Green Chemistry

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N-Chlorosuccinimide-promoted synthesis of thiophosphates from thiols and phosphonates under mild conditions†

Cite this: *Green Chem.*, 2014, **16**, 357

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Received 4th September 2013,
Accepted 26th October 2013

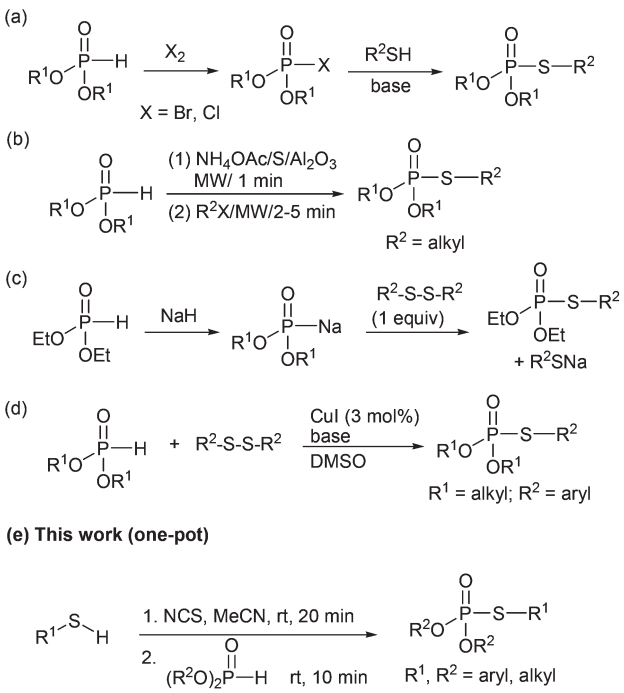
DOI: 10.1039/c3gc41839a

www.rsc.org/greenchem

A very simple *N*-chlorosuccinimide-promoted synthesis of thiophosphates through the coupling of thiols and phosphonates is reported. Notably, the reactions were carried out in the absence of a base. Functional groups including fluoro, bromo and trifluoromethyl are all tolerated by the reaction conditions employed. Both aryl and alkyl thiols are coupled smoothly with a broad spectrum of phosphonates to afford the corresponding thiophosphates in good to excellent yields.

Introduction

Thiophosphates are important skeletons in biology[1] and organic synthesis,[2] as a result, the synthesis of thiophosphates has gained much attention. Timperley and coworkers reported the formation of thiophosphates through the coupling of the corresponding phosphorochloridates or phosphorobromidates with thiols in the presence of a base; however, the preparation of phosphorochloridates and phosphorobromidates is required [Scheme 1(a)]. A typical procedure for preparing phosphorochloridates and phosphorobromidates relied on reacting H-phosphonates with chlorine and bromine in an organic solvent, respectively. Chlorine and bromine are both toxic and difficult to control.[3] Kaboudin described a one-pot procedure by the treatment of diethyl phosphonate with ammonium acetate/sulfur/Al_2O_3 followed by addition of alkyl halides to give thiophosphates; unfortunately, the substrate is limited to diethyl phosphonate, and only alkyl substituents are introduced to the sulfur atom in this system [Scheme 1(b)], moreover, microwave-heating is required in this approach.[4] Jensen *et al.* reported that thiophosphates can be synthesized through the coupling of sodium diethyl phosphonate with organic disulfides [Scheme 1(c)],[5] but again there are several limitations to using this approach. First, a strong base (*i.e.*, NaH) is necessary to generate the sodium diethyl phosphonate. Notably, a strong base will generally reduce the functional group compatibility. Second, one equiv. of disulfide is required to produce the thiophosphate as the target molecule; however, one equiv. of sodium thiolate[6,7] will be generated as a waste. Recently, a copper-catalyzed coupling of dialkyl phosphonates with organic disulfides was reported by Zhao and coworkers [Scheme 1(d)];[8] again several synthetic limitations have been observed by using this approach. First, the reaction is limited to dialkyl phosphonates. Second, no alkyl disulfides are involved in this system. Third, an additional base is required. In addition, thiophosphates have shown potential applications in chemical biology; and transition metals are generally



Scheme 1 Preparation of thiophosphates.

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†Electronic supplementary information (ESI) available: Spectral data for new products. See DOI: 10.1039/c3gc41839a

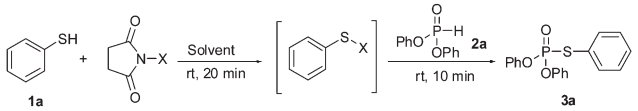
avoided for use in the final step for the preparation of biological molecules in order to exclude the presence of transition metal-contaminant.

From the substrate generality and conditions employed, a general direct coupling of thiols with H-phosphonates in transition metal-free and mild conditions is highly desirable for preparing thiophosphates. Building on our previous work,[9] we now report a general method to prepare thiophosphates through *N*-chlorosuccinimide-promoted[10–12] P–S bond formation between phosphonates and thiols. Importantly, this approach is simple and the reactions are carried out in one pot without an additive base [Scheme 1(e)].

Results and discussion

Thiophenol **1a** and diphenyl phosphonate **2a** were used as model substrates to determine the optimized reaction conditions. The results are summarized in Table 1. A trace amount of desired product was detected using 1.1 equiv. of *N*-iodosuccinimide (Table 1, entry 1), because the intermediate sulfenyliodide is too reactive to react with diphenyl phosphonate; this results in the formation of diphenyl disulfide as a side product. Interestingly, a 23% yield of the target, **3a** was afforded when *N*-bromosuccinimide was used instead of *N*-iodosuccinimide (Table 1, entry 2). To our delight, a 78% yield of **3a** was achieved when the reaction was carried out by using 1.1 equiv. of *N*-chlorosuccinimide (NCS, Table 1, entry 3). No improvement was observed when Et_3N was added as a base (Table 1, entry 4).[9] The control experiment showed that no product was formed in the absence of *N*-chlorosuccinimide (Table 1, entry 5). We then studied the influence of solvent (Table 1, entries 6–11) and found that MeCN was superior to THF, ether, dioxane, DMF and DMSO.

