



Oxidative cross-coupling between secondary phosphine selenides and thiols or dithiols: a facile regio-selective synthesis of thioselenophosphinic S-esters and S-diester

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ABSTRACT

Reactions between secondary phosphine selenides and a wide range of aliphatic, aromatic and heteroaromatic thiols or dithiols proceed in the Et₃N/CCl₄ oxidative system under mild conditions (rt 1–3 h) to give thioselenophosphinic S-esters or S-diester in 80–92% isolated yields.

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Chalcogenophosphinic thioesters have attracted considerable attention due to their applications as ligands for the design of metal-complexes,¹ drug intermediates,^{1a–c,2} flame retardants,³ RAFT-agents for controlled styrene polymerization⁴ and building blocks in organic and elementoorganic synthesis.⁵

Thioselenophosphinic S-esters are of particular interest as promising selenium sources for the fabrication of selenium-containing nanoparticles. However, the syntheses of these S-esters are very limited⁶ and have difficulties associated with the typical initial reagents such as phosphorus chlorides and organometallic compounds, which exhibit their own problems, including moisture- and air-sensitivity and issues in handling.

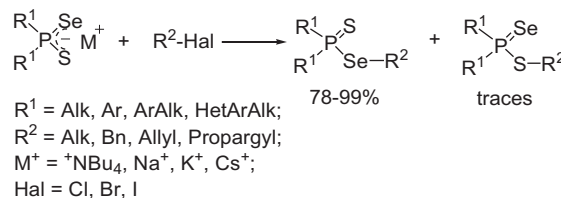
For example, Murai et al. published^{6d} a method for the preparation of chiral thioselenophosphinic S-esters which utilized phenyldichlorophosphane, elemental selenium, Grignard reagents and alkali metal thiolates (Scheme 1).

Esters of thioselenophosphinic acids have also been synthesized by alkylation of their ammonium^{6d,7} or alkali metal⁸ salts. However, the main products of these reactions were thioselenophosphinic Se-esters (Scheme 2).

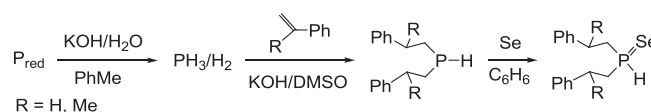
The goal of this work was to elaborate a novel, general and simple approach to the regio-selective synthesis of thioselenophosphinic S-esters and S-diester.



Scheme 1. Synthesis of thioselenophosphinic S-esters from phenyldichlorophosphane.



Scheme 2. Regio-selective reaction of thioselenophosphinates with organic halides.

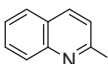


Scheme 3. Synthesis of secondary phosphine selenides.

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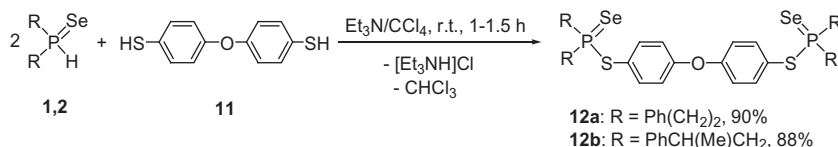
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Table 1
Synthesis of thioselenophosphinic S-esters **10a–i**^a

