10	Cs <sub>2</sub> CO <sub>3</sub>	DMSO	80	10	NR
11	Cs <sub>2</sub> CO <sub>3</sub>	1,4-dioxane	80	10	NR
12	Cs <sub>2</sub> CO <sub>3</sub>	DMF	80	10	trace
13	Cs <sub>2</sub> CO <sub>3</sub>	THF	80	10	40
14	Cs <sub>2</sub> CO <sub>3</sub>	DCE	80	10	43
15	Cs <sub>2</sub> CO <sub>3</sub>	EA	100	10	43
16	Cs <sub>2</sub> CO <sub>3</sub>	EA	80	8	49
17	Cs <sub>2</sub> CO <sub>3</sub>	EA	80	16	54
18	Cs <sub>2</sub> CO <sub>3</sub>	EA	80	24	39

<sup>a</sup>Reaction conditions: **1a** (0.6 mmol), diethyl phosphite **2a** (0.4 mmol), and base (40 mol %), under N<sub>2</sub> atmosphere at 80-100 °C heated for 8-24 h. <sup>b</sup>Isolated yield based on **2a**.

Subsequently, the generality of the developed P-S bond formation protocol was examined, and the results are summarized in Table 2. The diverse variety of sulfur surrogates **1a-k** possessing EDGs and EWGs were successfully reacted with diethyl phosphite (**2a**) under the optimized reaction conditions. Sulfur surrogates having EDGs (3-Me/4-OMe) reacted successfully with diethyl phosphite (**2a**) to afford the phosphorothioates **3b-f** in 35-61% yields. Sulfur surrogates having EWGs (4-F, 4-Cl, 3-Br, 4-Br, and 4-I) also reacted with diethyl phosphite (**2a**) to afford the phosphorothioates **3g-k** in 30-50% yields. Furthermore, naphthyl moiety containing sulfur surrogate **1l** and heterocyclic thiophene containing sulfur surrogates **1m** reacted with diethyl phosphite (**2a**) to lead to phosphorothioates **3l** and **3m** in 60% and 42% yield, respectively. The reactivity of di-*i*-butyl phosphite (**2b**) with various sulfur surrogates **1a-e** which possess EDGs (2-Me, 3-Me, 3-OMe and 4-OMe) and EWGs (4-F, 4-Cl, 3-Br, 4-Br, 4-I, 4-NO<sub>2</sub>) has been investigated. Thus, the phosphorothioates **3n-y** were successfully synthesized in 30-70% yields. 2-Naphthyl **1l** and 2-thienyl sulfur surrogate **1m**, were also reacted with di-*i*-butyl phosphite (**2b**) and afforded the phosphorothioates **3z** and **3aa** in yield 61% and 42% respectively. The structures of compounds **3a-3z** and **3aa** were confirmed through characterization techniques including <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>31</sup>P NMR, and HRMS data collection. Notably, we performed a large-scale reaction (5.0 mmol) using substrate **1a**, which yielded the desired product **3a** with 60% (Scheme 2).

Table 2. Substrate scope <sup>a,b</sup>

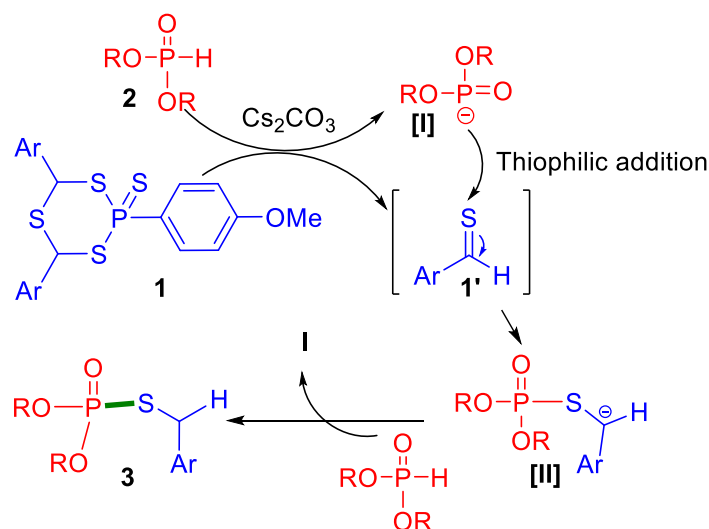
<sup>a</sup>Reaction conditions: **1** (0.6 mmol), phosphites **2** (0.4 mmol),  $\text{Cs}_2\text{CO}_3$  (40 mol%), and ethyl acetate (2 mL) under  $\text{N}_2$  at 80 °C for 10 h. <sup>b</sup>Isolated yields based on **2**.



### Scheme 2. Gram scale synthesis.

Based on the previous reports<sup>31-36</sup> and our experimental observations, we propose a mechanistic pathway illustrated in Scheme 3. Initially, phosphite **2** interacts with  $\text{Cs}_2\text{CO}_3$  and transforms into cesium-stabilized phosphite anion **I**. Trithiaphosphinane sulfides **1** in the presence of  $\text{Cs}_2\text{CO}_3$  *in-situ* generated thialdehyde **1'**.

Later on **I** reacted with thialdehyde **1'** through thiophilic addition to provide intermediate species **II** which upon protonation with another molecule phosphite **2** provided the resulting thiophosphates **3**.



**Scheme 3.** Plausible reaction mechanism.

## Conclusions

This protocol developed provides the  $\text{Cs}_2\text{CO}_3$ -catalytic synthetic strategy for the synthesis of thiophosphates *via* a thiophilic addition of *H*-phosphites on *in-situ* generated thialdehydes. A wide variety of sulfur surrogates were well tolerated under these conditions and provided a good library of thiophosphates compounds. The developed protocol exhibits remarkable functional group tolerance, and the reactivity pattern was dependent on the substituents that attached the moieties. The gram scale synthesis, base-catalysis, and mild conditions are the main feature of this developed protocol which proves the effectiveness of this protocol.

