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Phosphinoyl Radical-Initiated 1,2-Bifunctional Thiocyanodiphenylphosphinoylation of Alkenes

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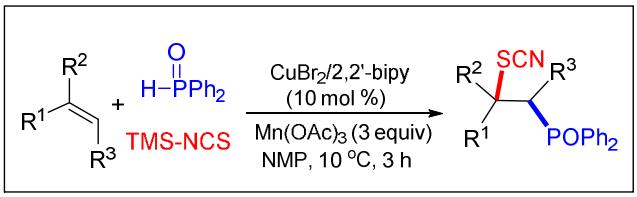
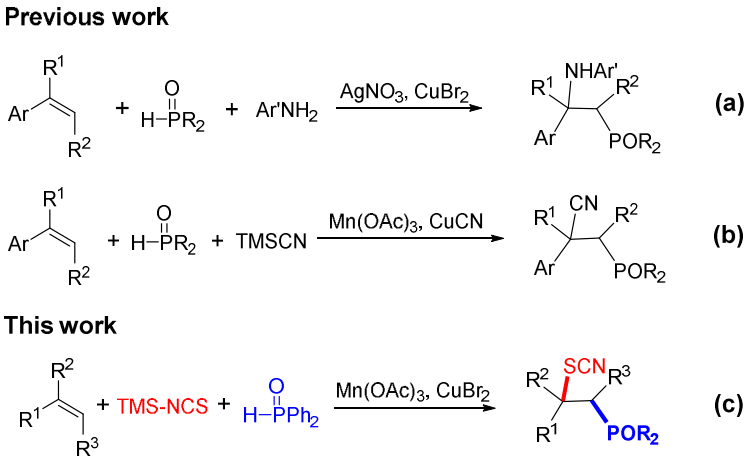


ABSTRACT: 1,2-Bifuctional thiocyanodiphenylphosphinoylation of alkenes is established through phosphinoyl radical addition followed by Cu-catalyzed thiocyanation. This one-pot reaction is applicable to a range of aromatic, aliphatic, and cyclic alkenes to afford thiocyanodiphenylphosphinoylated compounds in satisfactory yields.

Radical-initiated bifunctionalization of alkenes is an attractive method for introducing a set of groups during a one-pot reaction process.[1] On the basis of successful vicinal oxyphosphinoylation,[2] hydroxyphosphinoylation, acetoxyphosphinoylation,[3] and halophosphinoylation[4] reactions reported in the literature, we recently developed phosphinoyl radical-initiated aminophosphinoylation and cyanophosphinoylation reactions (Scheme 1, a and b)[5]. Introduced in this paper is the extension of the new method for bifunctional thiocyanodiphenylsphinoylation (Scheme 1, c). Both phosphinoyl and thiocyano are functional groups commonly found in biologically active compounds. Bifunctional thiocyanosphinoylated compounds could be useful in the development of new agricultural and pharmaceutical chemicals,[6,7] as well as phosphine ligands for metal-catalyzed reactions.

Thiocyanates are ubiquitous moieties in bioactive compounds such as antimicrobial[7b,8] or antiproliferative activitiy.[7c] as well as key building blocks for construction of various heterocyclic skeletons.[9] Furthermore, organic thiocyanates could be easily isomerized to isothiocyanates under heating. The later have been widely applied for synthesis of agrochemicals and polymers.[10] In addition, thiocyano is a versatile group which can be used for the synthesis of other organosulfur compounds such as thiols, thioethers, disulfides, thiocarbamates, and heterocycles.[6]

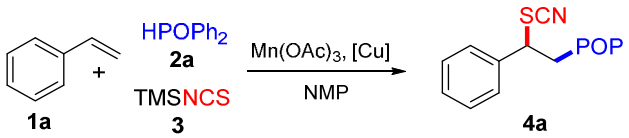
Scheme 1. Phosphorus Radical-initiated Bifunctionalizations



The development of reaction conditions was carried out using styrene **1a**, $HP(O)Ph_2$ **2a**, and trimethylsilylisothiocyanate (TMSNCS, **3**) as substrates. The initial reaction using CuSCN as a catalyst, $Mn(OAc)_3$ as an oxidant and *N*-methyl-2-pyrrolidone (NMP) as a solvent at room temperature gave desired product **4a** in 41% yield (Table 1, entry 1). The -SCN group of **4a** was confirmed by a week IR peak at 2158 cm^{-1} and a ^{13}C-NMR peak at 110.7 ppm, which are in accordance with that reported in literature.[11] If it is a -NCS group, it should have a strong IR peak at 2020-2100 cm^{-1} and a broad ^{13}C-NMR peak at 134-143 ppm.[10] Conducting reactions between 0 to 55 ^{o}C indicated that 10 ^{o}C was a good temperature which gave 54% yield (Table 1, entry 3). The effort of exploring other oxidants including DTBP, TBHP, Ag_2CO_3, and $AgNO_3$; alternative SCN sources such as KSCN, NH_4SCN and TsSCN; and different solvents such as DMSO, MeOH, toluene, and

MeCN, all failed to give better results (see supporting information (SI), Tables S1-S3). The screening of Cu-catalysts including CuI, CuBr, CuCl, and $Cu(OAc)_2$ indicated that $CuBr_2$ is better than CuSCN to give product in 63% yield at 10 mol % loading (Table 1, entries 5-8, see also SI, Table S4), whereas a control reaction without using a copper catalyst gave no product (Table 1, entry 9). Exploring different ligands including 2,2'-dipyridine (2,2'-dipy), *N,N*-dimethylethylenediamine (DMEDA), *N,N,N,N*-tetramethylethylenediamine (TMEDA), and 1,10-phenanthroline (phen) (Table 1, entries 10−13), and fine tuning the ratio of reaction components revealed that a reaction of 1:3:3:3 of **1a**/**2a**/**3**/$Mn(OAc)_3$ with 10 mol % each of $CuBr_2$ and 2,2'-bipy in NMP at 10 °C for 3 h under argon is an optimized condition to afford product **4a** in 69% yield (Table 1, entry 14, see SI, Table S5).

Table 1. Optimization of the reaction conditions[a]

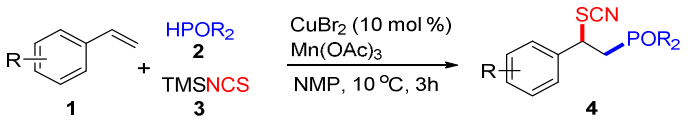


entry	Cu-cat (mol %)	ligand (mol %)	temp (°C)	yield[b] (%)
1	CuSCN (20)	—	25	41
2	CuSCN (20)	—	55	33
3	CuSCN (20)	—	10	54
4	CuSCN (20)	—	0	20
5	$CuBr_2$ (20)	—	10	58
6	$CuBr_2$ (5)	—	10	50
7	$CuBr_2$ (10)	—	10	63
8	$CuBr_2$ (1	—	10	30
9	—	—	10	nd[c]
10	$CuBr_2$ (10)	2,2'-dipy (10)	10	68
11	$CuBr_2$ (10)	DMEDA (10)	10	62
12	$CuBr_2$ (10)	TMEDA (10)	10	50
13	$CuBr_2$ (10)	phen (10)	10	66
14[d]	**$CuBr_2$ (10)**	2,2'-dipy (10)	**10**	**69**

[a]Conditions: **1a** (0.5 mmol), **2a** (2.5 mmol), **3** (4 mmol), $Mn(OAc)_3.2H_2O$ (2.5 mmol) in NMP (3 mL) at 10 °C for 3 h under Ar. [b]Isolated yield. [c]nd means not detected. [d]**1a** (0.5 mmol), **2a** (1.5 mmol), **3** (1.5 mmol) and $Mn(OAc)_3.2H_2O$ (1.5 mmol) were used.