Table 1 Optimize the reaction conditions[a]



Entry	X	Solvent	Yield[b] (%)
1	I	Toluene	Trace
2	Br	Toluene	23
3	Cl	Toluene	78
4[c]	Cl	Toluene	76
5	—	Toluene	—
6	Cl	THF	81
7	Cl	Ether	75
8	Cl	Dioxane	79
9	Cl	DMF	76
10	Cl	DMSO	Trace
11	Cl	MeCN	85

[a] Reaction conditions: thiophenol (1.0 mmol), *N*-halosuccinimide (1.1 mmol), under a nitrogen atmosphere in solvent (1.5 mL) at rt for 20 min for the first step; diphenyl phosphonate (1.0 mmol) was added, and reacted at rt for 10 min for the second step. [b] Isolated yield. [c] Et_3N (1.0 mmol) was added in the second step.

We examined the scope of the substrates based on the optimized reaction conditions above as demonstrated in Table 2. Aryl thiols bearing electron-donating and electron-withdrawing groups reacted with a variety of phosphonates to give the corresponding thiophosphates in good to excellent yields. Notably, this system shows good functional group compatibility. Functional groups including fluoro (Table 2, entries 2 and 19), bromo (Table 2, entries 3 and 7), trifluoromethyl (Table 2, entries 9, 10, 16 and 17) are all tolerated by the reaction conditions. Sterically demanding substituted aryl thiols did not decrease the reactivity of the reactions, and afforded the products with satisfying yields (Table 2, entries 7, 8, 14 and 18).

Based on the promising results for aryl thiols in Table 2, we then turned our attention to the coupling reaction of alkyl thiols with phosphonates. The results are summarized in Table 3. Alkyl thiols such as cyclohexanethiol (**4a**), 2-methylbutane-1-thiol (**4b**), hexanethiol (**4c**) and benzylthiol (**4d**) were coupled smoothly with phosphonates to give the corresponding thiophosphates in good to excellent yields.

Conclusions

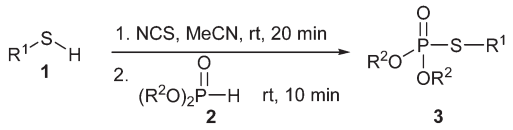
In conclusion, we report a convenient protocol for the synthesis of thiophosphates through the *N*-chlorosuccinimide-promoted coupling of thiols with phosphates. Both aryl and alkyl thiols are coupled smoothly with a variety of phosphates to provide the corresponding thiophosphates in good to excellent yields in the absence of a base. Importantly, it is not necessary to functionalize the starting materials, and this one-pot procedure can be completed within 30 min. Functional groups including fluoro, bromo and trifluoromethyl are all tolerated by the reaction conditions employed. Applications of *N*-chlorosuccinimide-promoted coupling reaction for carbon–carbon and carbon–heteroatom bond formations are underway in our laboratory.

Experimental

General information

All chemicals were purchased from commercial suppliers and used without further purification. TLC analyses were performed on Merck DC-Alufolien with Kieselgel 60F-254, and were visualized with UV light. Purifications were performed by flash chromatography on silica gel 60 (Merck, 230–400 mesh ASTM). NMR spectra were recorded on a Varian Unity Inova-600 or a Varian Mercury-400 instrument using $CDCl_3$ as the solvent. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent resonance. Coupling constants (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, q = quartet, m = multiplet. IR spectra were measured using a Bruker Equinox 55 or Bruker Tensor 27 spectrophotometer. High resolution mass spectra (HRMS) were recorded on an electron ionization

Table 2 NCS-promoted synthesis of thiophosphates from aryl thiols and phosphonates[a]



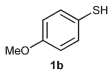
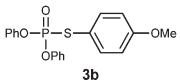
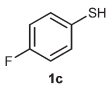
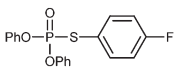
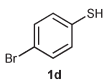
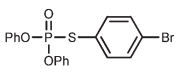
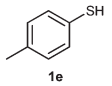
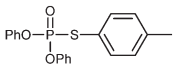
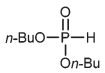
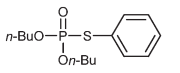
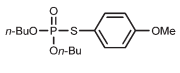
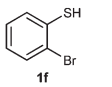
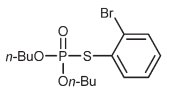
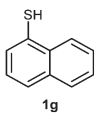
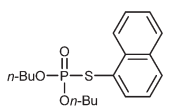
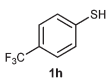
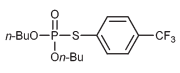
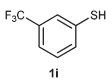
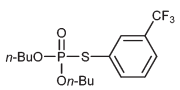
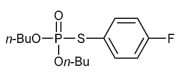
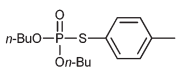
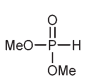
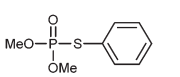
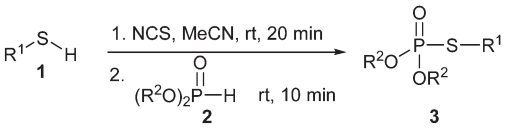
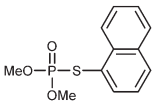
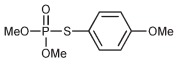
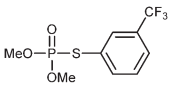
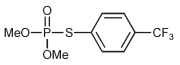
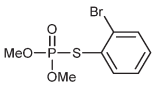
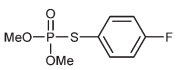
Entry	1	2	3	Yield (%)
1	 1b	2a	 3b	81
2	 1c	2a	 3c	53
3	 1d	2a	 3d	50
4	 1e	2a	 3e	50
5	1a	 2b	 3f	85
6	1b	2b	 3g	94
7	 1f	2b	 3h	96
8	 1g	2b	 3i	82
9	 1h	2b	 3j	58
10	 1i	2b	 3k	84
11	1c	2b	 3l	60
12	1e	2b	 3m	83
13	1a	 2c	 3n	72