## Experimental Section

**General:** Reagents, substrates, and solvents were purchased from commercial suppliers and used without purification. Anhydrous toluene uses calcium hydride to remove water, dry, and distill. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F<sub>254</sub> (Merck). Chromatography was performed using silica gel 60 (43-63  $\mu\text{m}$ ) (Merck) and Aluminum oxide 90 neutral (MN).  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ , and  $^{19}\text{F}$  NMR spectra were using  $\text{CDCl}_3$  on Jeol 400 MHz spectrometers. Tetramethylsilane (TMS) served as an internal standard for  $^1\text{H}$  and  $^{13}\text{C}$  NMR analysis. Chemical shifts in  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra are reported as follows: Chloroform-*d* (referenced to 7.26 ppm for  $^1\text{H}$  and 77.10 ppm for  $^{13}\text{C}$ ). Coupling constants (*J*) are reported in hertz and peak multiplicities are reported using the following abbreviations: m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, td = triplet of doublets, tq = triplet of quartets, qd = quartet of doublets, br = broad signal. Low-Resolution Mass Spectrometry (LRMS) experiments were recorded on an Agilent Technologies 5977A with Agilent Technologies 7890B. High-Resolution Mass Spectrometry (HRMS) experiments were recorded on Jeol JMS-HX-110 with EI (Electron Impact)

method. All the phosphites 2a & 2b commercially purchased and used without purification and all the thioaldehydes 1a-m were prepared from known literature methods.<sup>37</sup>

**General procedure for Table 1.** In a sealed tube, 2-(4-methoxyphenyl)-4,6-diphenyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1a**) (267.9 mg, 0.6 mmol), base (40 mol %) was added in a glove box, followed by diethyl phosphites **2a** (55.24 mg, 0.4 mmol) and solvent (2 mL) were added, and stir at 80-100 °C for 8-10 hours. After completion of the reaction, the reaction mixture was diluted with ethyl acetate and filtered through a celite pad and concentrated under reduced pressure. The crude product thus obtained was then purified by column chromatography using silica gel (300-400 mesh) (15% ethyl acetate in hexanes) to obtain the pure product of **3a**.

**Representative example of Table 1. S-Benzyl O,O-diisobutyl phosphorothioate (3a).**<sup>38</sup> Yield: 77.66 mg, 65%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.37-7.24 (m, 5H), 4.16-3.96 (m, 6H), 1.28 (t, *J* 7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 137.4 (d, *J* 6.0 Hz), 128.9, 128.6, 127.6, 63.5 (d, *J* 6.0 Hz), 34.9 (d, *J* 3.0 Hz), 15.9 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.3.

**General procedure for Table 2.** In a sealed tube, added **1** (0.6 mmol), cesium carbonate (40 mol %) in a glove box, then dialkyl phosphites **2** (0.4 mmol) and ethyl acetate (2 mL) were added, the reaction mixture was then heated for 10 hours at 80 °C. After completion of the reaction, the reaction mixture was diluted with ethyl acetate and filtered through a celite pad and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography using silica gel (300-400 mesh) (10-20% ethyl acetate in hexanes) to obtain the pure products **3**.

**O,O-Diethyl S-(3-methylbenzyl) phosphorothioate (3b).**<sup>39</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*m*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1b**) (284.7 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3b** (66.92 mg, 61% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.27-7.14 (m, 3H), 7.08 (d, *J* 7.2 Hz, 1H), 4.18-3.98 (m, 6H), 2.34 (s, 3H), 1.29 (t, *J*=7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 138.2, 137.3 (d, *J* 6.0 Hz), 129.6, 128.6, 128.4, 125.9, 63.5 (d, *J* 5.0 Hz), 34.9 (d, *J* 4.0 Hz), 21.3, 15.9 (d, *J* 8.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.4. HRMS (EI) calcd for C<sub>12</sub>H<sub>19</sub>O<sub>3</sub>PS [M]<sup>+</sup> 274.0793 found: 274.0784.

**O,O-Diethyl S-(2-methylbenzyl) phosphorothioate (3c).**<sup>39</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*o*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1c**) (284.7 mg, 0.6 mmol), diethyl phosphite **2a** (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3c** (65.82 mg, 60% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.31 (d, *J* 6.8 Hz, 1H), 7.21-7.13 (m, 3H), 4.18-3.99 (m, 6H), 2.40 (s, 3H), 1.30 (td, *J* 7.2 & 0.8 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 136.6, 135.1 (d, *J* 6.0 Hz), 130.6, 130.0, 128.1, 126.2, 63.5 (d, *J* 6.0 Hz), 33.1 (d, *J* 3.0 Hz), 19.2, 16.0 (d, *J* 8.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.4.

**O,O-Diethyl S-(4-methylbenzyl) phosphorothioate (3d).**<sup>39</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*p*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1d**) (284.7 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3d** as a colorless liquid (66.92 mg, 61% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.23 (d, *J* 8.0 Hz, 2H), 7.20 (d, *J* 8.0 Hz, 2H), 4.73-3.98 (m, 6H), 2.32 (s, 3H), 1.29 (t, *J* 7.2 Hz, 6H). <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>) δ 137.2, 134.2 (d, *J* 6.0 Hz), 129.2, 128.7, 63.4 (d, *J* 5.0 Hz), 34.6 (d, *J* 4.0 Hz), 21.0 (s), 15.8 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 27.5. HRMS (EI) calcd for C<sub>12</sub>H<sub>19</sub>O<sub>3</sub>PS [M]<sup>+</sup> 274.0793 found: 274.0784.