A series of styrene derivatives were used for bifunctional thiocyanodiphenylphosphinoylation under the optimized conditions. As shown in Scheme 2, starting materials with substitution groups at different positions of aromatic ring reacted smoothly to give the corresponding difunctionalization products **4b**−**n** in moderate to good yields. In general, the yields of electron-rich substrates are higher than that of electron-withdrawing substrates. For instance, substrates bearing Me- or MeO-substituents, regardless of substitution position, afforded products in 69-79% yields (Scheme 2, **4b**−**g**). Whereas substrates containing electron-withdrawing groups such as Cl, Br, F, CN and NO_2 groups gave products in 44−60% yields (Scheme 2, **4h**−**n**). The reaction of 2-vinylnaphthalene was also attempted to give **4o** in 67% yield. But the reaction of 2-vinylpyridine produced a complicated mixture, the desired product **4p** was not isolated. In addition to diphenylphosphine oxide **2a**, dimethyl- and diethyl phosphites were also used to form difunctionalization compounds **4q** and **4r,** but alkenylphosphonates **4q′** and **4r′** were observed as by-products. The by-products were generated from the deprotonation process after the phosphinoyl radical addition. Reactions of vinyl substituted aryl alkenes were also attempted. α-Methylstyrene and β-phenylstyrene gave product **4t** and **4u** in 35% and 48% yields, respectively. But no products were detected from the reactions of β-methylstyrene and α-phenylstyrene. Only 2,2-diphenylvinyl diphenylphosphine oxide was isolated (see mechanism discussion later). Reactions of cyclic aromatic alkenes 1,2-dihydronaphthalene and indene gave 4v and 4w in 65% and 69% yields, respectively.

Scheme 2. Reactions of Styrene Derivatives[a,b]



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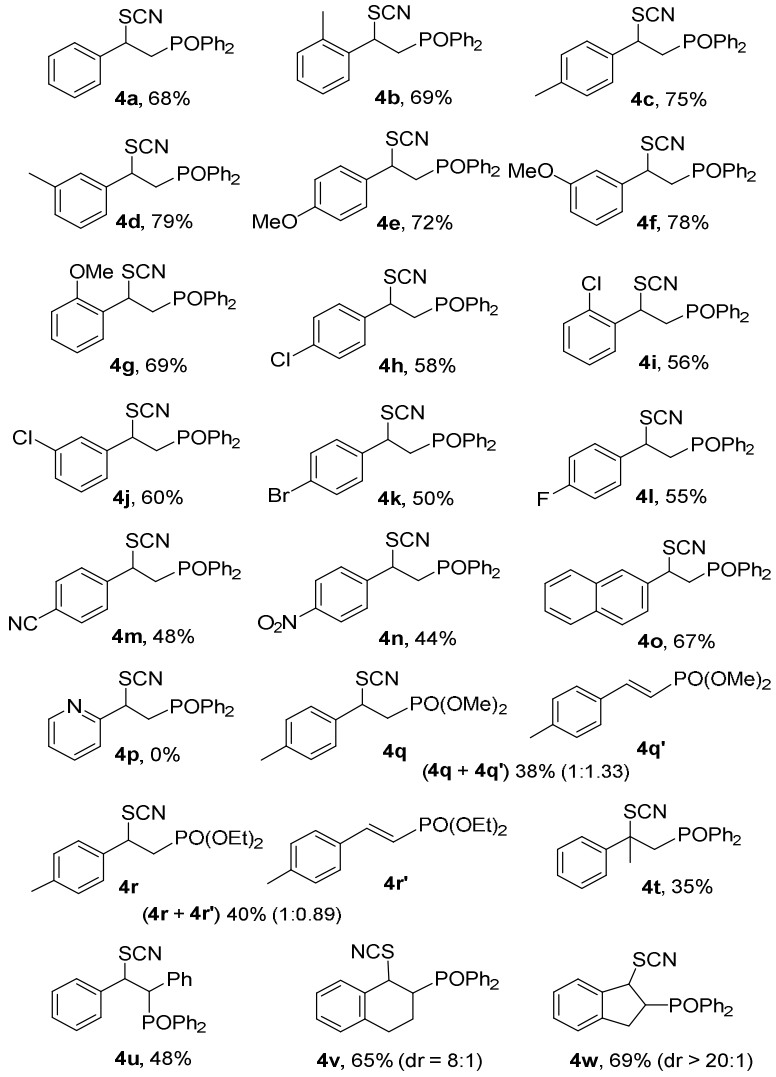
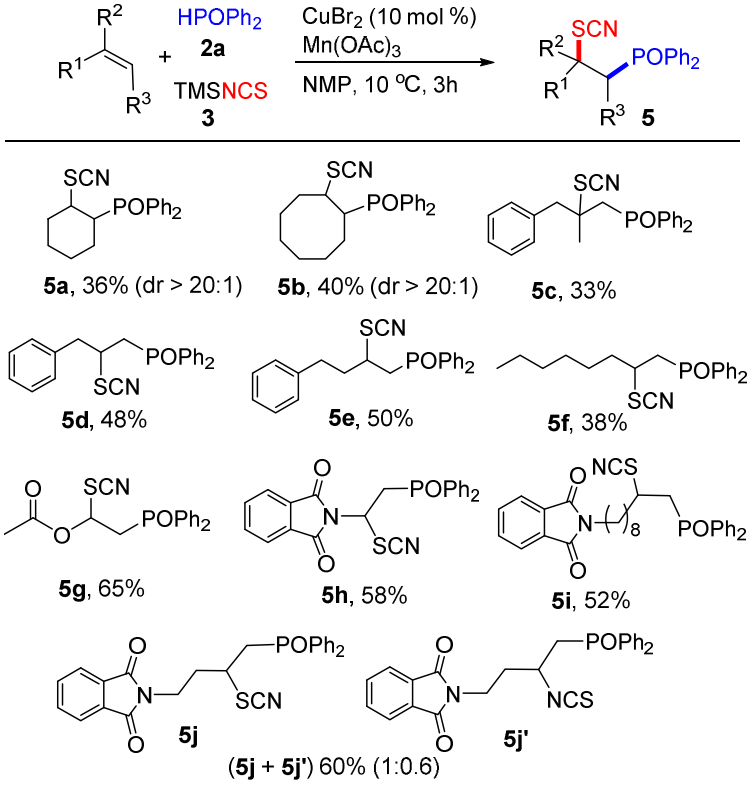


[a]Conditions: **1** (0.5 mmol), **2a** (1.5 mmol), **3** (1.5 mmol), $CuBr_2$ (0.05 mmol), 2,2'-bipy (0.05 mmol), $Mn(OAc)_3.2H_2O$ (1.5 mmol) in NMP (3 mL) at 10 °C, 3 h under Ar. [b]Isolated yield.

The thiocyanophosphinoylation reaction is also applicable to non-aromatic alkenes such as cyclohexene and cyclooctene to give **5a** and **5b** in 36% and 40% yields, respectively (Scheme 3). Reactions of aliphatic alkenes containing non-conjugated phenyl, conjugated ester, conjugated or non-conjugated phthalimide all processed smoothly to afford corresponding products **5c**–**j** in

satisfactory yields. Interestingly, the reaction for thiocyanated (-SCN) **5j** produced an isothiocyanated (-NCS) isomer **5j'** as a byproduct through isomerizayion under heating.[10]

Scheme 3. Reactions of alkenes[a]

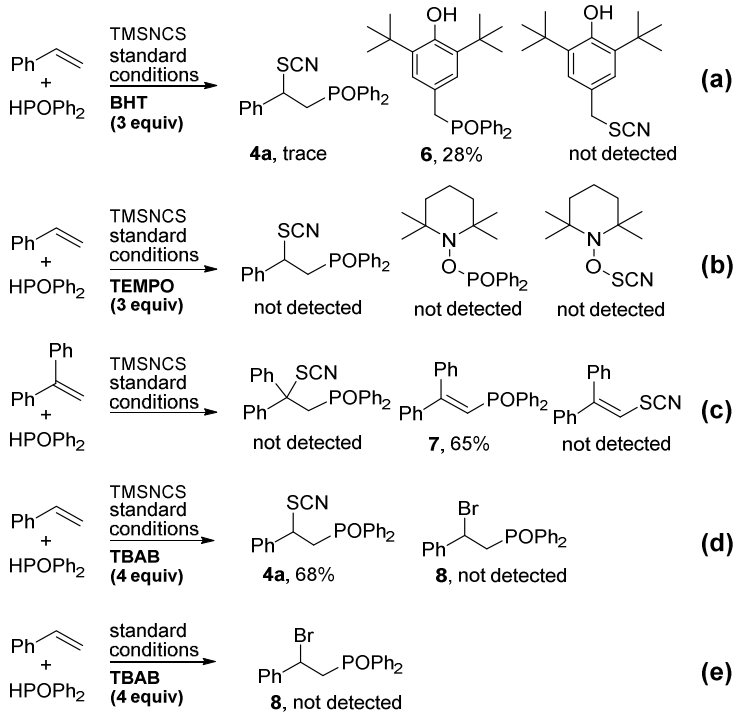


[a]Conditions: **1** (0.5 mmol), **2a** (1.5 mmol), **3** (1.5 mmol), $CuBr_2$ (0.05 mmol), 2,2'-bipy (0.05 mmol), $Mn(OAc)_3.2H_2O$ (1.5 mmol) in NMP (3 mL) at 10 °C, 3 h under Ar. Isolated yield.