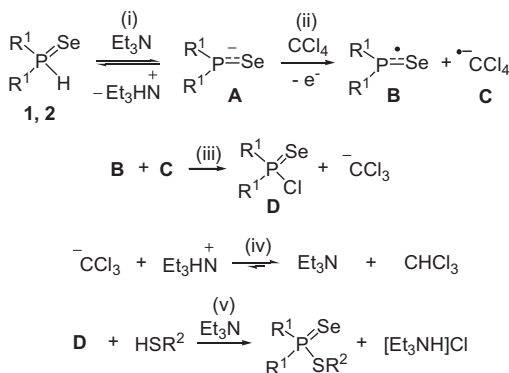
$ \begin{array}{c} R^1 \\ \diagup \\ R^1-P-Se \\ \diagdown \\ H \\ 1, 2 \end{array} + R^2SH \xrightarrow[Et_3N/CCl_4, \text{ r.t.}]{- [Et_3NH]Cl, - CHCl_3} \begin{array}{c} R^1 \\ \diagup \\ R^1-P-Se \\ \diagdown \\ SR^2 \\ 10a-i \end{array} $							
Entry	$R^1P(Se)H$ (1 mmol)	R^1	R^2SH (1 mmol)	R^2	Time (h)	S-ester	Yield ^b (%)
1	1	$Ph(CH_2)_2$	3	Et	2	10a	91
2	1	$Ph(CH_2)_2$	4	<i>n</i> -hept	2	10b	90
3	1	$Ph(CH_2)_2$	5		2	10c	80
4	1	$Ph(CH_2)_2$	6	Ph	1	10d	92
5	2	$PhCH(Me)CH_2$	6	Ph	1	10e	85
6	1	$Ph(CH_2)_2$	7		3	10f	90
7	1	$Ph(CH_2)_2$	8		2	10g	88
8	1	$Ph(CH_2)_2$	9		1.5	10h	90
9	2	$PhCH(Me)CH_2$	9		2	10i	87

^a All experiments were carried out under an argon atmosphere at rt for 1–3 h; Et_3N (1 mmol) and CCl_4 (4 mL) were used.

^b Isolated yield.



Scheme 4. Synthesis of thioselenophosphinic S-diester **12a,b**.



Scheme 5. A possible mechanism for the formation of thioselenophosphinic S-esters **10a–i**.

To achieve this goal we have studied, for the first time, the oxidative transition metal free cross-coupling between secondary phosphine selenides and various thiols or dithiols in a Et_3N/CCl_4 system.

The starting secondary phosphine selenides were easily prepared via a halogen-free method from red phosphorus, styrenes and elemental selenium (Scheme 3).⁹

The experiments showed¹⁰ that bis(2-phenylalkyl)phosphine selenides **1** and **2** react with aliphatic **3–5**, aromatic **6** and hetero-aromatic **7–9** thiols in the Et_3N/CCl_4 system under mild conditions

(20–22 °C, 1–3 h) to afford thioselenophosphinic S-esters **10a–i** in 80–92% isolated yields (Table 1).

The generality and preparative efficiency of the developed method was demonstrated by the synthesis of S-diester **12a** and **b** in 88–90% yield from phosphine selenides **1,2** and dithiol **11** in a 2:1 molar ratio under the same conditions¹¹ (Scheme 4).

It should be noted that triethylammonium chloride and $CHCl_3$ are also formed in the studied reactions (Table 1; Scheme 4). The experimental results obtained are in good agreement with the reaction mechanism (Scheme 5), which we proposed earlier for the cross-coupling of secondary phosphine chalcogenides with primary and secondary amines,¹² alcohols and phenols.¹³ The deprotonation of secondary phosphine selenides **1,2** by triethylamine produces P,Se-amidant selenophosphinite-anion **A** (step i). The latter participates in a one-electron transfer with CCl_4 (oxidizer) to give secondary phosphine selenide free radical **B** and anion radical **C** (step ii). The interaction of species **B** and **C** affords phosphinoselenoic chloride **D** and the $^-CCl_3$ carbanion (step iii). Protonation of the latter by a triethylammonium cation leads to regeneration of triethylamine and formation of chloroform (step iv). The reaction between chloride **D** and the thiol in the presence of triethylamine results in the final product, a thioselenophosphinic S-ester, and triethylammonium chloride (step v).

The structures of thioselenophosphinic S-esters **10a–i** and S-diester **12a,b** were established using multinuclear 1H , ^{13}C , ^{31}P and ^{77}Se NMR spectroscopy, as well as X-ray diffraction analysis (for compound **10h**) (Fig. 1).¹⁴

