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Cs_2CO_3-Mediated synthetic strategy for iprobenfos derivatives *via* thiophilic addition of *H*-phosphites on *in situ* generated thioaldehydes

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

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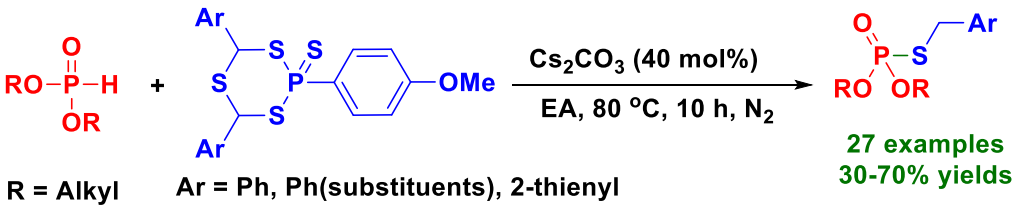
Abstract

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 tolerences
* 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.[1-3] Phosphorothioates molecules such as demeton-*S are* used as insecticides whereas omethoate is used in the agrochemical industry.[4-6] Phosphorothioate molecule echothiopate (AChE inhibitor) is used in cardioprotective therapeutics (Figure 1).[7-8] Furthermore, phosphorothioates are also used as a key intermediate for synthesizing value-added complex molecules.[9-10] 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.[11-17]

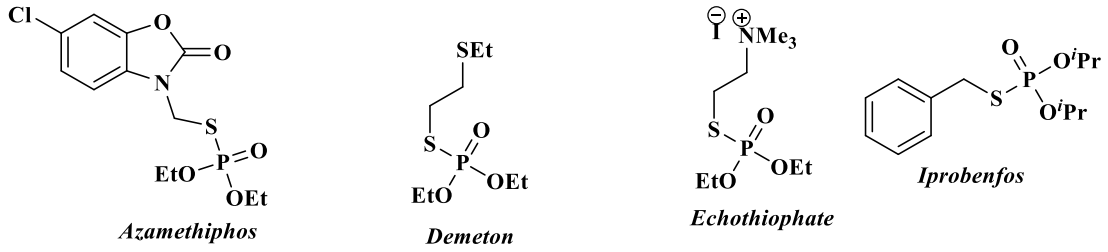
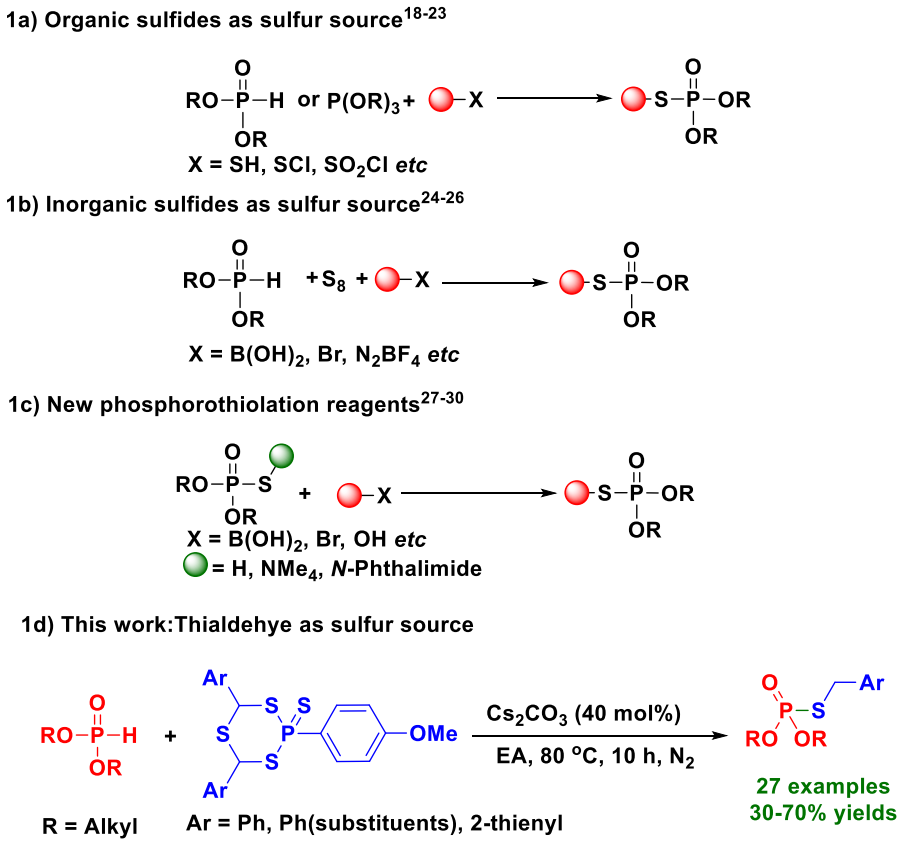


Figure 1. Pharmaceutically privileged molecules containing phosphorothioates system.