Table 2 *(Contd.)*



Entry	1	2	3	Yield (%)
14	1g	2c	 3o	71
15	1b	2c	 3p	62
16	1i	2c	 3q	76
17	1h	2c	 3r	93
18	1f	2c	 3s	70
19	1c	2c	 3t	66

[a] Reaction conditions unless otherwise stated: aryl thiol (1.0 mmol), NCS (1.1 mmol), under a nitrogen atmosphere in MeCN (1.5 mL) at rt for 20 min for the first step; phosphonate (1.0 mmol) was added, and reacted at rt for 10 min for the second step.

time-of-flight (EI-TOF) mass spectrometer at the National Chung Hsing University.

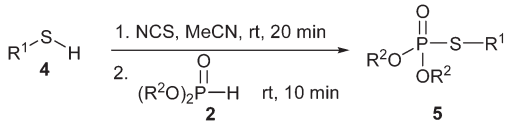
General procedure for Table 1

A Schlenk tube equipped with a magnetic stir bar was charged with *N*-chlorosuccinimide (0.15 g, 1.1 mmol), thiophenol **1a** (1.0 mmol) and solvent (1.5 mL). After the mixture was stirred for 20 min, diphenylphosphonate **2a** (1.0 mmol) was added by a syringe under a nitrogen-filled balloon. After being stirred for another 10 min at room temperature, the resulting solution was directly filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to afford **3a**.

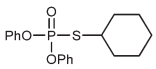
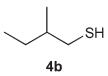
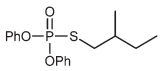
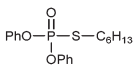
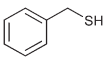
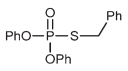
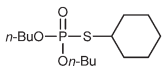
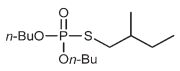
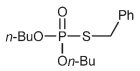
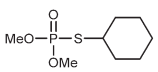
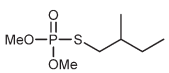
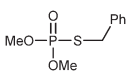
Representative example of Table 1

***O*,*O*,*S*-Triphenylphosphorothioate (entry 11, 3a).** Following the general procedure for Table 1, using thiophenol (0.103 mL, 1.0 mmol, 1.0 equiv.), *N*-chlorosuccinimide (0.15 g, 1.1 mmol, 1.1 equiv.), MeCN (1.5 mL) and diphenylphosphonate

Table 3 NCS-mediated coupling of alkyl thiols with phosphonates[a]



4 2 5

Entry	4	2	5	Yield [%]
1	 4a	2a	 5a	88
2	 4b	2a	 5b	87
3	$C_6H_{15}SH$ 4c	2a	 5c	75
4	 4d	2a	 5d	74
5	4a	2b	 5e	74
6	4b	2b	 5f	92
7	4d	2b	 5g	71
8	4a	2c	 5h	68
9	4b	2c	 5i	89
10	4d	2c	 5j	67

[a] Reaction conditions unless otherwise stated: alkyl thiol (1.0 mmol), NCS (1.1 mmol), under a nitrogen atmosphere in MeCN (1.5 mL) at rt for 20 min for the first step; phosphonate (1.0 mmol) was added, and reacted at rt for 10 min for the second step.

(0.192 mL, 1.0 mmol) and then purification by column chromatography (SiO_2, hexane) provides **3a** as a colorless oil (290 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.30 (m, 6 H), 7.31–7.37 (m, 7 H), 7.48–7.51 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.3, 120.3, (d, J = 2.7 Hz), 125.5, 129.2, 129.4, 129.5, 129.7, 135.1 (d, J = 5.4 Hz), 150.2 (d, J = 9.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.52; IR ($CHCl_3$): ν 3064, 2959, 2929, 2871, 1949, 1868, 1775, 1718, 1593, 1489, 1457, 1442, 1367, 1270, 1157, 1071, 1025, 1007, 920, 827, 746 cm^{-1}; HRMS-EI calcd for $C_{18}H_{15}O_3PS$: 342.0480, found: 342.0484.

General procedure for Table 2

A Schlenk tube equipped with a magnetic stir bar was charged with *N*-chlorosuccinimide (0.15 g, 1.1 mmol), aryl thiol **1** (1.0 mmol) and MeCN (1.5 mL). After the mixture was stirred for 20 min, phosphonate **2** (1.0 mmol) was added by a syringe under a nitrogen-filled balloon. After being stirred for another 10 min at room temperature and diluted with ethyl acetate (20 mL), the resulting solution was directly filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to yield **3**.

***S*-(4-Methoxyphenyl) *O*,*O*-diphenylphosphorothioate (3b).** Following the general procedure for Table 2, using 4-methoxythiophenol (0.123 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3b** as a colorless oil (301 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3 H), 6.83–6.85 (m, 2 H), 7.17–7.22 (m, 6 H), 7.31–7.39 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 114.7 (d, J = 8.2 Hz), 115.0 (d, J = 2.7 Hz), 120.3 (d, J = 5.4 Hz), 125.4, 129.6, 136.8 (d, J = 5.5 Hz), 150.2 (d, J = 8.2 Hz), 160.8 (d, J = 2.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.17; IR ($CHCl_3$): ν 3069, 3013, 2919, 2839, 1592, 1491, 1459, 1408, 1271, 1251, 1206, 1184, 1161, 1107, 1071, 1026, 1007, 938, 829, 769, 689 cm^{-1}; HRMS-EI calcd for $C_{19}H_{17}O_4PS$: 372.0585, found: 372.0595.