Several control reactions were carried out to understand the mechanism of thiocyanodiphenylphosphinoylation reaction and thiocyanation (Scheme 4). In the presence of 2,6-di-*tert*-butyl-4-methylphenol (BHT), the reaction of styrene under the standard conditions resulted in a trace amount of expected product **4a** together with radical trapping compound **6** (Scheme 4, a). A similar reaction with TEMPO completely stopped the formation of **4a** (Scheme 4, b). These results suggest that phosphinoyl radical is involved in the reaction of thiocyanodiphenylphosphinoylation. The reaction of 1,1-diphenylethylene without a radical tapping agent only gave (2,2-diphenylvinyl) diphenylphosphine oxide **7** (Scheme 4, c). The reaction of styrene under the standard conditions with

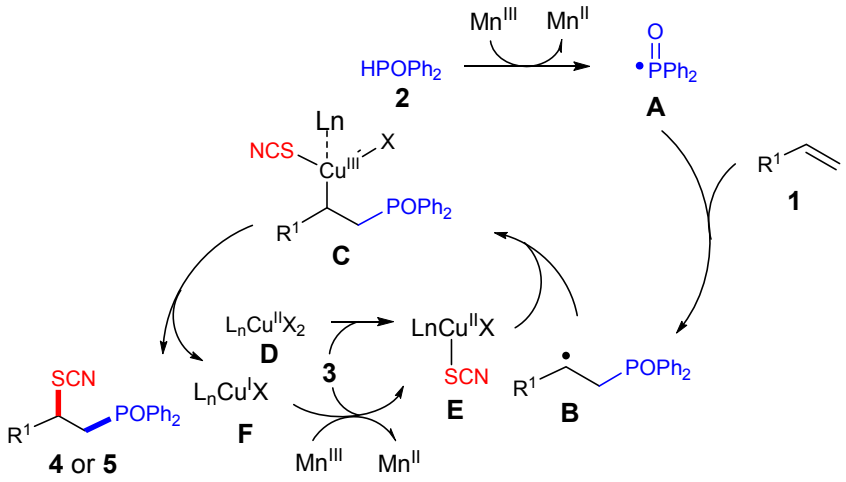
the addition of 4.0 equiv of tetrabutylammonium bromide (TBAB) provided product **4a** in 68% yield, but without brominated product **8** (Scheme 4, d and e). This result cannot prove an ionic process, which is different from the result of previously reported cyanophosphinoylation reaction.[5b] Furthermore, no evidence indicates that SCN radical was involved in the reaction process since no SCN radical was trapped by 1,1-diphenylethylene and BHT (see SI, Scheme S1).

Scheme 4. Control Reactions



A reaction mechanism for thiocyanodiphenylphosphinoylation is proposed based on the analysis of the results from the control reactions (Scheme 5). The initial phosphinoyl radical **A**, generated from the oxidation of $HPOPh_2$ **2a** with Mn^{III}, adds to alkene **1** to form radical **B**.[12,13] It then reacts with a Cu^{II} complex **E** which is formed through the interaction of TMSNCS **3** with Cu^{II} to form complex **C**.[14] Complex **C** undergoes elimination of **F** to form thiocyanodiphenylphosphinoylation products **4** or **5**.

Scheme 5. Mechanism for thiocyanodiphenylphosphinoylation



In summary, phosphinoyl radical-initiated bifunctionalization has been developed for thiocyanodiphenylphosphinoylation through $Mn(OAc)_3$ oxidation of diphenylphosphine oxide followed phosphinoyl addition to alkene and then Cu-catalyzed thiocyanation. This one-pot reaction is applicable to a range of aromatic, aliphatic, and cyclic alkenes to afford thiocyanodiphenylphosphinoylation compounds in satisfactory yields.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were obtained using $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as internal standard or 85% H_3PO_4 as external standard for ^{31}P NMR (162 MHz). Chemical shifts δ were reported in ppm using TMS as an internal stand. All coupling constants (J values) were reported in Hertz (Hz). High resolution mass spectra were recorded on a TOF machine (ESI). Column chromatography was performed with 300-400 mesh silica gel using flash column techniques. All alkenes were purified by flash column chromatography (Al_2O_3) before use.

Typical procedure for the preparation of diphenyl(2-phenyl-2-thiocyanatoethyl)phosphine oxide (4a). To a Schlenk tube charged with a magnetic stirring bar, $CuBr_2$ (0.05 mmol), 2,2'-dipyridyl (0.05 mmol) and $Mn(OAc)_3 \cdot 2H_2O$ (1.5 mmol) were added and flushed with argon gas three

times. A solution of styrene (**1a**, 0.50 mmol), $HP(O)Ph_2$ (**2a**, 0.75 mmol) and TMSNCS (**3**, 0.75 mmol) in NMP (2 mL) was injected. The mixture was allowed to stir at 10 °C for 0.5 h, then a solution of $HP(O)Ph_2$ (**2a**, 0.75 mmol) and TMSNCS (**3**, 0.75 mmol) in NMP (1 mL) was injected again. The mixture was stirred at 10 °C for 2.5 h (monitored with TLC). After the substrate was consumed, water (60 mL) was added to the reaction mixture, then extracted with ethyl acetate (20 mL×3). The combined organic layer was washed with saturated sodium bicarbonate solution (20 mL×3) and dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (1:10 AcOEt:CH_2Cl_2) to afford product **4a**.

*Diphenyl(2-phenyl-2-thiocyanatoethyl)phosphine oxide (**4a**).* White solid, Mp: 157.8-159.5 °C, 68% yield (123.42 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.74 (m, 2H), 7.58 – 7.46 (m, 5H), 7.41 – 7.36 (m, 1H), 7.31 – 7.24 (m, 4H), 7.20 – 7.12 (m, 3H), 5.04 – 4.92 (m, 1H), 3.30 – 3.10 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.9 (d, J = 4.8 Hz), 131.8 (d, J = 2.7 Hz), 131.3 (d, J = 2.7 Hz), 130.2 (d, J = 5.3 Hz), 130.1 (d, J = 5.4 Hz), 128.7, 128.5, 128.43, 128.40, 128.1, 128.0, 127.0, 110.7, 46.6, 36.0 (d, J = 66.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.78. IR (cm^{-1}): ν 2158. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{18}NOPSNa$ 386.0744, found 386.0754.

*Diphenyl(2-thiocyanato-2-(o-tolyl)ethyl)phosphine oxide (**4b**).* White solid, mp: 117.2-119.2 °C, 69% yield (130.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.75 (m, 2H), 7.60 – 7.46 (m, 5H), 7.41 – 7.36 (m, 1H), 7.21 – 7.31 (m, 3H), 7.11 – 7.03 (m, 2H), 7.01-6.95 (m, 1H), 5.35 – 5.23 (m, 1H), 3.41 – 3.19 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.7, 134.3 (d, J = 4.2 Hz), 131.8 (d, J = 2.7 Hz), 131.2 (d, J = 2.7 Hz), 130.4, 130.1, 130.0 (d, J = 1.4 Hz), 129.9, 128.5, 128.4, 128.0, 127.9, 126.2, 126.1, 110.7, 42.5, 36.0 (d, J = 66.1 Hz), 18.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.91. IR (cm^{-1}): ν 2151. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NOPSNa$ 400.0901, found 400.0892.