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).[18-23] Tang and co-workers reported a Cu-catalyzed multicomponent reaction (MCR) using aryl boronic acids, elemental sulfur, and P(O)H compounds.[24] Later on, the Tang group successfully achieved direct C(sp^2)-H and C(sp^3)-H phosphorothiolation *via* a multi-component composition strategy as shown in Scheme 1b.[25-26] 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).[27-30] 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).

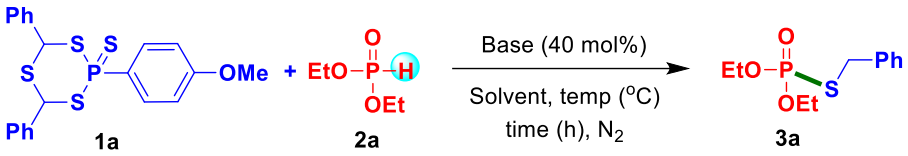


Scheme 1. Synthetic strategies for P-S bond formation.

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_2CO_3, NEt_3, DBU, CsF, ^tBuOK, NaOH, pyridine, and Cs_2CO_3. Among them, Cs_2CO_3 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_2CO_3 (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[a]

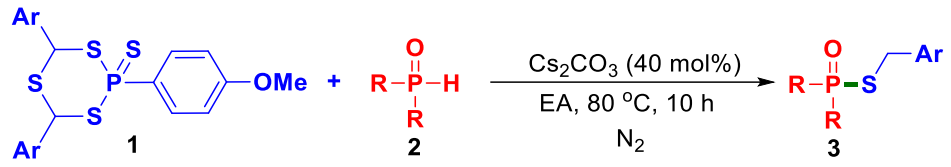


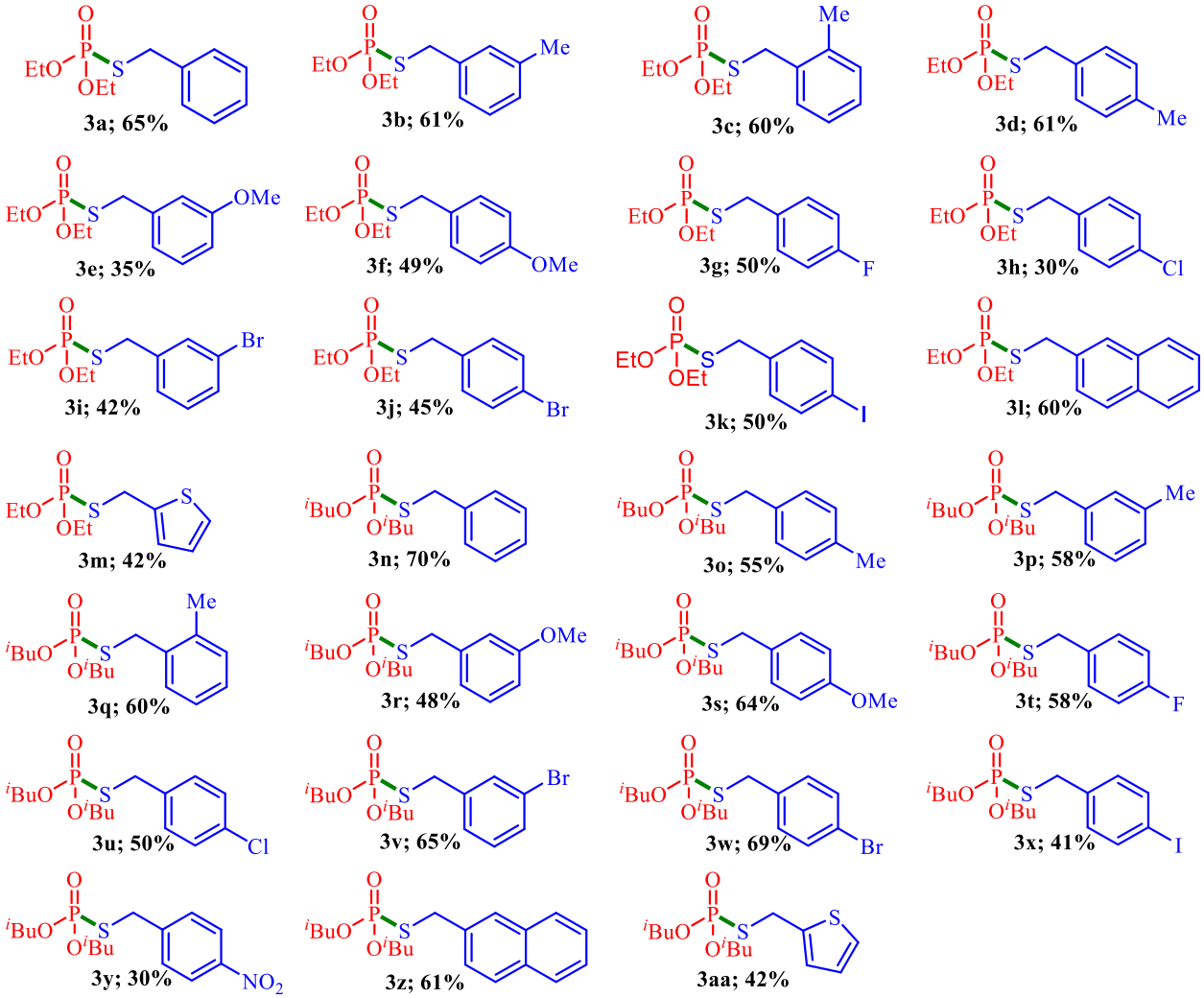
Entry	Base	Solvent (2 mL)	Temp (°C)	Time (h)	Yield (3a)[b]
1	K_2CO_3	EA	80	10	25
2	NEt_3	EA	80	10	15
3	DBU	EA	80	10	trace
4	CsF	EA	80	10	trace
5	^{t}BuOK	EA	80	10	NR
6	NaOH	EA	80	10	trace
7	Pyridine	EA	80	10	NR