***S*-(4-Fluorophenyl) *O*,*O*-diphenylphosphorothioate (3c).** Following the general procedure for Table 2, using 4-fluorothiophenol (0.107 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3c** as a colorless oil (190 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00–7.05 (m, 2 H), 7.19–7.26 (m, 6 H), 7.33–7.37 (m, 4 H), 7.43–7.47 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 115.3, 116.7 (dd, J = 2.4, 21.8 Hz), 120.4 (d, J = 4.8 Hz), 125.7, 129.8, 137.4 (q, J = 4.7 Hz), 150.2 (d, J = 8.6 Hz), 163.7 (dd, J = 3.8, 250.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.19; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.8 (s); IR ($CHCl_3$): ν 3069, 1590, 1488, 1457, 1399, 1272, 1182, 1158, 1093, 1071, 1025, 1008, 939, 833, 766, 688 cm^{-1}; HRMS-EI calcd for $C_{18}H_{14}FO_3PS$: 360.0385, found: 360.0376.

***S*-(4-Bromophenyl) *O*,*O*-diphenylphosphorothioate (3d).** Following the general procedure for Table 2, using 4-bromothiophenol (0.189 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3d** as a colorless oil (212 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.23 (m, 6 H), 7.31–7.35 (m, 6 H), 7.42–7.44 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.3, 120.3 (d, J = 4.6 Hz), 125.7, 129.2, 129.8, 132.5 (d, J = 2.8 Hz), 136.6 (d, J = 5.4 Hz), 150.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.49; IR ($CHCl_3$): ν 3068, 2919, 2851, 1942, 1899, 1778, 1590, 1488, 1387, 1273, 1181, 1085, 1070, 1025, 1009, 939, 817, 765, 689, 619, 590, 545, 512 cm^{-1}; HRMS-EI calcd for $C_{18}H_{14}BrO_3PS$: 419.9585, found: 419.9592.

***O,O*-Diphenyl *S*-*p*-tolylphosphorothioate (3e).** Following the general procedure for Table 2, using 4-methylbenzenethiol (0.124 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3e** as a yellow oil (160 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 7.11–7.21 (m, 8 H), 7.30–7.38 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 115.4, 120.4 (d, J = 5.5 Hz), 125.5, 129.2, 129.7, 130.2 (d, J = 2.8 Hz), 135.2 (d, J = 5.5 Hz), 140.0, 150.3 (d, J = 9.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.93; IR ($CHCl_3$): ν 3097, 3072, 3043, 2962, 2922, 2869, 1942, 1906, 1865, 1639, 1594, 1488, 1456, 1400, 1378, 1263, 1158, 1071, 1025, 919, 809, 757, 689 cm^{-1}; HRMS-EI calcd for $C_{19}H_{17}O_3PS$: 356.0636, found: 356.0630.

***O,O*-Dibutyl *S*-phenyl phosphorothioate (3f).**[8] Following the general procedure for Table 2, using thiophenol (0.103 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3f** as a yellow oil (257 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.4 Hz, 6 H), 1.30–1.40 (m, 4 H), 1.59–1.66 (m, 4 H), 4.06–4.17 (m, 4 H), 7.33–7.36 (m, 3 H), 7.55–7.58 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 18.5, 31.9 (d, J = 7.3 Hz), 67.6 (d, J = 6.3 Hz), 126.5, 128.8 (d, J = 2.8 Hz), 129.1 (d, J = 1.9 Hz), 134.3 (d, J = 4.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.60; IR ($CHCl_3$): ν 3063, 2961, 2934, 2874, 1641, 1583, 1471, 1442, 1383, 1258, 1194, 1120, 1060, 1021, 819, 783, 747, 692 cm^{-1}.

***O,O*-Dibutyl *S*-(4-methoxyphenyl)phosphorothioate (3g).** Following the general procedure for Table 2, using 4-methoxythiophenol (0.123 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3g** as a yellow oil (310 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 6 H), 1.33–1.41 (m, 4 H), 1.60–1.66 (m, 4 H), 3.80 (s, 3 H), 4.06–4.15 (m, 4 H), 6.86–6.88 (m, 2 H), 7.46–7.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 18.5, 32.0 (d, J = 9.4 Hz), 55.2, 67.6 (d, J = 7.3 Hz), 114.8 (d, J = 1.8 Hz), 116.4 (d, J = 8.2 Hz), 136.2 (d, J = 2.7 Hz), 160.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.32; IR ($CHCl_3$): ν 3070, 2960, 2937, 1634, 1593, 1574, 1494, 1463, 1383, 1290, 1245, 1176, 1043, 1016, 1008, 993, 906, 830, 798, 731 cm^{-1}; HRMS-EI calcd for $C_{15}H_{25}O_4PS$: 332.1211, found: 332.1204.

***S*-(2-Bromophenyl) *O,O*-dibutylphosphorothioate (3h).** Following the general procedure for Table 2, using 2-bromothiophenol (0.124 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3h** as a yellow oil (366 mg, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88–0.93 (m, 6 H), 1.32–1.41 (m, 4 H), 1.61–1.67 (m, 4 H), 4.11–4.20 (m, 4 H), 7.17–7.21 (m, 1 H), 7.28–7.32 (m, 1 H), 7.32–7.63 (m, 1 H), 7.79–7.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 18.4, 31.9 (d, J = 7.3 Hz), 67.9 (d, J = 6.4 Hz), 127.8 (d, J = 1.8 Hz), 128.1 (d, J = 7.3 Hz), 128.5 (d, J = 5.5 Hz), 129.9, 133.3, 136.1 (d, J = 4.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.03; IR ($CHCl_3$): ν 3062, 2962, 2934, 2874, 1633, 1562, 1452, 1428, 1383, 1260, 1149, 1109, 1060, 1018, 900, 836, 753 cm^{-1}; HRMS-EI calcd for $C_{17}H_{21}BrO_3PS$: 380.0211, found: 380.0207.