**O,O-Diethyl S-(3-methoxybenzyl) phosphorothioate (3e).** The title compound was prepared following the general procedure for table 2, using 4,6-bis(3-methoxyphenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1e**) (304.0 mg, 0.6 mmol), diethyl phosphite **2a** (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3e** as a colorless liquid (40.66 mg, 35% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.23 (t, *J* 8.0 Hz, 1H), 6.95-6.90 (m, 2H), 6.80 (dd, *J* 8.4 & 2.4 Hz, 1H), 4.17-3.98 (m, 6H), 3.80 (s, 3H), 1.29 (t, *J* 7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 159.6, 138.9 (d, *J* 6.0 Hz), 129.6, 121.0, 114.3, 113.2, 63.4 (d, *J* 6.0 Hz), 55.1, 34.8 (d, *J* 4.0 Hz), 15.8 (d, *J* 8.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.3. HRMS (EI) calcd for C<sub>12</sub>H<sub>19</sub>O<sub>4</sub> PS [M]<sup>+</sup> 290.0742 found: 290.0743.

**O,O-Diethyl S-(4-methoxybenzyl) phosphorothioate (3f).**<sup>40</sup> The title compound was prepared following the general procedure for table 2, using 2,4,6-tris(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1f**) (304.0 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3f** (56.90 mg, 49% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.27 (d, *J* 8.8 Hz, 2H), 6.84 (d, *J* 8.8 Hz, 2H), 4.17-3.98 (m, 6H), 3.79 (s, 3H), 1.29 (t, *J* 7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 159.0, 130.1, 129.4 (d, *J* 6.0 Hz), 114.0, 63.4 (d, *J* 6.0 Hz), 55.3, 34.5 (d, *J* 4.0 Hz), 15.9 (d, *J* 8.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.5.

**O,O-Diethyl S-(4-fluorobenzyl) phosphorothioate (3g).**<sup>41</sup> The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1g**) (289.4 mg, 0.6 mmol), diethyl phosphite **2a** (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3g** (55.65 mg, 50% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.35-7.31 (m, 2H), 7.03-6.97 (m, 2H), 4.16-3.97 (m, 6H), 1.29 (td, *J* 7.2 & 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 162.2 (d, *J* 236.0 Hz), 133.4 (dd, *J* 4.0 & 5.0 Hz), 130.4 (d, *J* 9.0 Hz), 115.4 (d, *J* 21.0 Hz), 63.5 (d, *J* 6.0 Hz), 34.1 (d, *J* 3.0 Hz), 15.8 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.1; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>): δ -114.5. HRMS (EI) calcd for C<sub>11</sub>H<sub>16</sub>FO<sub>3</sub>PS [M]<sup>+</sup> 278.0542 found: 278.0544.

**S-(4-Chlorobenzyl) O,O-diethyl phosphorothioate (3h).**<sup>39</sup> The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-chlorophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1h**) (309.2 mg, 0.6 mmol), diethyl phosphite **2a** (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3h** (35.28 mg, 30% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.32-7.27 (m, 4H), 4.16-3.97 (m, 6H), 1.29 (td, *J* 3.2 & 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 136.2 (d, *J* 5.0 Hz), 133.5, 130.3, 128.8, 63.6 (d, *J* 5.0 Hz), 34.2 (d, *J* 3.9 Hz), 15.9 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.0. HRMS (EI) calcd for C<sub>11</sub>H<sub>16</sub>ClO<sub>3</sub>PS [M]<sup>+</sup> 294.0246 found: 294.0238.

**S-(3-Bromobenzyl) O,O-diethyl phosphorothioate (3i).** The title compound was prepared following the general procedure for table 2, using 4,6-bis(3-bromophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1i**) (362.6 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3i** (56.98 mg, 42% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.52 (s, 1H), 7.40 (d, *J* 8.0 Hz, 1H), 7.29 (d, *J* 8.0 Hz, 1H), 7.19 (t, *J* 8.0 Hz, 1H), 4.17-3.97 (m, 6H), 1.30 (t, *J* 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 139.9 (d, *J* 4.0 Hz), 131.8, 130.6, 130.1, 127.5, 122.4, 63.6 (d, *J* 6.0 Hz), 34.2 (d, *J* 4.0 Hz), 15.9 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.7. HRMS (EI) calcd for C<sub>11</sub>H<sub>16</sub>BrO<sub>3</sub>PS [M]<sup>+</sup> 337.9741 found: 337.9739.

**S-(4-Bromobenzyl) O,O-diethyl phosphorothioate (3j).**<sup>42</sup> The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-bromophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1j**) (362.6 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3j** (61.05 mg, 45% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.46-7.43 (m, 2H), 7.27-7.22 (m, 2H), 4.16-3.96 (m, 6H), 1.28 (td, *J* 7.2 & 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 136.6 (d, *J* 5.0 Hz), 131.7, 130.6, 121.5, 63.6 (d, *J* 6.0 Hz), 34.2 (d,



*J* 4.0 Hz), 15.9 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.9. HRMS (EI) calcd for C<sub>11</sub>H<sub>16</sub>BrO<sub>3</sub>PS [M]<sup>+</sup> 337.9741 found: 337.9739.

***O,O*-Diethyl *S*-(4-iodobenzyl) phosphorothioate (3k).** The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-iodophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1k**) (419.0 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3k** (77.2 mg, 50% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.64 (d, *J* 8.4 Hz, 2H), 7.12 (d, *J* 8.4 Hz, 2H), 4.15-3.94 (m, 6H), 1.28 (td, *J* 7.2 & 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 137.6, 137.2 (d, *J* 5.0 Hz), 130.7, 93.0, 63.5 (d, *J* 6.0 Hz), 34.2, 15.8 (d, *J* 8.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 26.8; HRMS (EI) calcd for C<sub>11</sub>H<sub>16</sub>IO<sub>3</sub>PS [M]<sup>+</sup> 385.9602 found: 385.9599.