*Diphenyl(2-thiocyanato-2-(p-tolyl)ethyl)phosphine oxide (**4c**).* White solid, Mp: 151.9-154.2 °C, 75% yield (141.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.74 (m, 2H), 7.56 – 7.45 (m, 5H), 7.42

– 7.37 (m, 1H), 7.25–7.31 (m, 2H), 7.17 – 7.09 (m, 2H), 7.03–6.87 (m, 2H), 5.03 – 4.84 (m, 1H), 3.32 – 3.07 (m, 2H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.7, 133.8 (d, J = 4.6 Hz), 131.8 (d, J = 2.8 Hz), 131.0 (d, J = 2.8 Hz), 130.2 (d, J = 2.0 Hz), 130.1 (d, J = 2.2 Hz), 129.0, 128.5, 128.4, 128.0, 127.9, 127.0, 110.8, 46.6, 36.2 (d, J = 66.4 Hz), 20.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.85. IR (cm^{-1}): ν 2155. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NOPSNa$ 400.0901, found 400.0896.

*Diphenyl(2-thiocyanato-2-(m-tolyl)ethyl)phosphine oxide (**4d**)*. White solid, Mp: 122.3-124 ^oC, 79% yield (148.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 – 7.67 (m, 3H), 7.55 – 7.46 (m, 5H), 7.40 – 7.35 (m, 1H), 7.30 – 7.27 (m, 1H), 7.09 – 7.04 (m, 2H),7.01 – 6.95 (m, 2H), 5.05 – 4.89 (m, 1H), 3.27 – 3.12 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.1, 136.6, 131.8, 131.2, 130.2, 130.1, 129.5, 128.5, 128.39, 128.35, 127.9, 127.8, 127.7, 124.2, 110.8, 46.7, 36.2 (d, J = 66.3 Hz), 20.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.88. IR (cm^{-1}): ν 2152. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NOPSNa$ 400.0901, found 400.0890.

*(2-(4-Methoxyphenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4e**)*. White solid, Mp: 121.9-122.8 ^oC, 72% yield (141.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.73 (m, 2H), 7.59 – 7.32 (m, 8H), 7.24 – 7.08 (m, 2H), 6.84 – 6.64 (m, 2H), 5.50 – 5.10 (m, 1H), 3.73 (s, 3H), 3.07 – 2.94 (m, 1H), 2.87 – 2.60 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7, 133.9, 132.2, 131.8, 131.2 (d, J = 7.6 Hz), 130.8 (d, J = 9.2 Hz), 130.5 (d, J = 9.1 Hz), 129.0, 128.9, 128.7, 128.6, 127.3, 114.3, 55.3 (d, J = 13.2 Hz), 39.3 (d, J = 67.9 Hz), 29.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.89. IR (cm^{-1}): ν 2138. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NO_2PSNa$ 416.0850, found 416.0864.

*(2-(3-Methoxyphenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4f**)*. White solid, Mp: 138.4-141.3 ^oC, 78% yield (153.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.73 (m, 2H), 7.57 – 7.47 (m, 5H), 7.40 – 7.36 (m, 1H), 7.35 – 7.26 (m, 2H),7.14 – 7.04 (m, 1H), 6.89 – 6.83 (m, 1H), 6.78 – 6.67 (m, 2H), 5.13 – 4.82 (m, 1H), 3.71 (s, 3H), 3.29 – 3.02 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.2, 138.3 (d, J = 3.8 Hz), 131.9, 131.2, 130.2, 130.1 (d, J = 1.6 Hz), 129.54, 128.52, 128.4, 128.0,

127.9, 119.3, 114.4, 112.5, 110.7, 54.7, 46.5, 29.2; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.90. IR (cm^{-1}): ν 2141. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NO_2PSNa$ 416.0850, found 416.0851.

*(2-(2-Methoxyphenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4g**).* White solid, Mp: 136.6-137.1 ^{o}C, 69% yield (135.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 2H), 7.56 – 7.48 (m, 5H), 7.41 – 7.37 (m, 1H), 7.33 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 7.19 – 7.12 (m, 1H), 6.83 – 6.77 (m, 1H), 6.67 – 6.60 (m, 1H), 5.33 – 5.23 (m, 1H), 3.75 (s, 3H), 3.40 – 3.31 (m, 1H), 3.28 – 3.17 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 156.0, 131.7 (d, J = 2.6 Hz), 131.1 (d, J = 2.7 Hz), 130.2, 130.1 (d, J = 1.7 Hz), 130.0, 129.9, 128.4, 128.3, 128.2, 127.9, 127.8, 120.1, 111.5, 110.3, 54.8, 42.4, 34.6 (d, J = 66.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.98. IR (cm^{-1}): ν 2050. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NO_2PSNa$ 416.0850, found 416.0837.

*(2-(4-Chlorophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4h**).* White solid, Mp: 194.8-196.6 ^{o}C, 58% yield (115.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.72 (m, 2H), 7.60 – 7.39 (m, 6H), 7.34 – 7.27 (m, 2H), 7.22 – 7.14 (m, 2H), 7.14 – 7.01 (m, 2H), 5.02 – 4.90 (m, 1H), 3.28 – 3.04 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.2 (d, J = 4.2 Hz), 134.7, 132.0 (d, J = 2.8 Hz), 131.3 (d, J = 3.1 Hz), 131.2 (d, J = 4.0 Hz), 130.1, 130.0, 128.58, 128.55, 128.47, 128.1, 128.0, 110.3, 46.0, 36.2 (d, J = 65.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.62. IR (cm^{-1}): ν 2156. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{17}ClNOPSNa$ 420.0355, found 420.0338.

*(2-(2-Chlorophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4i**).* Yellow solid, Mp: 122.7-125 ^{o}C, 56% yield (111.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.72 (m, 2H), 7.67 – 7.49 (m, 5H), 7.46 – 7.41 (m, 1H), 7.40 – 7.31 (m, 3H), 7.31 – 7.26 (m, 1H), 7.21 – 7.09 (m, 2H), 5.49 – 5.29 (m, 1H), 3.42 – 3.12 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 134.8 (d, J = 5.2 Hz), 133.4, 132.4 (d, J = 2.3 Hz), 132.0 (d, J = 2.3 Hz), 130.8, 130.6 (d, J = 2.8 Hz), 130.5, 130.2, 130.1, 129.0, 128.9, 128.7, 128.6, 127.3, 110.8, 43.4, 35.4 (d, J = 66.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.59. IR (cm^{-1}): ν 2146. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{17}ClNOPSNa$ 420.0355, found 420.0364.

*(2-(3-Chlorophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4j**)*. White solid, Mp: 158.6-159.8 °C, 60% yield (119.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.72 (m, 2H), 7.63 – 7.45 (m, 5H), 7.43 – 7.37 (m, 1H), 7.36 – 7.28 (m, 2H), 7.21 – 7.00 (m, 4H), 5.02 – 4.91 (m, 1H), 3.25 – 3.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.7 (d, J = 4.4 Hz), 134.2, 132.0 (d, J = 2.8 Hz), 131.5 (d, J = 2.9 Hz), 130.1, 130.0, 129.7, 128.9, 128.6, 128.5, 128.1, 128.0, 127.2, 125.4, 110.1, 45.9, 35.9 (d, J = 65.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.48. IR (cm^{-1}): ν 2157. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{17}ClNOPSNa$ 420.0355, found 420.0357.