***O,O*-Dibutyl *S*-naphthalen-1-yl phosphorothioate (3i).** Following the general procedure for Table 2, using 1-naphthalenethiol (0.140 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3i** as a yellow oil (290 mg, 82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79–0.83 (m, 6 H), 1.18–1.27 (m, 4 H), 1.45–1.52 (m, 4 H), 3.97–4.10 (m, 4 H), 7.42 (t, J = 7.8 Hz, 1 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.56 (t, J = 7.6 Hz, 1 H), 7.82–7.91 (m, 3 H), 8.52 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 18.3, 32.0 (d, J = 6.4 Hz), 67.7 (d, J = 7.3 Hz), 123.5 (d, J = 8.2 Hz), 125.4 (d, J = 3.6 Hz), 125.8, 126.2, 126.8, 128.3, 130.0 (d, J = 3.6 Hz), 134.0 (d, J = 1.8 Hz), 134.5 (d, J = 3.6 Hz), 135.0 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.32; IR ($CHCl_3$): ν 3056, 2961, 2933, 2873, 1267, 1590, 1564, 1432, 1381, 1256, 1146, 1120, 1060, 985, 903, 799, 772, 730 cm^{-1}; HRMS-EI calcd for $C_{18}H_{25}O_3PS$: 352.1262, found: 352.1256.

***O,O*-Dibutyl *S*-(4-(trifluoromethyl)phenyl)phosphorothioate (3j).** Following the general procedure for Table 2, using 4-trifluoromethylthiophenol (0.137 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3j** as a colorless oil (226 mg, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88–0.94 (m, 6 H), 1.26–1.40 (m, 4 H), 1.61–1.68 (m, 4 H), 4.07–4.21 (m, 4 H), 7.60 (d, J = 8.4 Hz, 1 H), 7.72 (d, J = 8.0 Hz, 1 H), 7.78–7.84 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.3, 18.4, 31.9 (d, J = 6.8 Hz), 67.9 (d, J = 6.6 Hz), 123.6 (q, J = 270.9 Hz), 125.9, 130.7 (q, J = 32.8 Hz), 131.9 (d, J = 6.6 Hz), 134.1 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.06; ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.5 (s); IR ($CHCl_3$): ν 2963, 2936, 2876, 1640, 1608, 1465, 1401, 1326, 1264, 1168, 1130, 1106, 1091, 1063, 1015, 889, 836, 772, 702 cm^{-1}; HRMS-EI calcd for $C_{15}H_{22}F_3O_3PS$: 370.0979, found: 370.0970.

***O,O*-Dibutyl *S*-(3-(trifluoromethyl)phenyl)phosphorothioate (3k).** Following the general procedure for Table 2, using 3-trifluoromethylthiophenol (0.140 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3k** as a yellow oil (316 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88–0.96 (m, 6 H), 1.30–1.40 (m, 4 H), 1.60–1.67 (m, 4 H), 4.08–4.20 (m, 4 H), 7.49 (t, J = 7.8 Hz, 1 H), 7.61–7.63 (m, 1 H), 7.78–7.84 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.1, 18.4, 31.8 (d, J = 6.8 Hz), 67.8 (d, J = 6.8 Hz), 123.3 (q, J = 271.1 Hz), 125.4, 128.2 (d, J = 6.8 Hz), 129.5, 130.8, 131.4 (q, J = 32.0 Hz), 137.5 (d, J = 4.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.27; ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.5 (s); IR ($CHCl_3$): ν 3076, 2963, 2876, 1465, 1423, 1384, 1324, 1263, 1169, 1130, 1069, 986, 899, 799, 697 cm^{-1}; HRMS-EI calcd for $C_{15}H_{22}F_3O_3PS$: 370.0979, found: 370.0970.

***O,O*-Dibutyl *S*-(4-fluorophenyl)phosphorothioate (3l).** Following the general procedure for Table 2, using 4-fluorothiophenol (0.107 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3l** as a colorless oil (190 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 6 H), 1.31–1.41 (m, 4 H), 1.60–1.67 (m, 4 H), 4.04–4.18 (m, 4 H), 7.03–7.07 (m, 2 H), 7.53–7.57 (m, 2 H); ^{13}C NMR

(150 MHz, $CDCl_3$) δ 13.3, 18.4, 31.9 (d, J = 7.4 Hz), 67.7 (d, J = 6.6 Hz), 116.3 (dd, J = 2.6, 22.5 Hz), 121.6 (q, J = 9.2 Hz), 136.5 (q, J = 4.5 Hz), 163.1 (dd, J = 3.0, 248.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.37; ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.3 (s); IR ($CHCl_3$): ν 2962, 2935, 2875, 1640, 1590, 1491, 1465, 1383, 1258, 1232, 1158, 1060, 1017, 988, 891, 834, 783, 727 cm^{-1}; HRMS-EI calcd for $C_{14}H_{22}FO_3PS$: 320.1011, found: 320.1020.

***O*,*O*-Dibutyl *S*-*p*-tolylphosphorothioate (3m).** Following the general procedure for Table 2, using 4-methylbenzenethiol (0.124 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3m** as a colorless oil (262 mg, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88–0.92 (m, 6 H), 1.31–1.40 (m, 4 H), 1.59–1.66 (m, 4 H), 2.33 (s, 3 H), 4.05–4.17 (m, 4 H), 7.12–7.15 (m, 2 H), 7.42–7.45 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 18.4, 20.9, 31.9 (d, J = 7.3 Hz), 67.5 (d, J = 6.4 Hz), 122.6 (d, J = 6.3 Hz), 129.9, 134.4 (d, J = 5.4 Hz), 139.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.00; IR ($CHCl_3$): ν 3025, 2961, 2934, 2874, 1493, 1464, 1382, 1257, 1119, 1060, 1018, 893, 810, 728 cm^{-1}; HRMS-EI calcd for $C_{15}H_{25}O_3PS$: 316.1262, found: 316.1260.