***O,O*-Diethyl *S*-(naphthalen-2-ylmethyl) phosphorothioate (3l).** The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di(naphthalen-2-yl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1l**) (328.0 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3l** (74.48 mg, 60% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.05 (d, *J* 8.4 Hz, 1H), 7.84 (d, *J* 8.0 Hz, 1H), 7.77 (d, *J* 8.0 Hz, 1H), 7.57-7.47 (m, 3H), 7.37 (t, *J* 7.6 Hz, 1H), 4.49 (d, *J* 12.4 Hz, 2H), 4.16-3.95 (m, 4H), 1.25 (t, *J* 7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 133.6, 132.6 (d, *J* 6.0 Hz), 130.89, 128.8, 128.7, 127.6, 126.3, 125.8, 125.2, 123.4, 63.5 (d, *J* 6.0 Hz), 32.7 (d, *J* 3.0 Hz), 15.8 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.3. HRMS (EI) calcd for C<sub>15</sub>H<sub>19</sub>O<sub>3</sub>PS [M]<sup>+</sup> 310.0793 found: 310.0789.

***O,O*-Diethyl *S*-(thiophen-2-ylmethyl) phosphorothioate (3m).**<sup>43</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di(thiophen-2-yl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1m**) (275.1 mg, 0.6 mmol), diethyl phosphite (**2a**) (55.24 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3m** (44.69 mg, 42% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.23 (dd, *J* 5.2 & 2.0 Hz, 1H), 7.03 (d, *J* 3.2 Hz, 1H), 6.93-6.90 (m, 1H), 4.27 (d, *J* 14.0 Hz, 2H), 4.20-4.01 (m, 4H), 1.31(t, *J* 7.2 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 140.0 (d, *J* 6.0 Hz), 127.1, 126.9, 125.7, 63.6 (d, *J* 5.0 Hz), 29.5 (d, *J* 3.0 Hz), 15.9 (d, *J* 7.0 Hz); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.7. HRMS (EI) calcd for C<sub>9</sub>H<sub>15</sub>O<sub>3</sub>PS<sub>2</sub> [M]<sup>+</sup> 266.0200 found: 266.0206.

***S*-Benzyl *O,O*-diisobutyl phosphorothioate (3n).**<sup>41</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-diphenyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1a**) (267.9 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3n** (88.58 mg, 70% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.39-7.24 (m, 5H), 4.04 (d, *J* 14.0 Hz, 2H), 3.84-3.78 (m, 2H), 3.73-3.67 (m, 2H), 1.95-1.85 (m, 2H), 0.92 (d, *J* 1.2 Hz, 6H), 0.90 (d, *J* 1.2 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 137.5 (d, *J* 5.0 Hz), 128.9, 128.7, 127.6, 73.3 (d, *J* 7.0 Hz), 34.9 (d, *J* 3.0 Hz), 28.9 (d, *J* 8.0 Hz), 18.7; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.4.

***O,O*-Diisobutyl *S*-(4-methylbenzyl) phosphorothioate (3o).**<sup>41</sup> The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*p*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide (**1d**) (284.7 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3o** (72.69 mg, 55% yield); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 7.29-7.26 (m, 2H), 6.86-6.83 (m, 2H), 4.01 (d, *J* 13.2 Hz, 2H), 3.84-3.79 (m, 5H), 3.74-3.58 (m, 2H), 1.96-1.85 (m, 2H), 0.93(d, *J* 1.2 Hz, 6H), 0.91 (d, *J* 1.2 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 159.0, 130.1, 129.4 (d, *J* 6.0 Hz), 114.0, 73.3 (d, *J* 7.0 Hz), 55.3, 34.4, (d, *J* 4.0 Hz), 28.9 (d, *J* 7.0 Hz), 18.7. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 27.5. HRMS (EI) calcd for C<sub>16</sub>H<sub>27</sub>O<sub>3</sub> PS [M]<sup>+</sup> 330.1419 found: 330.1422.

***O,O*-Diisobutyl *S*-(3-methylbenzyl) phosphorothioate (3p).** The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*m*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide

**(1b)** (284.7 mg, 0.6 mmol), di-isobutyl phosphite **(2b)** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (53.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3p** (76.65 mg, 58% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.23 (t, *J* 8.0 Hz, 1H), 6.94 (d, *J* 7.6 Hz, 1H), 6.91 (t, *J* 2.0 Hz, 1H), 6.81 (dd, *J* 8.4 & 2.4 Hz, 1H), 4.02 (d, *J* 13.6 Hz, 2H), 3.85-3.79 (m, 5H), 3.75-3.69 (m, 2H), 1.96-1.86 (m, 2H), 0.93 (d, *J* 1.2 Hz, 6H), 0.91 (d, *J* 1.2 Hz, 6H). <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 159.7, 139.0 (d, *J* 5.0 Hz), 129.7, 121.2, 114.4, 113.3, 73.4 (d, *J* 6.0 Hz), 55.3, 34.9, (d, *J* 4.0 Hz), 29.0 (d, *J* 7.0 Hz), 18.7. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 27.4. HRMS (EI) calcd for C<sub>16</sub>H<sub>27</sub>O<sub>3</sub> PS [M]<sup>+</sup> 330.1419 found: 330.1422.