*(2-(4-Bromophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4k**)*. White solid, Mp: 196-198.4 °C, 50% yield (110.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.69 (m, 2H), 7.61 – 7.39 (m, 6H), 7.34 – 7.22 (m, 4H), 7.17 – 7.04 (m, 2H), 5.04 – 4.87 (m, 1H), 3.30 – 3.03 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.7 (d, J = 3.8 Hz), 132.0 (d, J = 1.9 Hz), 131.5, 131.2 (d, J = 2.2 Hz), 130.14, 130.05, 128.7, 128.6, 128.5, 128.2, 128.0, 122.9, 110.3, 46.0, 36.2 (d, J = 66.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.49. IR (cm^{-1}): ν 2156. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{17}BrNOPSNa$ 463.9850, found 463.9856.

*(2-(4-Fluorophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4l**)*. White solid, Mp: 176.6-178.8 °C, 55% yield (104.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 – 7.69 (m, 2H), 7.65 – 7.38 (m, 6H), 7.35 – 7.27 (m, 2H), 7.26 – 7.18 (m, 2H), 6.95 – 6.64 (m, 2H), 5.09 – 4.91 (m, 1H), 3.38 – 2.78 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.6, 161.1, 132.5 (d, J = 3.9 Hz), 131.9 (d, J = 2.7 Hz), 131.3 (d, J = 2.7 Hz), 130.1, 130.0, 129.0 (d, J = 8.6 Hz), 128.5 (d, J = 12.0 Hz), 128.0 (d, J = 12.1 Hz), 115.5, 115.3, 110.5, 46.0, 36.3 (d, J = 66.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.64. IR (cm^{-1}): ν 2156. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{17}FNOPSNa$ 404.0650, found 404.0652.

*(2-(4-Cyanophenyl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4m**)*. White solid, Mp: 155.6-157.6 °C, 48% yield (93.12 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.66 (m, 3H), 7.58 – 7.51 (m, 2H), 7.51 – 7.47 (m, 2H), 7.41 – 7.34 (m, 6H), 7.29 – 7.26 (m, 1H), 5.59 – 5.50 (m, 1H), 3.50 – 3.22

(m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.0 (d, J = 3.1 Hz), 131.9 (d, J = 2.8 Hz), 131.6, 131.2 (d, J = 2.7 Hz), 130.1, 130.04 (d, J = 1.8 Hz), 129.96, 128.5, 128.4, 128.0, 127.9, 126.6, 117.7, 111.8, 44.1, 40.8 (d, J = 63.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.32. IR (cm^{-1}): ν 2230. HRMS (ESI-TOF) *m/z*: $(M+H)^+$ calcd for $C_{22}H_{18}N_2OPS$ 389.0877, found 389.0866.

*(2-(4-Nitrophenyl)-2-thiocyanatoethyl) diphenylphosphine oxide (**4n**).* White solid, Mp: 168.1-171.1 °C, 44% yield (89 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 8.3 Hz, 2H), 7.80 – 7.63 (m, 2H), 7.60 – 7.30 (m, 8H), 7.23 (t, J = 6.8 Hz, 2H), 5.70-5.50 (m, 1H), 3.60 – 3.18 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.4 (d, J = 16.0 Hz), 132.4, 131.7, 130.7, 130.62, 130.57, 130.49, 129.0 (d, J = 9.1 Hz), 128.7, 128.4 (d, J = 10.1 Hz), 123.6, 44.1, 29.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.34. IR (cm^{-1}): ν 2156. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ Calcd for $C_{21}H_{17}N_2NaO_3PS$ 431.0595, found 431.0595.

*(2-(Naphthalen-2-yl)-2-thiocyanatoethyl)diphenylphosphine oxide (**4o**).* White solid, Mp: 161.1-162.5 °C, 67% yield (138.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 2H), 7.73 – 7.62 (m, 4H), 7.57 – 7.33 (m, 8H), 7.18 – 7.10 (m, 1H), 7.09 – 6.92 (m, 2H), 5.25 – 5.12 (m, 1H), 3.37 – 3.19 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 133.9 (d, J = 4.1 Hz), 132.8, 132.2, 131.9 (d, J = 1.8 Hz), 130.9 (d, J = 2.1 Hz), 130.2, 130.1 (d, J = 4.4 Hz), 130.0, 128.6, 128.5, 128.4, 127.74, 127.70, 127.6, 127.1, 127.0, 126.4, 126.1, 110.6, 47.0, 36.2 (d, J = 66.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.84. IR (cm^{-1}): ν 2043. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ Calcd for $C_{25}H_{20}NOPSNa$ 436.0901, found 436.0895.

*Mixture of dimethyl (2-thiocyanato-2-(p-tolyl)ethyl)phosphonate (**4q**) and dimethyl (4-methylstyryl) phosphonate (**4q'**).* Colorless liquid. 15% (**4q**) and 23% (**4q'**) yield (47.3 mg), respectively, **4q** : **4q'** =1 : 1.33, analyzed by ^{1}H NMR spectrum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (dd, J = 22.6, 17.5 Hz, 1.34H), 7.40 (d, J = 8.1 Hz, 2.66H), 7.28 (d, J = 8.2 Hz, 2H), 7.23 – 7.17 (m, 4.66H), 6.16 (t, J = 17.8 Hz, 2H), 4.75 (dd, J = 16.0, 8.2 Hz, 1H), 3.77 (d, J = 11.1 Hz, 8H), 3.64 (d, J = 11.1 Hz, 3H), 3.47 (d, J = 11.0 Hz, 3H), 2.70 (dd, J = 19.0, 7.4 Hz, 2H), 2.37 (s, 4H), 2.35 (s,

3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.2 (d, J = 6.8 Hz), 140.4, 139.1, 133.8 (d, J = 6.0 Hz), 131.6, 129.4, 129.1, 127.3, 126.9, 111.5, 109.6, 52.2, 52.1 (d, J = 4.3 Hz), 52.01, 51.96, 51.91, 47.0, 32.3, 31.0, 21.0, 20.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.68, 22.89. IR (cm^{-1}): ν 2054. HRMS (ESI-TOF) of **4q** *m/z*: $(M+Na)^+$ Calcd for $C_{12}H_{16}NO_3PSNa$ 308.0486, found 308.0472; HRMS (ESI-TOF) of **4q'** *m/z*: $(M+Na)^+$ Calcd for $C_{11}H_{15}O_3PNa$ 249.0657, found 249.0650.

*Mixture of diethyl (2-thiocyanato-2-(p-tolyl)ethyl)phosphonate (**4r**) and diethyl (4-methylstyryl) phosphonate (**4r'**).* Colorless liquid. 21% (**4r**) and 19% (**4r'**) yield (245.5 mg), respectively, **4r** : **4r**' =1 : 0.89, analyzed by ^{1}H NMR spectrum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (dd, J = 22.6, 17.5 Hz, 0.89H), 7.30 – 7.23 (m, 2.79H), 7.21 – 7.16 (m, 3.77H), 6.19 (t, J = 17.7 Hz, 0.89H), 4.76 (dt, J = 15.5, 7.7 Hz, 1H), 4.17 – 4.07 (m, 3.56H), 4.04 – 3.96 (m, 2H), 3.93 – 3.73 (m, 2H), 2.72 – 2.63 (m, 2H), 2.36 (s, 2.67H), 2.34 (s, 3H), 1.34 (t, J = 7.1 Hz, 5.34H), 1.22 (t, J = 7.1 Hz, 3H), 1.13 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.7, 167.6, 133.7, 133.4, 131.6, 131.4, 130.4 (d, J = 9.3 Hz), 130.3 (d, J = 9.3 Hz), 129.98 (d, J = 9.4 Hz), 129.95 (d, J = 9.6 Hz), 128.4 (d, J = 3.7 Hz), 128.3 (d, J = 3.8 Hz), 123.0, 122.8, 109.8, 44.6, 42.0 (d, J = 1.8 Hz), 39.9 (d, J = 64.0 Hz), 37.7 (d, J = 3.7 Hz), 36.4, 35.8, 34.7 (d, J = 4.9 Hz), 34.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 23.88, 20.02. IR (cm^{-1}): ν 2150. HRMS (ESI-TOF) of **4r** *m/z*: $(M+Na)^+$ Calcd for $C_{14}H_{20}NO_3PSNa$ 336.0799, found 336.0808; HRMS (ESI-TOF) of **4r'** *m/z*: $(M+Na)^+$ Calcd for $C_{13}H_{19}O_3PNa$ 277.0970, found 277.0957.

