Tetrahedron Letters 52 (2011) 6985–6987

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A three-component reaction between alkenes, secondary phosphanes, and elemental selenium: a novel, efficient, atom-economic synthesis of diselenophosphinic esters

Nina K. Gusarova, Alexander V. Artem'ev, Svetlana F. Malysheva, Ol'ga A. Tarasova, Boris A. Trofimov *

A.E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russian Federation

ARTICLE INFO

Article history:
Received 6 September 2011
Revised 29 September 2011
Accepted 17 October 2011
Available online 20 October 2011

Keywords:
Alkenes
Esters
Multicomponent reactions
Phosphanes
Selenium

ABSTRACT

A novel, convenient, atom-economic approach toward the synthesis of diselenophosphinic esters has been developed via the three-component reaction between aryl- or hetarylalkenes secondary phosphanes, and elemental selenium. The reaction proceeds without a catalyst (85 °C, 3 h, 1,4-dioxane) to afford the target compounds in good to high yields.

Currently, the chemistry of diselenophosphinates is progressing rapidly.[1–5] These compounds are used extensively as convenient single-source precursors of nanocrystalline materials,[2] anionic ligands for metal complexes,[6] promising extractants of heavy metals, and as building blocks for organic synthesis.[3]

Recently, increasing attention has been paid to the synthesis of diselenophosphinic esters,[3] $R^1_2P(Se)SeR^2$ (R^1, R^2 = alkyl or aryl), which are selenium heteroanalogues of dithiophosphinates, $R^1_2P(S)SR^2$. The latter are a known class of biologically active chalcogenophosphorus compounds.[7] Taking into account that selenium itself is a biologically important element and represents a key active factor in numerous drugs,[8] it might be expected that replacement of the two sulfur atoms of the dithiophosphinates by Se would allow new, promising drugs and pesticides to be developed. In addition, diselenophosphinic esters are efficient iniferters (RAFT-agents) for pseudo-living radical polymerization of alkenes.[3c,d]

At the same time, only two synthetic methods for the preparation of diselenophosphinic esters have been described. The most common[3a,c,d] is based on a two-step sequence involving the oxidation of monochlorophosphanes by elemental selenium (toluene, 120 °C, 3 h) and treatment of the intermediate selenophosphinic chlorides with $R^2SeMgCl$, prepared via an insertion reaction of Grignard reagents with elemental selenium (Scheme 1).

Recently, a new approach[3e] for the synthesis of diselenophosphinic esters by the alkylation of diverse alkali metal diselenophosphinates with primary organic halides has been reported (Scheme 2). The starting alkali metal diselenophosphinates were prepared from secondary phosphanes, elemental selenium, and alkali metal hydroxides.[4c]

The objective of this Letter was to develop a conceptually new, one-pot, atom-economic approach to the synthesis of diselenophosphinic esters. We herein describe the three-component reaction between secondary phosphanes, elemental selenium, and alkenes.

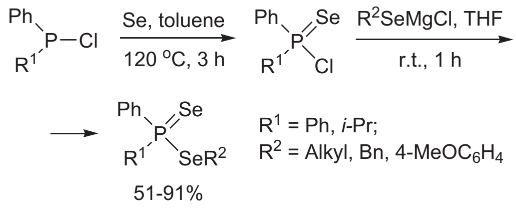
The experimental results show that secondary phosphanes **1–3** react with elemental selenium and various aryl- or hetarylalkenes **4–9** under mild conditions (85 °C, 3 h, 1,4-dioxane, molar ratio **1**–**3**:Se:**4**–**9** being 1:2:1.2) to furnish previously unknown racemic mixtures of chiral deiselenophosphinic esters **10a–i** in good to high yields (Table 1).[9]

The results (Table 1) demonstrate the generality of this new reaction for the aryl- and hetarylalkene series. Indeed, diverse aryl- and hetarylalkenes having functional, heterocyclic, and bulky substituents participate readily in this reaction. In many cases the synthesis of the diselenophosphinic esters was almost quantitative. The only exception was product **10d**, the moderate yield of which probably resulted from the presence of the bulky naphthyl group in starting alkene **7** (Table 1, entry 4). In this case, the major by-product was bis(selenophosphoryl)selenide, $(R_2PSe)_2Se$ [$R = Ph(CH_2)_2$], which was formed via a side reaction, as recently described,[10] between secondary phosphane **1** and elemental selenium.