**O,O-Diisobutyl S-(2-methylbenzyl) phosphorothioate (3q)**. The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di-*o*-tolyl-1,3,5,2-trithiaphosphinane 2-sulfide **(1c)** (284.7 mg, 0.6 mmol), di-isobutyl phosphite **(2b)** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3q** (79.30 mg, 60% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.32-7.30 (m, 1H), 7.20-7.12 (m, 3H), 4.06 (d, *J* 12.0 Hz, 2H), 3.85-3.80 (m, 2H), 3.75-3.70 (m, 2H), 2.40 (s, 3H), 1.97-1.87 (m, 2H), 0.93 (d, *J* 1.2 Hz, 6H), 0.91 (d, *J* 1.2 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 136.6, 135.1 (d, *J* 6.0 Hz), 130.5, 129.9, 128.0, 126.2, 73.3 (d, *J* 7.0 Hz), 33.0 (d, *J* 3.0 Hz), 28.9 (d, *J* 7.0 Hz), 19.1, 18.6. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.5. HRMS (EI) calcd for C<sub>16</sub>H<sub>27</sub>O<sub>3</sub>PS [M]<sup>+</sup> 330.1419 found: 330.1416.

**O,O-Diisobutyl S-(3-methoxybenzyl) phosphorothioate (3r)**. The title compound was prepared following the general procedure for table 2, using 4,6-bis(3-methoxyphenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide **(1e)** (304.0 mg, 0.6 mmol), di-isobutyl phosphite **(2b)** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3r** (66.50 mg, 48% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.23 (t, *J* 8.0 Hz, 1H), 6.95-6.91 (m, 2H), 6.80 (dd, *J* 8.0 & 2.0 Hz, 1H), 4.02 (d, *J* 14.0 Hz, 2H), 3.83-3.79 (m, 5H), 3.75-3.71 (m, 2H), 1.96-1.86 (m, 2H), 0.92 (d, *J* 1.2 Hz, 6H), 0.91 (d, *J* 1.2 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>) δ 159.7, 138.9 (d, *J* 6.0 Hz), 129.7, 121.2, 114.3, 113.2, 73.3 (d, *J* 6.0 Hz), 55.2, 34.8 (d, *J* 4.0 Hz), 28.9 (d, *J* 7.0 Hz), 18.7. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.4. HRMS (EI) calcd for C<sub>16</sub>H<sub>27</sub>O<sub>4</sub>PS [M]<sup>+</sup> 346.1368 found: 346.1363.

**O,O-Diisobutyl S-(4-methoxybenzyl) phosphorothioate (3s)**.<sup>44</sup> The title compound was prepared following the general procedure for table 2, using 2,4,6-tris(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide **(1f)** (304.0 mg, 0.6 mmol), di-isobutyl phosphite **(2b)** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3s** (88.67 mg, 64% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.30-7.26 (m, 2H), 6.87-6.82 (m, 2H), 4.02 (d, *J* 13.2 Hz, 2H), 3.84-3.78 (m, 5H), 3.74-3.68 (m, 2H), 1.96-1.87 (m, 3H), 0.93 (d, *J* 3.0 Hz, 6H), 0.91 (d, *J* 3.0 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 159.0, 130.1, 129.4 (d, *J* 5.0 Hz), 114.4, 73.3 (d, *J* 7.0 Hz), 55.3 (s), 34.5 (d, *J* 4.0 Hz), 28.9 (d, *J* 8.0 Hz), 18.6; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.6. HRMS (EI) calcd for C<sub>16</sub>H<sub>27</sub>O<sub>4</sub>PS [M]<sup>+</sup> 346.1368 found: 346.1363.

**S-(4-Fluorobenzyl) O,O-diisobutyl phosphorothioate (3t)**. The title compound was prepared following the general procedure for table 2 using 4,6-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide **(1g)** (289.4 mg, 0.6 mmol), di-isobutyl phosphite **(2b)** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3t** (77.57 mg, 58% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.36-7.32 (m, 2H), 7.03-6.98 (m, 2H), 4.03 (d, *J* 14.0 Hz, 2H), 3.84-3.78 (m, 2H), 3.74-3.68 (m, 2H), 1.95-1.87 (m, 2H), 0.92 (d, *J* 6.8 Hz, 12H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 161.6 (d, *J* 170.0 Hz), 133.2 (d, *J* 125.0 Hz), 130.4 (d, *J* 9.0 Hz), 115.6 (d, *J* 21.0 Hz), 73.4 (d, *J* 7.0 Hz), 34.2 (d, *J* 4.0 Hz), 29.0 (d, *J* 7.0 Hz), 18.7; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.1; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>): δ -114.5. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>FO<sub>3</sub>PS [M]<sup>+</sup> 334.1168 found: 334.1172.

**S-(4-Chlorobenzyl) O,O-diisobutyl phosphorothioate (3u)**. The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-chlorophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-

sulfide (**1h**) (309.2 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3u** (70.16 mg, 50% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.32-7.27 (m, 4H), 4.01 (d, *J* 14.4 Hz, 2H), 3.83-3.77 (m, 2H), 3.73-3.67 (m, 2H), 1.95-1.85 (m, 2H), 0.91 (d, *J* 6.8 Hz, 12H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 136.2 (d, *J* 5.0 Hz), 133.4, 130.3, 128.8, 73.4 (d, *J* 7.0 Hz), 34.2 (d, *J* 4.0 Hz), 28.9 (d, *J* 7.0 Hz), 18.6. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 27.0. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>ClO<sub>3</sub>PS [M]<sup>+</sup> 350.0872 found: 350.0869.