8	Cs_2CO_3	EA	80	10	65
9	Cs_2CO_3	EtOH	80	10	NR
10	Cs_2CO_3	DMSO	80	10	NR
11	Cs_2CO_3	1,4-dioxane	80	10	NR
12	Cs_2CO_3	DMF	80	10	trace
13	Cs_2CO_3	THF	80	10	40
14	Cs_2CO_3	DCE	80	10	43
15	Cs_2CO_3	EA	100	10	43
16	Cs_2CO_3	EA	80	8	49
17	Cs_2CO_3	EA	80	16	54
18	Cs_2CO_3	EA	80	24	39

[a]Reaction conditions**: 1a** (0.6 mmol), diethyl phosphite **2a** (0.4 mmol), and base (40 mol %), under N_2 atmosphere at 80-100 °C heated for 8-24 h. [b]Isolated yield based on **2a**.

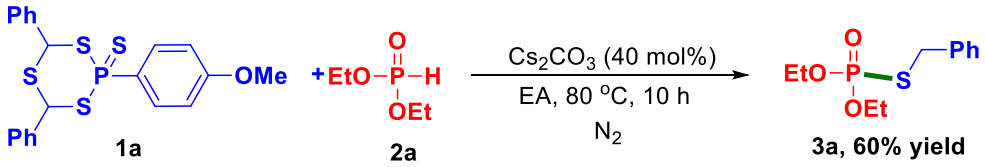
Subsequently, the generality of the developed P-S bond formation protocol was examined, and the results are summarized in Table 2. The diverse variety of sulfur surrogates **1a**-**k** possessing EDGs and EWGs were successfully reacted with diethyl phosphite (**2a**) under the optimized reaction conditions. 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_2) 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 yield61% and 42% respectively. The structures of compounds **3a**-**3z** and **3aa** were confirmed through characterization techniques including ^{1}H NMR, ^{13}C NMR, ^{31}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 [a,b]