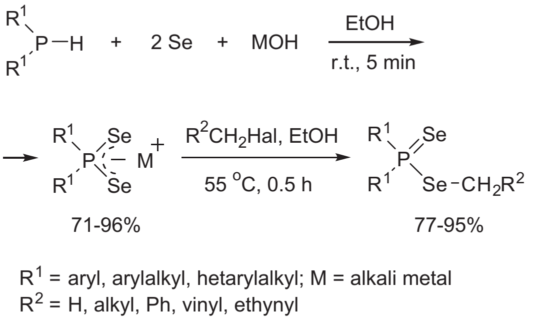
---

* Corresponding author. Tel.: +7 395242 14 11; fax: +7 395241 93 46.
E-mail address: boris_trofimov@irioch.irk.ru (B.A. Trofimov).

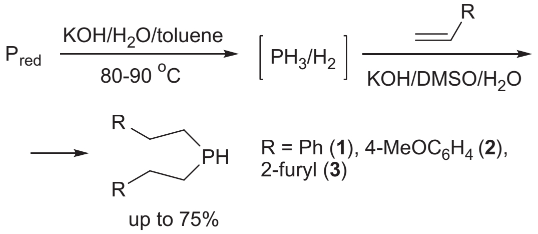
0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.10.094



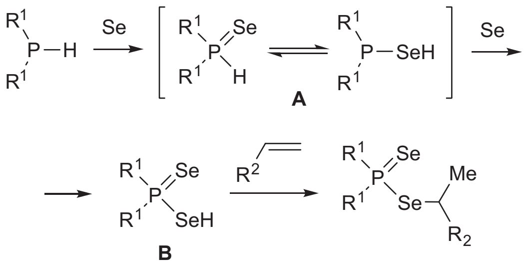
Scheme 1. Conventional synthesis of diselenophosphinic esters.



Scheme 2. Synthesis of diselenophosphinic esters via reaction of organic halides with alkali metal diselenophosphinates prepared from secondary phosphanes, elemental selenium, and MOH.



Scheme 3. Synthesis of the starting secondary phosphanes **1–3** from red phosphorus and styrenes or 2-vinylfuran.



Scheme 4. Possible mechanism for the three-component reaction between secondary phosphanes, elemental selenium, and alkenes.

The preparative advantages of the developed method are the following: atom-economic, halogen-free and organometallic-free protocols, simple experimental procedure and relatively mild conditions. In addition, this new approach allows the synthesis of hitherto unknown diselenophosphinic esters bearing heterocyclic or functional substituents. Bearing in mind that the starting secondary phosphanes **1–3** employed in this Letter are readily accessible[11] from red phosphorus and vinylarenes or vinylhetarenes (Scheme 3), this three-component reaction represents a concise and expedient route to diselenophosphinic esters.

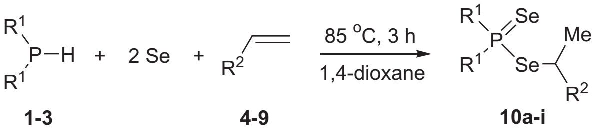
All the compounds synthesized are air-stable oils which are soluble in most organic solvents and insoluble in water. Their structures were established by ^{1}H, ^{13}C, ^{31}P and ^{77}Se NMR and IR spectroscopy.