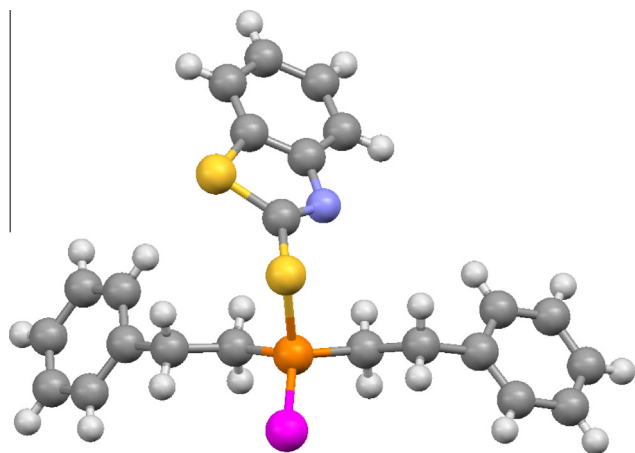


Figure 1. ORTEP diagram of the molecular structure of **10h**. Selected bond lengths [Å] and angles [deg]: P–Se 2.0963(16), P–S 2.127(2), P–C 1.804(5) and 1.815(5) Å; Se–P–S 108.60(7), Se–P–C 113.8(2) and 116.1(2), S–P–C 105.2(2) and 106.4(2), C–P–C 106.0(2).

In summary, the oxidative transition metal free cross-coupling between secondary phosphine selenides and thiols or dithiols in the $\text{Et}_3\text{N}/\text{CCl}_4$ system at room temperature for 1–3 h affords regioselectively thioselenophosphinic S-esters and S-diester in high yields. The compounds synthesized are novel representatives of rare derivatives of thioselenophosphinic acids, which can be used as single-source precursors of nanomaterials, RAFT-agents for pseudo-living radical polymerization and as potential drug candidates.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2013.04.117>.

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- General procedure for the synthesis of thioselenophosphinic S-esters 10a–i.** A mixture of secondary phosphine selenide **1** or **2** (1.0 mmol) and Et_3N (1.0 mmol) in CCl_4 (4 mL) was stirred at 20–22 °C for 10 min. Thiols **3–9** (1.0 mmol) were added, and the reaction mixture was stirred at 20–22 °C for 1–3 h. The solvent was removed under reduced pressure, and 1,4-dioxane (3 mL) was added. The precipitated white solid (triethylammonium chloride) was removed by filtration, and the 1,4-dioxane was evaporated. Hexane (2 mL) was added to the residue obtained, and the resulting mixture was allowed to stand for 12 h at 0–1 °C. The solution was removed from the precipitate by decantation, the solvent was evaporated and the residue was dried under vacuum to give thioesters **10a–c**, **e**, **i**. In the cases of thioesters **10d,f–h** the residue (after 1,4-dioxane was evaporated under vacuum) was washed with hexane (3 × 1 mL) and dried under vacuum to afford **10d**, **f–h**.
- General procedure for the synthesis of thioselenophosphinic S-diester 12a and b.** A mixture of secondary phosphine selenide **1** or **2** (1.0 mmol) and Et_3N (1.0 mmol) in CCl_4 (4 mL) was stirred at 20–22 °C for 10 min. The dithiol **11** (0.5 mmol) was added, and the mixture was stirred at 20–22 °C for 1–1.5 h. The solvent was removed under reduced pressure and 1,4-dioxane (3 mL) was added. The precipitated white solid (triethylammonium chloride) was removed by filtration, and the 1,4-dioxane was evaporated. The residue was reprecipitated from CHCl_3 (1 mL) into hexane (10 mL) to give **12a** and **b**.
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- X-ray crystallographic data for compound 10h.** $\text{C}_{23}\text{H}_{22}\text{NPS}_2\text{Se}$, $M_r = 486.493$, R -factor is 0.0446 (2609 $I > 2\sigma(I)$), monoclinic, space group $P2_1/n$, $a = 5.4327(6)$, $b = 38.793(4)$, $c = 10.8139(11)$ Å, $\beta = 90.369(3)^\circ$, $V = 2279.0(4)$ Å³, $Z = 4$, $D_{\text{calcd}} = 1.418$ g cm^{−3}. CCDC 927802. X-ray analysis was carried out using a Bruker APEX-II CCD diffractometer at 200 K using graphite-monochromated Mo- K_α radiation ($\lambda = 0.71073$ Å). Absorption corrections were applied using the SADABS program. The crystal structure was solved by direct methods followed with Fourier synthesis using SHELXS-97.¹⁵ All nonhydrogen atoms were refined using anisotropic full-matrix approximation using SHELXL-97.¹⁵ The coordinates of the hydrogen atoms were calculated from geometrical positions.
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