**S-(3-Bromobenzyl) O,O-diisobutyl phosphorothioate (3v).** The title compound was prepared following the general procedure for table 2, using 4,6-bis(3-bromophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1i**) (362.6 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3v** (102.77 mg, 65% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.52 (t, *J* 1.6 Hz, 1H), 7.40-7.37 (m, 1H), 7.31-7.27 (m, 1H), 7.19 (t, *J* 8.0 Hz, 1H), 3.98 (d, *J* 14.8 Hz, 2H), 3.84-3.79 (m, 2H), 3.74-3.67 (m, 2H), 1.95-1.85 (m, 2H), 0.92 (d, *J* 0.8 Hz, 6H), 0.90 (d, *J* 1.2 Hz, 6H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 134.0 (d, *J* 5.0 Hz), 125.8, 124.6, 124.1, 121.5, 116.4, 67.3 (d, *J* 7.0 Hz), 28.1, 22.8 (d, *J* = 8.0 Hz), 12.6; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.85. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>BrO<sub>3</sub>PS [M]<sup>+</sup> 394.0367 found: 394.0358.

**S-(4-Bromobenzyl) O,O-diisobutyl phosphorothioate (3w).** The title compound was prepared following the general procedure for table 2, using 4,6-bis(4-bromophenyl)-2-(4-methoxyphenyl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1j**) (362.6 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3w** (109.10 mg, 69% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.46-7.43 (m, 2H), 7.26-7.23 (m, 2H), 3.99 (d, *J* 14.8 Hz, 2H), 3.83-3.77 (m, 2H), 3.73-3.67 (m, 2H), 1.95-1.85 (m, 2H), 0.91 (d, *J* 6.8 Hz, 12H). <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 136.7 (d, *J* 5.0 Hz), 131.7, 130.6, 121.5, 73.4 (d, *J* 6.0 Hz), 34.2 (d, *J* 4.0 Hz), 28.8 (d, *J* 8.0 Hz), 18.6. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.9. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>BrO<sub>3</sub>PS [M]<sup>+</sup> 394.0367 found: 394.0364.

**S-(4-Iodobenzyl) O,O-diisobutyl phosphorothioate (3x).** The title compound was prepared following the general procedure for table 2, using 4-iodobenzothialdehyde **1k** (148.8 mg, 0.6 mmol), di-isobutyl phosphite **2b** (419.0 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3x** (72.53 mg, 41% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.64 (dt, *J* 8.8 & 2.4 Hz, 2H), 7.12 (dt, *J* 8.8 & 2.4 Hz, 2H), 3.98 (d, *J* 14.8 Hz, 2H), 3.82-3.77 (m, 2H), 3.72-3.66 (m, 2H), 1.94-1.84 (m, 2H), 0.91 (d, *J* 0.8 Hz, 6H), 0.90 (d, *J* 0.8 Hz, 6H); <sup>13</sup>C{H}NMR (100 MHz, CDCl<sub>3</sub>): δ 137.7, 137.5 (d, *J* 5.0 Hz), 130.9, 93.0, 73.4 (d, *J* 7.0 Hz), 34.4 (d, *J* 4.0 Hz), 28.9 (d, *J* 8.0 Hz), 18.7; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.9. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>I O<sub>3</sub>PS [M]<sup>+</sup> 442.0228 found: 442.0234.

**O,O-Diisobutyl S-(4-nitrobenzyl) phosphorothioate (3y).** The title compound was prepared following the general procedure for table 2, using 4-nitrobenzothialdehyde **1n** (100.3 mg, 0.6 mmol), di-isobutyl phosphite **2b** (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3y** (43.36 mg, 30% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.20-8.16 (m, 2H), 7.58-7.55 (m, 2H), 4.12 (d, *J* 15.6 Hz, 2H), 3.84-3.75 (m, 2H), 3.74-3.68 (m, 2H), 1.95-1.85 (m, 2H), 0.85 (d, *J* 6.9 Hz, 12H); <sup>13</sup>C{H} NMR (100 MHz, CDCl<sub>3</sub>): δ 147.2, 145.4 (d, *J* 4.0 Hz), 129.7, 123.8, 73.6 (d, *J* 7.0 Hz), 34.0 (d, *J* 4.0 Hz), 29.8 (d, *J* 7.0 Hz), 18.6; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 26.2. HRMS (EI) calcd for C<sub>15</sub>H<sub>24</sub>NO<sub>5</sub>PS [M]<sup>+</sup> 361.1113 found: 361.1117.

**O,O-Diisobutyl S-(naphthalen-2-ylmethyl) phosphorothioate (3z).** The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di(naphthalen-2-yl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1l**) (328.0 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol), Cs<sub>2</sub>CO<sub>3</sub> (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO<sub>2</sub>, ethyl acetate/hexane) to provide **3z** (89.41 mg, 61% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.07 (d, *J* 8.4 Hz, 1H), 7.83 (d, *J* 8.0 Hz, 1H), 7.76

(d, *J* 8.0 Hz, 1H), 7.57-7.47 (m, 3H), 7.39-7.35 (m, 1H), 4.51 (d, *J* 12.4 Hz, 2H), 3.83-3.76 (m, 2H), 3.73-3.67 (m, 2H), 1.92-1.82 (m, 2H), 0.89 (d, *J* 4.0 Hz, 6H), 0.87 (d, *J* 4.0 Hz, 6H);  $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  133.7, 132.6 (d, *J* 6.0 Hz), 130.9, 128.77, 128.70, 127.6, 126.3, 125.8, 125.2, 123.5, 73.2 (d, *J* 7.0 Hz), 32.6 (d, *J* 4.0 Hz), 28.7 (d, *J* 7.0 Hz), 18.5;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  27.4. HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{27}\text{O}_3\text{PS}$   $[\text{M}]^+$  366.1419 found: 366.1416.