*Diphenyl(2-phenyl-2-thiocyanatopropyl)phosphine oxide (**4t**).* White solid, Mp: 154.6–155.5 ^{o}C, 35% yield (66.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.70 (m, 2H), 7.60 – 7.54 (m, 2H), 7.53 – 7.45 (m, 3H), 7.44 – 7.32 (m, 5H), 7.26 – 7.14 (m, 3H), 3.03 – 2.89 (m, 2H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.13, 143.07, 131.8 (d, J = 2.6 Hz), 131.5 (d, J = 2.5 Hz), 130.7 (d, J = 9.4 Hz), 130.4 (d, J = 9.2 Hz), 128.9, 128.8, 128.64, 128.58, 128.5, 128.0, 124.7, 64.6 (d, J = 3.3 Hz), 43.9 (d, J = 67.5 Hz), 30.3 (d, J = 1.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.96. IR (cm^{-1}): ν 2229. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ Calcd for $C_{22}H_{20}NOPSNa$ 400.0901, found 400.0887.

*1,2-Diphenyl-2-thiocyanatoethyl diphenylphosphine oxide (**4u**).* White solid, Mp: 135.6–136.5 ^{o}C, 48% yield (105.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.44 (m, 6H), 7.39 – 7.35 (m, 2H), 7.29 – 7.15 (m, 9H), 7.08 – 6.99 (m, 3H), 5.45 (dd, J = 11.0, 8.0 Hz, 1H), 4.26 (dd, J = 11.2, 6.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.5 (d, J = 1.6 Hz), 133.8 (d, J = 4.7 Hz), 132.3, 131.8, 130.6 (d, J = 2.7 Hz), 130.5 (d, J = 2.9 Hz), 130.1, 130.0, 129.9, 129.5, 128.6, 128.3, 128.2, 128.0, 127.7 (d, J = 11.8 Hz), 127.4 (d, J = 11.9 Hz), 111.0, 55.4 (d, J = 3.0 Hz), 51.7 (d, J = 62.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.86. IR (cm^{-1}): ν 2148. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ Calcd for $C_{27}H_{22}NNaOPS$ 462.1057, found 462.1065.

*Diphenyl(1-thiocyanato-1,2,3,4-tetrahydronaphthalen-2-yl)phosphine oxide (**4v**).* White solid, Mp: 183.2–184.6 ^{o}C, 65% yield (127.1 mg), dr = 8:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 – 7.85 (m, 4H), 7.85 – 7.80 (m, 0.48H), 7.61 – 7.47 (m, 6.72H), 7.37 – 7.29 (m, 0.24H), 7.24 – 7.06 (m, 4.24H), 5.39 (t, J = 9.1 Hz, 0.12H), 5.08 (d, J = 9.0 Hz, 1H), 3.61 – 2.97 (m, 2H), 2.99 – 2.92 (m, 0.12H), 2.89 – 2.70 (m, 1.24H), 2.62 – 2.29 (m, 1H), 2.14 – 2.04 (m, 1H), 2.03 – 1.98 (m, 0.24H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.6, 135.5, 131.9, 131.7, 131.5, 131.1, 130.7, 130.6, 130.5, 130.4, 130.3, 130.2, 129.7, 129.3, 129.0, 128.6, 128.5 (d, J = 2.5 Hz), 128.4, 127.8, 127.1, 126.6, 126.2, 111.6, 54.1, 48.3 (d, J = 2.4 Hz), 38.5 (d, J = 65.1 Hz), 27.7 (d, J = 9.8 Hz), 26.0 (d, J = 3.5 Hz), 22.2, 21.0, 18.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 31.54, 30.92. IR (cm^{-1}): ν 2054. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ Calcd for $C_{23}H_{20}NNaOPS$ 412.0901, found 412.0894.

Diphenyl(1-thiocyanato-2,3-dihydro-1H-inden-2-yl)phosphine oxide (**4w**). Colorless liquid, 69% yield (245.5 mg), dr > 20:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.81 (m, 4H), 7.58 – 7.47 (m, 6H), 7.34 – 7.30 (m, 1H), 7.27 – 7.21 (m, 2H), 7.17 – 7.10 (m, 1H), 5.06 (dd, J = 14.0, 5.4 Hz, 1H), 3.71 – 3.57 (m, 1H), 3.46 – 3.27 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.8 (d, J = 5.0 Hz), 138.2 (d, J = 4.8 Hz), 132.0 (d, J = 2.7 Hz), 131.8 (d, J = 2.6 Hz), 130.8, 130.7, 130.5, 130.4, 129.1, 128.6, 128.4, 127.4, 124.4, 124.3, 110.3, 52.1, 44.9 (d, J = 69.3 Hz), 31.9. ^{31}P NMR (162 MHz, $CDCl_3$): δ

31.55. IR (cm^{-1}): ν 2046. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{18}NOPSNa$ 398.0744, found 398.0731.

*Diphenyl (2-thiocyanatocyclohexyl) phosphine oxide (**5a**).* Colorless liquid, 36% yield (61.3 mg), dr > 20:1. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.82 (m, 3H), 7.80 – 7.71 (m, 2H), 7.57-7.50 (m, 3H), 7.49-7.40 (m, 2H), 4.80-4.72 (m, 1H), 2.91-2.82 (m, 1H), 2.55-2.44 (m, 1H), 2.05 – 1.87 (m, 3H), 1.84 – 1.74 (m, 1H), 1.73 – 1.63 (m, 1H), 1.65 – 1.56 (m, 1H), 1.55 – 1.41 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 131.4, 131.2 (d, J = 2.0 Hz), 130.31, 130.26, 130.23, 130.18, 128.5, 128.4 (d, J = 8.6 Hz), 128.2, 52.2 (d, J = 3.3 Hz), 42.1 (d, J = 64.6 Hz), 33.5, 22.3 (d, J = 3.0 Hz), 21.9, 21.2. ^{31}P NMR (162 MHz, $CDCl_3$): δ 32.64. IR (cm^{-1}): ν 2150. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{19}H_{20}NNaOPS$ 364.0901, found 364.0910.

*Diphenyl (2-thiocyanatocyclooctyl) phosphine oxide (**5b**).* Colorless liquid, 40% yield (73.2 mg), dr > 20:1. ^1H NMR (400 MHz, $CDCl_3$): δ 7.88-7.80 (m, 4H), 7.58 – 7.37 (m, 6H), 5.01 – 4.66 (m, 1H), 3.04 – 2.94 (m, 1H), 2.35 – 2.22 (m, 1H), 2.14 – 2.05 (m, 2H), 2.03 – 1.80 (m, 2H), 1.73 – 1.58 (m, 5H), 1.58 – 1.45 (m, 1H), 1.38 – 1.28 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 131.2, 130.9, 130.8, 130.2, 130.1, 128.3, 128.2, 128.0, 127.9, 52.0, 45.6 (d, J = 71.5 Hz), 32.7 (d, J = 6.0 Hz), 27.8 (d, J = 8.9 Hz), 25.4, 25.3, 24.7, 24.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ 36.87. IR (cm^{-1}): ν 2150. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{24}NOPSNa$ 392.1214, found 392.1208.

*(2-Methyl-3-phenyl-2-thiocyanatopropyl)diphenylphosphine oxide (**5c**)*. Red liquid, 33% yield (34.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 – 7.80 (m, 2H), 7.78 – 7.70 (m, 2H), 7.54 – 7.42 (m, 6H), 7.36 – 7.21 (m, 5H), 3.38 (q, J = 14.1 Hz, 2H), 3.00 – 2.85 (m, 2H), 1.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 134.7, 131.7 (d, J = 2.7 Hz), 131.6 (d, J = 2.6 Hz), 130.7, 130.34, 130.25, 130.0, 129.9, 128.6 (d, J = 3.6 Hz), 128.5 (d, J = 3.6 Hz), 127.8, 127.1, 111.3, 58.6 (d, J = 2.4 Hz), 46.0 (d, J = 2.2 Hz), 39.8 (d, J = 64.5 Hz), 27.2 (d, J = 3.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.29. IR (cm^{-1}): ν 2152. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{23}H_{22}NOPSNa$ 414.1057, found 414.1042.