***O*,*O*-Dimethyl *S*-phenyl phosphorothioate (3n).** Following the general procedure for Table 2, using thiophenol (0.103 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3n** as a yellow oil (157 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80–3.84 (m, 6 H), 7.34–7.38 (m, 3 H), 7.55–7.58 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.1 (d, J = 5.4 Hz), 125.8 (d, J = 7.3 Hz), 129.0 (d, J = 2.8 Hz), 129.3 (d, J = 2.7 Hz), 134.4 (d, J = 5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.81; IR ($CHCl_3$): ν 3060, 3004, 2954, 2919, 2851, 1962, 1887, 1810, 1721, 1638, 1580, 1474, 1443, 1257, 1182, 1020, 918, 831, 796, 768, 694 cm^{-1}; HRMS-EI calcd for $C_8H_{11}O_3PS$: 218.0167, found: 218.0160.

***O*,*O*-Dimethyl *S*-naphthalen-1-yl phosphorothioate (3o).** Following the general procedure for Table 2, using 1-naphthalenethiol (0.140 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3o** as a yellow oil (191 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71–3.76 (m, 6 H), 7.42 (t, J = 7.8 Hz, 1 H), 7.50 (t, J = 7.4 Hz, 1 H), 7.59 (t, J = 7.4 Hz, 1 H), 7.81–7.88 (m, 3 H), 8.50 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.3 (d, J = 6.4 Hz), 122.8 (d, J = 8.2 Hz), 125.5 (d, J = 5.5 Hz), 126.4, 127.1, 128.5, 130.3 (d, J = 3.7 Hz), 134.1 (d, J = 1.9 Hz), 134.5 (d, J = 3.7 Hz), 135.1 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.31; IR ($CHCl_3$): ν 3056, 3006, 2954, 2851, 1722, 1637, 1590, 1564, 1503, 1456, 1380, 1336, 1256, 1183, 1020, 914, 831, 801, 771, 601, 569 cm^{-1}; HRMS-EI calcd for $C_{12}H_{13}O_3PS$: 268.0323, found: 268.0320.

***S*-(4-Methoxyphenyl) *O*,*O*-dimethyl phosphorothioate (3p).** Following the general procedure for Table 2, using 4-methoxythiophenol (0.123 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3p** as a yellow oil (154 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79–3.84 (m, 9 H), 6.87–6.90 (m, 2 H), 7.45–7.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.0 (d, J = 6.3 Hz), 55.2, 115.0 (d, J = 1.8 Hz), 115.8 (d, J = 6.4 Hz), 136.2 (d, J = 4.5 Hz), 160.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.46; IR ($CHCl_3$): ν 3070, 3007, 2955, 2849, 1639, 1592, 1494, 1462, 1408, 1291, 1250, 1177, 1024, 832, 791, 768 cm^{-1}; HRMS-EI calcd for $C_9H_{13}O_4PS$: 248.0272, found: 248.0269.

***O*,*O*-Dimethyl *S*-(3-(trifluoromethyl)phenyl)phosphorothioate (3q).** Following the general procedure for Table 2, using 3-trifluoromethylthiophenol (0.140 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3q** as a colorless oil (216 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82–3.87 (m, 6 H), 7.50 (t, J = 7.8 Hz, 1 H), 7.63–7.65 (m, 1 H), 7.77–7.82 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 54.3 (d, J = 6.0 Hz), 123.3 (q, J = 271.1 Hz), 125.8, 127.5 (d, J = 2.7 Hz), 129.8 (d, J = 1.8 Hz), 131.0 (t, J = 4.3 Hz), 131.6 (q, J = 32.8 Hz), 137.7 (d, J = 4.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.47; ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.4 (s); IR ($CHCl_3$): ν 2958, 2855, 1640, 1449, 1423, 1325, 1263, 1169, 1127, 1022, 898, 833, 799, 766, 697 cm^{-1}; HRMS-EI calcd for $C_9H_{10}F_3O_3PS$: 286.0040, found: 286.0033.

***O*,*O*-Dimethyl *S*-(4-(trifluoromethyl)phenyl)phosphorothioate (3r).** Following the general procedure for Table 2, using 4-trifluoromethylthiophenol (0.137 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3r** as a colorless oil (265 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84–3.89 (m, 6 H), 7.20–7.25 (m, 1 H), 7.30–7.34 (m, 1 H), 7.64–7.66 (m, 1 H), 7.74–7.77 (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 54.3 (d, J = 6.0 Hz), 128.0 (d, J = 2.4 Hz), 128.0 (dd, J = 7.8, 106.2 Hz), 130.3 (d, J = 3.0 Hz), 133.4 (d, J = 2.4 Hz), 136.4 (d, J = 4.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.14; ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.4 (s); IR ($CHCl_3$): ν 3062, 3003, 2954, 2851, 1636, 1562, 1450, 1427, 1257, 1182, 1109, 1030, 833, 757, 720, 646 cm^{-1}; HRMS-EI calcd for $C_9H_{10}F_3O_3PS$: 286.0040, found: 286.0044.

***S*-(2-Bromophenyl) *O*,*O*-dimethyl phosphorothioate (3s).** Following the general procedure for Table 2, using 2-bromothiophenol (0.124 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3s** as a yellow oil (208 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83–3.87 (m, 6 H), 7.60–7.62 (m, 2 H), 7.70–7.72 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.2 (d, J = 5.5 Hz), 122.2, 124.9, 126.0, 130.7, 131.1, 134.2 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.30; IR ($CHCl_3$): ν 3097, 3046, 3005, 2958, 2855, 1688, 1576, 1496, 1459, 1401, 1328, 1264, 1173, 1091, 1011, 837, 759, 767 cm^{-1}; HRMS-EI calcd for $C_8H_{10}BrO_3PS$: 295.9272, found: 295.9265.