***O,O*-Diisobutyl *S*-(thiophen-2-ylmethyl) phosphorothioate (3aa).** The title compound was prepared following the general procedure for table 2, using 2-(4-methoxyphenyl)-4,6-di(thiophen-2-yl)-1,3,5,2-trithiaphosphinane 2-sulfide (**1m**) (275.1 mg, 0.6 mmol), di-isobutyl phosphite (**2b**) (77.68 mg, 0.4 mmol),  $\text{Cs}_2\text{CO}_3$  (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography ( $\text{SiO}_2$ , ethyl acetate/hexane) to provide **3aa** (54.16 mg, 42% yield);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.22 (dd, *J* 5.2 & 1.2 Hz, 1H), 7.03 (dd, *J* 3.6 & 1.2 Hz, 1H), 6.91 (dd, *J* 5.2 & 3.6 Hz, 1H), 4.28 (d, *J* 13.6 Hz, 2H), 3.88-3.82 (m, 2H), 3.78-3.72 (m, 2H), 1.99-1.88 (m, 2H), 0.93 (d, *J* 17.0 Hz, 12H);  $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  140.0 (d, *J* 6.0 Hz), 127.1, 126.8, 125.6, 73.3 (d, *J* 7.0 Hz), 29.4 (d, *J* 3.0 Hz), 28.9 (d, *J* 8.0 Hz), 18.6;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  26.7. HRMS (EI) calcd for  $\text{C}_{13}\text{H}_{23}\text{O}_3\text{PS}_2$   $[\text{M}]^+$  322.0826 found: 322.0819.

## Acknowledgements

This work was financially supported by the Ministry of Science and Technology, Taiwan (Most 110-2113-M-005-014-MY3), National Chung Hsing University, i-Center for Advanced Science and Technology (iCAST), the "Innovation and Development Centre of Sustainable Agriculture (IDCSA)" from The Featured Areas Research Centre Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan and Science and Engineering Research Board-Department of Science.

## Supplementary Material

Experimental for the preparation of trithiaphosphinanes **1a-n**, and copies of  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  &  $^{19}\text{F}$  NMR spectra of compounds **1** & **3** are available in the supplementary material associated with this manuscript.

## References

1. Li, N. S.; Frederiksen, J. K.; Piccirilli, J. A. *Acc. Chem. Res.*, **2011**, *44*, 1257.  
<https://doi.org/10.1021/ar200131t>
2. McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R., *Chem. Rev.* **2004**, *104*, 2239.  
<https://doi.org/10.1021/cr020109k>
3. Ozturk, T.; Ertas, E.; Mert, O., *Chem. Rev.* **2010**, *110*, 3419.  
<https://doi.org/10.1021/cr900243d>
4. Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley Interscience: New York, 2000.
5. Murphy, P. J. *Organophosphorus Reagents*; Oxford University Press: Oxford, U.K., 2004.  
<https://doi.org/10.1093/oso/9780198502623.001.0001>
6. Cogoi, S.; Rapozzi, V.; Quadrifoglio, F.; Xodo, L. *Biochemistry* **2001**, *40*, 1135.  
<https://doi.org/10.1021/bi0012639>

7. Schrader, G. U.S. Patent US259753419520520, **1952**.
8. Johnston, F. U.S. Patent US261691819521104, **1952**.
9. Qiu, Y.; Worch, J. C.; Chirdon, D. N.; Kaur, A.; Maurer, A. B.; Amsterdam, S.; Collins, C. R.; Pintauer, T.; Yaron, D.; Bernhard, S.; Noonan, K. J. T. *Chem. Eur. J.* **2014**, *20*, 7746.  
<https://doi.org/10.1002/chem.201402561>
10. Lauer, A. M.; Mahmud, F.; Wu, J. J. *Am. Chem. Soc.* **2011**, *133*, 9119.  
<https://doi.org/10.1021/ja202954b>
11. Morrison, D. C. *J. Am. Chem. Soc.* **1955**, *77*, 181.  
<https://doi.org/10.1021/ja01606a062>
12. Panmand, D. S.; Tiwari, A. D.; Panda, S. S.; Monbaliu, J. C. M.; Beagle, L. K.; Asiri, A. M.; Stevens, C. V.; Steel, P. J.; Hall, C. D.; Katritzky, A. R. *Tetrahedron Lett.* **2014**, *55*, 5898.  
<https://doi.org/10.1016/j.tetlet.2014.07.057>
13. Wang, J.; Huang, X.; Ni, Z.; Wang, S.; Wu, J.; Pan, Y. *Green Chem.* **2015**, *17*, 314.  
<https://doi.org/10.1039/C4GC00944D>
14. Li, Y.; Yang, Q.; Yang, L.; Lei, N.; Zheng, K. *Chem. Commun.* **2019**, *55*, 4981.  
<https://doi.org/10.1039/C9CC01378D>
15. Zhu, Y.; Chen, T.; Li, S.; Shimada, S.; Han, L. B. *J. Am. Chem. Soc.* **2016**, *138*, 5825.  
<https://doi.org/10.1021/jacs.6b03112>
16. Song, S.; Zhang, Y.; Yeerlan, A.; Zhu, B.; Liu, J.; Jiao, N. *Angew. Chem., Int. Ed.* **2017**, *56*, 2487.  
<https://doi.org/10.1002/anie.201612190>
17. Li, C.-Y.; Liu, Y.-C.; Li, Y.-X.; Reddy, D. M.; Lee, C.-F. *Org. Lett.* **2019**, *21*, 7833.  
<https://doi.org/10.1021/acs.orglett.9b02825>
18. Bai, J.; Cui, X.; Wang, H.; Wu, Y. *Chem. Commun.* **2014**, *50*, 8860.  
<https://doi.org/10.1039/C4CC02693D>
19. Sun, J.G; Weng, W.Z.; Li, P.; Zhang, B. *Green Chem.* **2017**, *19*, 1128.  
<https://doi.org/10.1039/C6GC03115C>
20. Kumaraswamy, G.; Raju, R. *Adv. Synth. Catal.* **2014**, *356*, 2591.  
<https://doi.org/10.1002/adsc.201400116>
21. Moon, Y.; Moon, Y.; Choi, H.; Hong, S. *Green Chem.* **2017**, *19*, 1005.  
<https://doi.org/10.1039/C6GC03285K>
22. Wang, J.; Huang, X.; Ni, Z.; Wang, S.; Wu, J.; Pan, Y. *Green Chem.* **2015**, *17*, 314.  
<https://doi.org/10.1039/C4GC00944D>
23. Choudhary, R.; Singh, P.; Bai, R. Sharma, M. C. Badsara, S. S. *Org. Biomol. Chem.* **2019**, *17*, 9757.  
<https://doi.org/10.1039/C9OB01921A>
24. Xu, J.; Zhang, L.; Li, X.; Gao, Y.; Tang, G.; Zhao, Y. *Org. Lett.* **2016**, *18*, 1266.  
<https://doi.org/10.1021/acs.orglett.6b00118>
25. Shi, S.; Chen, J.; Zhuo, S.; Wu, Z.A.; Fang, M.; Tang, G.; Zhao, Y. *Adv. Synth. Catal.* **2019**, *361*, 3210.  
<https://doi.org/10.1002/adsc.201900291>
26. Shi, S.; Zhang, P.; Luo, C.; Zhuo, S.; Zhang, Y.; Tang, G.; Zhao, Y. *Org. Lett.* **2020**, *22*, 1760.  
<https://doi.org/10.1021/acs.orglett.0c00044>
27. Han, X.; Wu, J. *Org. Lett.* **2010**, *12*, 5780.  
<https://doi.org/10.1021/ol102565b>
28. Kovács, S.; Bayarmagnai, B.; Aillerie, A.; Gooßen, L. J. *Adv. Synth. Catal.* **2018**, *360*, 1913.  
<https://doi.org/10.1002/adsc.201701549>