*Diphenyl(3-phenyl-2-thiocyanatopropyl)phosphine oxide (**5d**).* White solid, Mp: 108.2–110.6 °C, 48% yield (91.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.78 (m, 2H), 7.75 – 7.69 (m, 2H), 7.57 – 7.46 (m, 6H), 7.31 – 7.25 (m, 3H), 7.19 – 7.15 (m, 2H), 4.60 – 4.41 (m, 1H), 3.57 (dd, J = 14.6, 3.7 Hz, 1H), 3.17 – 3.01 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 131.7 (d, J = 2.5 Hz), 131.6 (d, J = 2.5 Hz), 130.5, 130.4, 130.1, 130.0, 129.0, 128.9, 128.5 (d, J = 5.1 Hz), 128.4 (d, J = 5.0 Hz), 127.8, 126.5, 48.0, 45.4 (d, J = 4.0 Hz), 39.3 (d, J = 64.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.32. IR (cm^{-1}): ν 2147. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{22}H_{20}NOPSNa$ 400.0901, found 400.0894.

*Diphenyl(4-phenyl-2-thiocyanatobutyl)phosphine oxide (**5e**).* Colorless liquid, 50% yield (98.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 – 7.70 (m, 4H), 7.55 – 7.46 (m, 6H), 7.25 – 7.15 (m, 3H), 7.11 – 7.09 (m, 2H), 3.56 – 3.35 (m, 1H), 2.94 – 2.77 (m, 3H), 2.70 – 2.63 (m, 1H), 2.54 – 2.42 (m, 1H), 2.13 – 2.03 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.4, 132.2 (d, J = 2.7 Hz), 130.8, 130.7, 130.5, 130.4, 129.0, 128.9, 128.6, 128.42 (d, J = 6.7 Hz), 128.38, 126.4, 110.5, 44.2 (d, J = 2.0 Hz), 37.3 (d, J = 24.8 Hz), 36.9 (d, J = 37.0 Hz), 32.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.50. IR (cm^{-1}): ν 2151. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{23}H_{22}NOPSNa$ 414.1057, found 414.1044.

*Diphenyl (2-thiocyanatooctyl) phosphine oxide (**5f**).* Colorless liquid, 38% yield (70.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.65 (m, 4H), 7.58 – 7.41 (m, 6H), 4.49 – 4.29 (m, 1H), 3.15-3.03 (m, 1H), 3.01 – 2.83 (m, 1H), 2.13 – 1.94 (m, 1H), 1.83 – 1.70 (m, 1H), 1.30 – 1.11 (m, 8H), 0.87 – 0.82 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 131.6 (d, J = 2.7 Hz), 131.5 (d, J = 2.7 Hz), 130.5, 130.4, 130.1, 130.0, 128.4 (d, J = 3.9 Hz), 128.30, 128.26, 48.8, 40.2 (d, J = 64.4 Hz), 39.3 (d, J = 3.6 Hz), 31.0, 27.8, 26.9, 22.0, 13.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.39. IR (cm^{-1}): ν 2058. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{21}H_{26}NNaOPS$ 394.1370, found 394.1359.

*2-(Diphenylphosphoryl)-1-thiocyanatoethyl acetate (**5g**).* Colorless liquid, 65% yield (112.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.70 (m, 4H), 7.60 – 7.47 (m, 6H), 6.48 – 4.28 (m, 1H), 3.45 – 3.29 (m, 1H), 3.09-2.89 (m, 1H), 1.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.6, 132.1, 131.8,

130.5 (d, J = 7.9 Hz), 130.1 (d, J = 8.0 Hz), 128.63, 128.57, 128.4, 128.3, 108.4, 76.7, 72.0, 19.5; ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.27. IR (cm^{-1}): ν 2054. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd. for $C_{17}H_{16}NO_3PSNa$ 368.0486, found 368.0480.

*2-((2-Diphenylphosphoryl-1-thiocyanato)ethyl)isoindoline-1,3-dione (**5h**).* Yellow liquid, 58% yield (125.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.68 (m, 6H), 7.65 – 7.57 (m, 3H), 7.55 – 7.50 (m, 2H), 7.21 – 7.12 (m, 3H), 6.49 – 6.32 (m, 1H), 4.15 – 3.95 (m, 1H), 3.00 (t, J = 13.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.2, 134.1, 132.2 (d, J = 1.9 Hz), 131.3 (d, J = 1.9 Hz), 130.5, 130.2 (d, J = 1.5 Hz), 130.1 (d, J = 1.3 Hz), 128.7, 128.6, 128.1, 128.0, 123.4, 108.9, 51.0, 32.9 (d, J = 64.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.30. IR (cm^{-1}): ν 2150. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{23}H_{17}N_2O_3PSNa$ 455.0595, found 455.0584.

*2-((10-Diphenylphosphoryl-9-thiocyanato)decyl)isoindoline-1,3-dione (**5i**).* Colorless liquid, 52% yield (141.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.67 (m, 8H), 7.56 – 7.44 (m, 6H), 4.59 – 4.22 (m, 1H), 3.65 (t, J = 7.3 Hz, 2H), 3.20 – 3.02 (m, 1H), 3.00 – 2.90 (m, 1H), 2.09 – 1.97 (m, 1H), 1.80 – 1.71 (m, 1H), 1.68 – 1.58 (m, 2H), 1.48 – 1.40 (m, 1H), 1.35 – 1.15 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.0, 133.4, 132.3, 132.0, 131.7, 131.6 (d, J = 2.8 Hz), 131.5 (d, J = 2.7 Hz), 131.1, 130.4 (d, J = 9.3 Hz), 130.0 (d, J = 9.3 Hz), 128.4 (d, J = 4.0 Hz), 128.3 (d, J = 4.0 Hz), 122.7, 48.8, 40.5, 39.9, 39.2 (d, J = 3.5 Hz), 37.6, 28.7, 28.6, 28.0 (d, J = 10.2 Hz), 26.8, 26.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.07. IR (cm^{-1}): ν 2150. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{31}H_{33}N_2O_3PSNa$ 567.1847, found 567.1850.

*Mixture of 2-((4-diphenylphosphoryl-3-thiocyanato)butyl)isoindoline-1,3-dione (**5j**) and 2-((4-diphenylphosphoryl-3-isothiocyanato)butyl)isoindoline-1,3-dione (**5j'**).* Colorless liquid. 23% (**5j**) and 37% (**5j'**) yield (144.9 mg), respectively, **5j** : **5j**' =1 : 0.6, analyzed by ^{1}H NMR spectrum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.77 (m, 3H), 7.74 – 7.65 (m, 9.4H), 7.57 – 7.31 (m, 10H), 4.32 – 4.22 (m, 1H), 3.89 – (m, 3.2H), 3.49 – 3.35 (m, 0.6H), 3.13 – 2.95 (m, 2H), 2.94 – 2.78 (m, 1.2H), 2.69 – 2.59 (m, 1H), 2.55 – 2.44 (m, 0.6H), 2.28 – 2.17 (m, 1H), 2.15 – 2.05 (m, 0.6H); ^{13}C NMR

(101 MHz, $CDCl_3$): δ 167.7, 167.6, 133.7, 133.4, 131.8 (d, J = 2.7 Hz), 131.7 (d, J = 2.8 Hz), 131.6 (d, J = 4.3 Hz), 131.5 (d, J = 2.9 Hz), 131.4, 130.5, 130.4, 130.3, 130.2, 130.03, 130.00, 129.94, 129.90, 128.5, 128.43, 128.40, 128.36, 128.31, 128.28, 128.25, 123.0, 122.8, 109.8, 44.6, 42.0 (d, J = 1.9 Hz), 40.2, 39.6, 37.7 (d, J = 3.8 Hz), 35.8, 34.70 (d, J = 4.9 Hz), 34.65; ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.85, 27.39. IR (cm^{-1}): ν 2224, 2152. HRMS (ESI-TOF) *m/z*: $(M+Na)^+$ calcd for $C_{25}H_{21}N_2O_3PSNa$ 483.0908, found 483.0918.