***S*-(4-Fluorophenyl) *O*,*O*-dimethyl phosphorothioate (3t).** Following the general procedure for Table 2, using 4-fluorothiophenol (0.107 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **3t** as a colorless oil

(156 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80–3.85 (m, 6 H), 7.04–7.09 (m, 2 H), 7.53–7.57 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 54.1 (d, J = 6.6 Hz), 116.5 (d, J = 21.5 Hz), 120.9 (q, J = 3.5 Hz), 136.6 (q, J = 12.8 Hz), 163.2 (dd, J = 3.2, 248.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.51; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.8 (s); IR ($CHCl_3$): ν 2957, 2853, 1642, 1590, 1491, 1460, 1399, 1258, 1232, 1183, 1160, 1022, 835, 792, 767 cm^{-1}; HRMS-EI calcd for $C_8H_{10}FO_3PS$: 236.0072, found: 236.0081.

General procedure for Table 3

A Schlenk tube equipped with a magnetic stir bar was charged with *N*-chlorosuccinimide (1.1 mmol), alkyl thiol **4** (1.0 mmol) and MeCN (1.5 mL). After the mixture was stirred for 20 min, phosphonate **2** (1.0 mmol) was added by a syringe under a nitrogen-filled balloon. After being stirred for another 10 min at room temperature and diluted with ethyl acetate (20 mL) the resulting solution was directly filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to yield **5**.

***S*-Cyclohexyl *O*,*O*-diphenylphosphorothioate (5a).** Following the general procedure for Table 3, using cyclohexanethiol (0.126 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5a** as a colorless oil (306 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19–1.37 (m, 3 H), 1.41–1.53 (m, 3 H), 1.64–1.69 (m, 2 H), 1.96–2.00 (m, 2 H), 3.44–3.47 (m, 2 H), 7.17–7.21 (m, 2 H), 7.25–7.36 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 25.6, 34.9 (d, J = 4.4 Hz), 46.9 (d, J = 3.6 Hz), 120.5 (d, J = 4.5 Hz), 125.3, 129.5, 150.0 (d, J = 8.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.64; IR ($CHCl_3$): ν 3069, 3043, 2934, 2855, 2793, 1592, 1496, 1480, 1451, 1340, 1275, 1241, 1193, 1180, 1166, 1157, 1100, 1025, 1006, 996, 950, 940, 903, 814, 772, 689 cm^{-1}; HRMS-EI calcd for $C_{18}H_{21}O_3PS$: 348.0949, found: 348.0956.

***S*-(2-Methylbutyl) *O*,*O*-diphenylphosphorothioate (5b).** Following the general procedure for Table 3, using 2-methyl-1-butanethiol (0.136 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5b** as a colorless oil (291 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, J = 7.4 Hz, 3 H), 0.88–0.90 (m, 3 H), 1.11–1.18 (m, 1 H), 1.35–1.41 (m, 1 H), 1.55–1.60 (m, 1 H), 2.76–2.84 (m, 1 H), 2.91–2.99 (m, 1 H), 7.17–7.21 (m, 2 H), 7.28–7.36 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 18.2, 28.0, 35.4 (d, J = 5.4 Hz), 38.1 (d, J = 3.6 Hz), 120.4 (d, J = 4.6 Hz), 125.4, 129.6, 150.0 (d, J = 8.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.58; IR ($CHCl_3$): ν 3070, 3044, 2963, 2930, 2876, 1591, 1489, 1458, 1430, 1380, 1333, 1272, 1185, 1161, 1071, 1025, 1007, 929, 770, 689 cm^{-1}; HRMS-EI calcd for $C_{17}H_{21}O_3PS$: 336.0949, found: 336.0952.

***S*-Hexyl *O*,*O*-diphenylphosphorothioate (5c).** Following the general procedure for Table 3, using 1-hexanethiol (0.145 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5c** as a colorless oil (261 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83–0.87 (m, 3 H), 1.17–1.33 (m, 6 H), 1.55–1.62 (m, 2H), 2.89–2.96 (m, 2 H), 7.18–7.25 (m, 2 H), 7.28–7.38 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.2, 27.8, 30.4 (d, J = 5.4 Hz), 30.9, 31.6 (d, J = 3.7 Hz), 120.5 (d, J = 4.6 Hz), 125.4, 129.6, 150.0 (d, J = 8.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.23; IR ($CHCl_3$): ν 3069, 3044, 2957, 2930, 2857, 1591, 1489, 1457, 1378, 1272, 1185, 1161, 1071, 1025, 930, 770, 689 cm^{-1}; HRMS-EI calcd for $C_{18}H_{23}O_3PS$: 350.1106, found: 350.1101.

***S*-Benzyl *O*,*O*-diphenylphosphorothioate (5d).** Following the general procedure for Table 3, using α-toluenethiol (0.120 mL, 1.0 mmol) and diphenylphosphonate (0.192 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5d** as a yellow oil (263 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11–4.15 (m, 2 H), 7.18–7.28 (m, 11 H), 7.30–7.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.7 (d, J = 3.6 Hz), 120.6 (d, J = 4.6 Hz), 125.6, 127.8, 128.7, 128.9, 129.7, 136.4 (d, J = 6.4 Hz), 150.1 (d, J = 8.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.69; IR ($CHCl_3$): ν 3065, 3032, 2942, 2851, 1950, 1867, 1637, 1592, 1488, 1455, 1272, 1241, 1160, 1071, 1025, 1007, 922, 703, 691 cm^{-1}; HRMS-EI calcd for $C_{19}H_{17}O_3PS$: 356.0636, found: 356.0644.