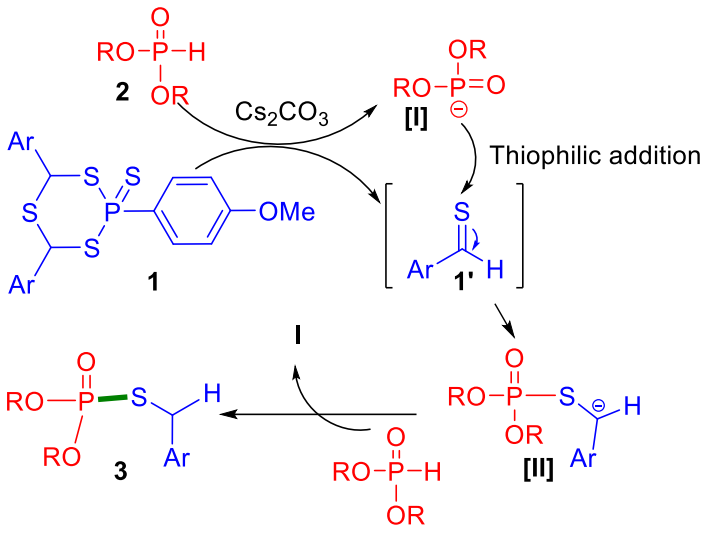
[a]Reaction conditions: **1** (0.6 mmol), phosphites **2** (0.4 mmol), Cs_2CO_3 (40 mol%), and ethyl acetate (2 mL) under N_2 at 80 °C for 10 h. [b]Isolated yields based on **2**.



Scheme 2. Gram scale synthesis.

Based on the previous reports[31-36] and our experimental observations, we propose a mechanistic pathway illustrated in Scheme 3. Initially, phosphite **2** interacts with Cs_2CO_3 and transforms into cesium-stabilized phosphite anion **I.** Trithiaphosphinane sulfides **1** in the presence of Cs_2CO_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 Cs_2CO_3-catalytic synthetic strategy for the synthesis of thiophosphates *via* a thiophilic addition of *H*-phosphites on *in-situ* generated thialdehyde*s*. 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_{254} (Merck). Chromatography was performed using silica gel 60 (43-63 um) (Merck) and Aluminum oxide 90 neutral (MN). ^{1}H, ^{13}C, ^{31}P, and ^{19}F NMR spectra were using $CDCl_3$ on *J*eol 400 MHz spectrometers. Tetramethylsilane (TMS) served as an internal standard for ^{1}H and ^{13}C NMR analysis. Chemical shifts in ^{1}H NMR and ^{13}C NMR spectra are reported as follows: Chloroform-d (referenced to 7.26 ppm for ^{1}H and 77.10 ppm for ^{13}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 *J*eol *J*MS-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.[37]

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).[38] Yield: 77.66 mg, 65%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.24 (m, 5H), 4.16-3.96 (m, 6H), 1.28 (t, *J* 7.2 Hz, 6H); ^{13}C{H}NMR (100 MHz, $CDCl_3$): 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); ^{31}P NMR (162 MHz, $CDCl_3$): 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).**[39] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3b** (66.92 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): 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); ^{31}P NMR (162 MHz, $CDCl_3$); δ 27.4. HRMS (EI) calcd for $C_{12}H_{19}O_3PS$ $[M]^+$ 274.0793 found: 274.0784.

***O,O*-Diethyl *S*-(2-methylbenzyl) phosphorothioate (3c).**[39] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3c** (65.82 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): 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); ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.4.

***O,O*-Diethyl *S*-(4-methylbenzyl) phosphorothioate (3d).**[39] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3d** as a colorless liquid (66.92 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$): 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). ^{13}C{H}NMR (100 MHz, $CDCl_3$) 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); ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.5. HRMS (EI) calcd for $C_{12}H_{19}O_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3e** as a colorless liquid (40.66 mg, 35% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.3. HRMS (EI) calcd for $C_{12}H_{19}O_4PS$ [M]$^+$ 290.0742 found: 290.0743.

***O,O*-Diethyl *S*-(4-methoxybenzyl) phosphorothioate (3f).**[40] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3f** (56.90 mg, 49% yield); ^{1}H NMR (400 MHz, $CDCl_3$); *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.5.

***O,O*-Diethyl *S*-(4-fluorobenzyl) phosphorothioate (3g).**[41] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3g** (55.65 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.1; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -114.5. HRMS (EI) calcd for $C_{11}H_{16}FO_3PS$ [M]$^+$ 278.0542 found: 278.0544.