*(3,5-Di-tert-butyl-4-hydroxybenzyl)diphenylphosphine oxide (BHT-POPh$_2$) (**6**).* White solid, Mp: 176.6-177.5 ^{o}C, 28% yield (58.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.60 (m, 4H), 7.54 – 7.48 (m, 2H), 7.47 – 7.37 (m, 4H), 6.73 (d, J = 2.1 Hz, 2H), 5.06 (s, 1H), 3.57 (d, J = 13.8 Hz, 2H), 1.28 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 152.3 (d, J = 3.4 Hz), 135.3 (d, J = 2.6 Hz), 132.0, 131.3 (d, J = 2.6 Hz), 131.0, 130.9, 128.0, 127.9, 126.5 (d, J = 5.0 Hz), 120.6 (d, J = 8.0 Hz), 37.5 (d, J = 67.2 Hz), 33.7, 29.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.91. HRMS (ESI-TOF) *m/z*: $(M+H)^+$ calcd for $C_{27}H_{33}O_2PNa$ 443.2116, found 443.2124.

(2,2-Diphenylvinyl)diphenylphosphine oxide (**7**). White solid, Mp: 205.3-207.5 ^{o}C, 65% yield (123.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 – 7.60 (m, 4H), 7.38 – 7.26 (m, 11H), 7.26 – 7.19 (m, 2H), 7.15 – 7.05 (m, 3H), 6.79 (d, J = 16 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.7 (d, J = 2.2 Hz), 141.4 (d, J = 16.2 Hz), 137.5 (d, J = 6.7 Hz), 133.7 (d, J = 106.2 Hz), 130.6 (d, J = 2.6 Hz), 130.4 (d, J = 9.5 Hz), 129.8, 129.1, 128.2, 127.9 (d, J = 3.2 Hz), 127.82, 127.75, 127.1, 119.9 (d, J = 103.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 19.21. HRMS (ESI-TOF) *m/z*: $(M+H)^+$ calcd for $C_{26}H_{22}OP$ 381.1408, found 381.1395.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.

^{1}H, ^{13}C and ^{31}P NMR spectra for compounds **4-7** (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Gao, Y. Z.; Tang, G.; Zhao, Y. F. *Phosphorus, Sulfur Silicon Relat. Elem.* **2017**, *192*, 589.

(2) (a) Wei, W.; Ji, J. X. *Angew. Chem. Int. Ed*. **2011**, *50*, 9097. (b) Gutierrez, V.; Mascar´o, E.; Alonso, F.; Moglie, Y.; Radivoy, G. *RSC Adv*. **2015**, *5*, 65739. (c) Zhang, G. Y.; Li, C. K.; Li, D. P.; Zeng, R. S.; Shoberu, A.; Zou, J. P. *Tetrahedron* **2016**, *72*, 2972.

(3) (a) Taniguchi, T.; Idota, A.; Yokoyama, S. I.; Ishibashi, H. *Tetrahedron Lett*. **2011**, *37*, 4768. (b) Gao, Y.; Wu, J.; Xu, J.; Zhang, P.; Tang, G.; Zhao, Y. *RSC Adv*. **2014**, *4*, 51776. (c) Zhou, S. F.; Li, D. P.; Liu, K.; Zou, J. P.; Asekun, O. T. *J. Org. Chem*. **2015**, *80*, 1214.

(4) (a) Zhang, C. W.; Li, Z. D.; Zhu, L.; Yu, L. M.; Wang, Z. T.; Li, C. Z. *J. Am. Chem. Soc*. **2013**, *135*, 14082. (b) Richard, V.; Fisher, H. C.; Montchamp, J. L. *Tetrahedron Lett*. **2015**, *23*, 3197.

(5) (a) Li, J. A.; Zhang, P. Z.; Liu, K. Shoberu, A.; Zou, J. P.; Zhang, W. *Org. Lett.* **2017**, *19,* 4704. (b) Zhang, P. Z.; Zhang, L.; Li, J. A.; Shoberu, A.; Zou, J. P.; Zhang, W. *Org. Lett.* **2017**, *19*, 5537.

(6) Selected book and reviews on organic thiocyanates: (a) Erian, A. W.; Sherif, S. M. *Tetrahedron*, **1999**, *55*, 7957. (b) Romanowski, F.; Klenk, H. *Ullmann's Encyclopedia of Industrial Chemistry, Thiocyanates and Isothiocyanates, Organic,* Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, **2012**. (c) Castanheiro, T.; Suffert, J.; Donnard, M.; Gulea, M. *Chem. Soc. Rev*., **2016**, *45*, 494.

(7) Bioactivities of organic thiocyanates, see: (a) Benn, M. *Pure Appl. Chem*., **1977**, *49*, 197. (b) Grishchuk, B. D.; Prodanchuk, N. G.; Sinchenko, V. G.; Gorbovoi, P. M.; Kudrik, E. Y. *Pharm. Chem. J*., **1994**, *28*, 657. (c) Szajnman, S. H.; Yan, W.; Bailey, B. N.; Docampo, R.; Elhalem, E.; Rodriguez, J. B. *J. Med. Chem*., **2000**, *43*, 1826.

(8) Long, J. K.; Hanagan, M. A.; Marshall, E. A.; Sharpe, P. L.; Ding, A. X. *WO 2012/030922A1*, **2012**.

(9) (a) Wood, J. L. *Org. React.* **1946**, *3*, 240. (b) Kelly, T. R.; Kim, M. H.; Curtis, A. D. M. *J. Org. Chem*. **1993**, *58*, 5855.

(10) (a) Tian, H.; Yu, J. P.; Yang, H. J.; Zhu, C. J.; Fu, H. *Adv. Synth. Catal*. **2016**, *358*, 1794. (b) Zhong, B. Y.; Al-Awar, R. S.; Shih, C.; Grimes, Jr., J. H.; Vieth, M.; Hamdouchi, C. *Tetrahedron Lett.,* **2006**, *47*, 2161.

(11) (a) Yadav, J. S.; Reddy, B. V. S.; Gupta, M. K. *Synthesis,* **2004**, 1983. (b) Yang, H.; Duan, X.-H.; Zhao, J.-F.; Guo, L.-N. *Org. Lett*. **2015**, *17*, 1998. (c) Liang, Z. L.; Wang, F.; Chen, P. H.; Liu, G. S. *Org. Lett.* **2015**, *17*, 2438.

(12) (a) Gao, Y.; Wu, J.; Xu, J.; Zhang, P.; Tang, G.; Zhao, Y. *RSC Adv*. **2014**, *4*, 51776. (b) Xu, J.; Li, X.; Gao, Y.; Zhang, L.; Chen, W.; Fang, H.; Tang, G.; Zhao, Y. F. *Chem. Commun*. **2015**, *51*, 11240. (c) Gutierrez, V.; Mascaró, E.; Alonso, F.; Moglie, Y.; Radivoy, G. *RSC Adv*. **2015**, *5*, 65739.

(13) Zhang, P.; Zhang, L. L.; Gao, Y. Z.; Xu, J.; Fang, H.; Tang, G.; Zhao, Y. F. *Chem. Commun.* **2015**, *51*, 7839.

(14) (a) Sun, N.; Che, L.; Mo, W.; Hu, B.; Shen, Z.; Hu, X. *Org. Biomol. Chem.* **2015**, *13*, 691. (b) Zhu, N.; Wang, F.; Chen, P.; Ye, J.; Liu, G. *Org. Lett.* **2015**, *17*, 3580. (c) Jiang, H.; Yu, W.; Tang, X.; Li, J.; Wu, W. *J. Org. Chem.* **2017**, *82*, 9312.