***O*,*O*-Dibutyl *S*-cyclohexylphosphorothioate (5e).** Following the general procedure for Table 3, using cyclohexanethiol (0.126 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5e** as a colorless oil (226 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86–0.96 (m, 6 H), 1.24–1.60 (m, 10 H), 1.65–1.77 (m, 6 H), 2.05–2.09 (m, 2 H), 3.26–3.29 (m, 1 H), 4.01–4.012 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 18.6, 25.1, 25.7, 32.0 (d, J = 7.3 Hz), 35.1 (d, J = 5.5 Hz), 45.3 (d, J = 3.6 Hz), 66.9 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.01; IR ($CHCl_3$): ν 2960, 2933, 2873, 2856, 1252, 1148, 1121, 1061, 1020, 979, 888, 784, 727 cm^{-1}; HRMS-EI calcd for $C_{14}H_{29}O_3PS$: 308.1575, found: 308.1570.

***O*,*O*-Dibutyl *S*-(2-methylbutyl)phosphorothioate (5f).** Following the general procedure for Table 3, using 2-methyl-1-butanethiol (0.136 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5f** as a colorless oil (271 mg, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89–1.00 (m, 12 H), 1.21–1.28 (m, 1 H), 1.38–1.52 (m, 5 H), 1.65–1.72 (m, 5 H), 2.66–2.74 (m, 1 H), 2.82–2.88 (m, 1 H), 4.02–4.16 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.8, 13.2, 18.2, 18.4, 28.0, 31.8 (d, J = 7.3 Hz), 35.3 (d, J = 6.4 Hz), 37.1 (d, J = 4.5 Hz), 66.7 (d, J = 6.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.45; IR ($CHCl_3$): ν 2962, 2934, 2875, 1258, 1064, 1020, 980, 784, 729 cm^{-1}; HRMS-EI calcd for $C_{13}H_{29}O_3PS$: 296.1575, found: 296.1576.

***S*-Benzyl *O*,*O*-dibutylphosphorothioate (5g).** Following the general procedure for Table 3, α-toluenethiol (0.120 mL, 1.0 mmol) and dibutylphosphonate (0.203 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5g** as a yellow oil (224 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 6 H), 1.32–1.41 (m, 4 H), 1.57–1.64 (m, 4 H), 3.92–4.08 (m, 6 H), 7.23–7.37 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 18.5, 31.9 (d, J = 7.3 Hz),

34.7 (d, J = 3.6 Hz), 67.0 (d, J = 5.4 Hz), 127.4, 128.4, 128.7, 137.4 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.49; IR ($CHCl_3$) : ν 3089, 3064, 3031, 2961, 2935, 2874, 1639, 1496, 1457, 1432, 1383, 1260, 1149, 1120, 1061, 980, 894, 780, 730, 701 cm^{-1}; HRMS-EI calcd for $C_{15}H_{25}O_3PS$: 316.1262, found: 316.12627.

***S*-Cyclohexyl *O*,*O*-dimethyl phosphorothioate (5h).** Following the general procedure for Table 3, using cyclohexanethiol (0.126 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5h** as a yellow oil (153 mg, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.44 (m, 3 H), 1.48–1.61 (m, 3 H), 1.73–1.79 (m, 2 H), 2.06–2.10 (m, 2 H), 3.23–3.31 (m, 1 H), 3.75–3.78 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 25.6, 34.9 (d, J = 5.4 Hz), 45.3 (d, J = 2.8 Hz), 53.4 (d, J = 5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.73; IR ($CHCl_3$): ν 2934, 2854, 1641, 1449, 1342, 1250, 1182, 1019, 888, 827, 773, 728 cm^{-1}; HRMS-EI calcd for $C_8H_{17}O_3PS$: 224.0636, found: 224.0633.

***O*,*O*-Dimethyl *S*-(2-methylbutyl)phosphorothioate (5i).** Following the general procedure for Table 3, using 2-methyl-1-butanethiol (0.136 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5i** as a yellow oil (189 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 6.8 Hz, 3 H), 1.00 (d, J = 6.4 Hz, 3 H), 1.21–1.28 (m, 1 H), 1.46–1.53 (m, 1 H), 1.66–1.71 (m, 1 H), 2.67–2.75 (m, 1 H), 2.82–2.89 (m, 1 H), 3.78–3.83 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 18.3, 28.0, 35.4 (d, J = 5.5 Hz), 37.2 (d, J = 3.6 Hz), 53.4 (d, J = 5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 32.80; IR ($CHCl_3$): ν 2961, 2931, 2877, 2853, 1638, 1461, 1380, 1334, 1258, 1182, 1022, 925, 829, 794, 774, cm^{-1}; HRMS-EI calcd for $C_7H_{17}O_3PS$: 212.0636, found: 212.0629.

***S*-Benzyl *O*,*O*-dimethyl phosphorothioate (5j).** Following the general procedure for Table 3, using α-toluenethiol (0.120 mL, 1.0 mmol) and dimethylphosphonate (0.094 mL, 1.0 mmol), and then purification by column chromatography (SiO_2, hexane) provides **5j** as a yellow oil (156 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66–3.70 (m, 6 H), 4.02 (d, J = 14.4 Hz, 2 H), 7.27–7.37 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.7 (d, J = 3.7 Hz), 53.5 (d, J = 5.5 Hz), 127.5, 128.5, 128.7, 137.2 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.94; IR ($CHCl_3$): ν 3063, 3030, 2953, 2851, 1638, 1496, 1455, 1261, 1183, 1015, 920, 829, 771, 702 cm^{-1}; HRMS-EI calcd for $C_9H_{13}O_3PS$: 232.0323, found: 232.0318.

Acknowledgements

The National Science Council, Taiwan (NSC 101-2113-M-005-008-MY3), the National Chung Hsing University and the Center of Nanoscience and Nanotechnology (NCHU) are gratefully acknowledged for financial support. We also thank Prof. Fung-E Hong (NCHU) for sharing his GC-MS instruments. C.F. L. is a Golden-Jade Fellow of Kenda Foundation, Taiwan.

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