***S*-(4-Chlorobenzyl) *O,O*-diethyl phosphorothioate (3h).**[39] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3h** (35.28 mg, 30% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.32-7.27 (m, 4H), 4.16-3.97 (m, 6H), 1.29 (td, *J* 3.2 & 0.8 Hz, 6H); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.0. HRMS (EI) calcd for $C_{11}H_{16}ClO_3PS$ [M]$^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3i** (56.98 mg, 42% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.7. HRMS (EI) calcd for $C_{11}H_{16}BrO_3PS$ [M]$^+$ 337.9741 found: 337.9739.

***S*-(4-Bromobenzyl) *O,O*-diethyl phosphorothioate (3j).**[42] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3j** (61.05 mg, 45% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.9. HRMS (EI) calcd for $C_{11}H_{16}BrO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3k** (77.2 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.8; HRMS (EI) calcd for $C_{11}H_{16}IO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3l** (74.48 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.3. HRMS (EI) calcd for $C_{15}H_{19}O_3PS$ $[M]^+$ 310.0793 found: 310.0789.

***O,O*-Diethyl *S*-(thiophen-2-ylmethyl) phosphorothioate (3m).**[43] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3m** (44.69 mg, 42% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.7. HRMS (EI) calcd for $C_9H_{15}O_3PS_2$ $[M]^+$ 266.0200 found: 266.0206.

***S*-Benzyl *O,O*-diisobutyl phosphorothioate (3n).**[41] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3n** (88.58 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.4.

***O,O*-Diisobutyl *S*-(4-methylbenzyl) phosphorothioate (3o).**[41] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3o** (72.69 mg, 55% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) 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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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. ^{31}P NMR (162 MHz, $CDCl_3$) *δ* 27.5. HRMS (EI) calcd for $C_{16}H_{27}O_3PS$ $[M]^+$ 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_2CO_3 (53.13 mg, 40 mo l%) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3p** (76.65 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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). ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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. ^{31}P NMR (162 MHz, $CDCl_3$) *δ* 27.4. HRMS (EI) calcd for $C_{16}H_{27}O_3$ PS $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3q** (79.30 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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. ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.5. HRMS (EI) calcd for $C_{16}H_{27}O_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3r** (66.50 mg, 48% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$) 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. ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.4. HRMS (EI) calcd for $C_{16}H_{27}O_4PS$ $[M]^+$ 346.1368 found: 346.1363.

***O,O*-Diisobutyl *S*-(4-methoxybenzyl) phosphorothioate (3s).**[44] 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3s** (88.67 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.6. HRMS (EI) calcd for $C_{16}H_{27}O_4PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3t** (77.57 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -114.5. HRMS (EI) calcd for $C_{15}H_{24}FO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3u** (70.16 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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. ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 27.0. HRMS (EI) calcd for $C_{15}H_{24}ClO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3v** (102.77 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.85. HRMS (EI) calcd for $C_{15}H_{24}BrO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3w** (109.10 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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). ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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. ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.9. HRMS (EI) calcd for $C_{15}H_{24}BrO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3x** (72.53 mg, 41% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H}NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.9. HRMS (EI) calcd for $C_{15}H_{24}IO_3PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3y** (43.36 mg, 30% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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); ^{13}C{H} NMR (100 MHz, $CDCl_3$): *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; ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 26.2. HRMS (EI) calcd for $C_{15}H_{24}NO_5PS$ $[M]^+$ 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_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3z** (89.41 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *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}C{H}NMR (100 MHz, $CDCl_3$) δ 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}P NMR (162 MHz, $CDCl_3$) *δ* 27.4. HRMS (EI) calcd for $C_{19}H_{27}O_3PS$ $[M]^+$ 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), Cs_2CO_3 (52.13 mg, 40 mol %) and EA (2.0 mL), then purified by column chromatography (SiO_2, ethyl acetate/hexane) to provide **3aa** (54.16 mg, 42% yield); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 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}C{H}NMR (100 MHz, $CDCl_3$): *δ* 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}P NMR (162 MHz, $CDCl_3$): *δ* 26.7. HRMS (EI) calcd for $C_{13}H_{23}O_3PS_2$ $[M]^+$ 322.0826 found: 322.0819.

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Supplementary Material

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

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