29. Chen, X.-Y.; Pu, M.; Cheng, H.-G.; Sperger, T.; Schoenebeck, F. *Angew. Chem., Int. Ed.* **2019**, *58*, 11395.  
<https://doi.org/10.1002/anie.201906063>
30. Nishiyama, Y.; Hosoya, T.; Yoshida, S. *Chem. Commun.* **2020**, *56*, 5771.  
<https://doi.org/10.1039/D0CC02039G>
31. Pallikonda, G.; Santosh, R.; Ghosal, S.; Chakravarty, M. *Tetrahedron Letters* **2015**, *56*, 3796.  
<https://doi.org/10.1016/j.tetlet.2015.04.073>
32. Kumaraswamy, S.; Selvi, R.S.; Swamy, K.K.; *Synthesis*, **1997**, 207.  
<https://doi.org/10.1055/s-1997-1166>
33. Kuroboshi, M.; Ishihara, T.; Ando, T. *J. Fluor. Chem.* **1988**, *39*, 293.  
[https://doi.org/10.1016/S0022-1139\(00\)82785-2](https://doi.org/10.1016/S0022-1139(00)82785-2)
34. Gancarz, R.; Gancarz, I.; Walkowiak, U.; *Phosphorus Sulfur Silicon Relat. Elem.* **1995**, *104*, 45.  
<https://doi.org/10.1080/10426509508042576>
35. Hayashi, M.; Nakamura, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 2249.  
<https://doi.org/10.1002/anie.201007568>
36. Sun, Y.M.; Xin, N.; Xu, Z.Y.; Liu, L.J.; Meng, F.J.; Zhang, H.; Fu, B.C.; Liang, Q.J.; Zheng, H.X.; Sun, L.J.; Zhao, C.Q. *Org. Biomol. Chem.* **2014**, *12*, 9457.  
<https://doi.org/10.1039/C4OB01574F>
37. Chen, Y.; Li, M.; Goug, Z.; Shen, Z.; *Phosphorus Sulfur Silicon Relat Elem.* **2021**, *196*, 19.  
<https://doi.org/10.1080/10426507.2020.1799369>
38. Mondal, M.; Saha, A. *Tetrahedron Letters*. **2019**, *60*, 150965.  
<https://doi.org/10.1016/j.tetlet.2019.150965>
39. Kaboudin, B.; Farjadian, F. *Beilstein. J. Org. Chem.* **2006**, *2*, 4.  
<https://doi.org/10.1186/1860-5397-2-4>
40. Xue, J.-W.; Zeng, M.; Zhang, S.; Chen, Z.; Yin, G. *J. Org. Chem.* **2019**, *84*, 4179.  
<https://doi.org/10.1021/acs.joc.9b00194>
41. Min, C.; Zhang, R.; Liu, Q.; Lin, S. *Synlett*, **2018**, *29*, 2027.  
<https://doi.org/10.1055/s-0037-1609556>
42. Pluempanupat, W.; Temyarasilp, P.; Widhalm, M.; Chavasiri, W. *J. Sulfur Chem.*, **2014**, *35*, 418.  
<https://doi.org/10.1080/17415993.2014.907408>
43. Han, X.; Wu, J. *Org Lett.*, **2010**, *12*, 5780.  
<https://doi.org/10.1021/ol102565b>
44. Ghantwal, S. R.; Samant, S. D. *Chem. Abstr.*, **1968**, *69*, 2627.

This paper is an open access article distributed under the terms of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>)