The formation of diselenophosphinic esters via the three-component reaction can be rationalized as follows: oxidation of the secondary phosphane by elemental selenium gives a secondary phosphane selenide **A** which is further oxidized by a second equivalent of elemental selenium to provide diselenophosphinic acid **B**. The addition of the latter to the alkene results in diselenophosphinates (Scheme 4).

Formally, this reaction is assumed to be the first example of the addition of diselenophosphinic acids $R_2P(Se)SeH$ (unknown so far) to alkenes. Certainly, this type of addition is electrophilic in nature and proceeds regioselectively in agreement with Markovnikov's rule allowing diselenophosphinates with a $SeCH(R^2)Me$ structural unit to be prepared. Until now, only one representative of such compounds has been described.[3d] The generation of the intermediate diselenophosphinic acids is in keeping with the result obtained for 2-vinylpyridine, which as an organic base gives, instead of the expected adduct, a salt-like product. According to the electrophilic character of the addition, the key intermediate of this step should be a carbocation $^{+}[CHR^2(Me)]$, which in the case of aryl- or hetarylalkenes is stabilized by the adjacent aromatic or heteroaromatic moieties, R^2. This is additionally supported by the fact that when R^2 = alkyl, and is less able to stabilize the neighboring

Table 1

One-pot atom-economic synthesis of diselenophosphinic esters **10a–i** from secondary phosphanes **1–3**, elemental selenium, and aryl- or hetarylalkenes **4–9**[a]

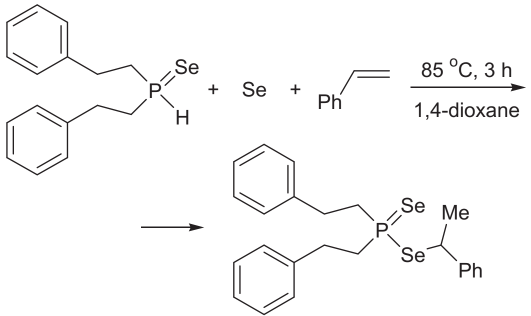


Entry	Phosphane	R^1	Alkene	R^2	Ester	Yield[b] (%)
1	**1**	$Ph(CH_2)_2$	**4**	Ph	**10a**	85
2	**1**	$Ph(CH_2)_2$	**5**	4-*t*-BuC_6H_4	**10b**	90
3	**1**	$Ph(CH_2)_2$	**6**	4-ClC_6H_4	**10c**	86
4	**1**	$Ph(CH_2)_2$	**7**	2-Naphthyl	**10d**	54[c]
5	**1**	$Ph(CH_2)_2$	**8**	2-Furyl	**10e**	91
6	**1**	$Ph(CH_2)_2$	**9**	1-Pyrrolyl	**10f**	95
7	**2**	4-$MeOC_6H_4(CH_2)_2$	**5**	4-*t*-BuC_6H_4	**10g**	89
8	**3**	2-Furyl$(CH_2)_2$	**8**	2-Furyl	**10h**	90
9	**3**	2-Furyl$(CH_2)_2$	**9**	1-Pyrrolyl	**10i**	94

[a] Reaction conditions: secondary phosphane **1–3** (1.0 mmol), alkene **4–9** (1.2 mmol), Se (2.0 mmol), 1,4-dioxane (8 mL), 85 °C, ca. 3 h.

[b] Yield of isolated product after flash chromatography.

[c] Yield of isolated product after column chromatography.



10a

Scheme 5. One-pot synthesis of diselenophosphinate **10a** from a secondary phosphane selenide, elemental selenium, and styrene.

positive charge, the three-component reaction does not take place (as was the case with 1-octene).

Besides, the mechanism proposed (Scheme 4) is in agreement with our finding that bis(2-phenethyl)phosphane selenide reacts with one equivalent of elemental selenium and one equivalent of styrene under the same conditions (85 °C, 3 h, 1,4-dioxane) to form diselenophosphinate **10a** in 86% yield[12] (Scheme 5).

The synthesis of diselenophosphinic esters reported here is strictly atom-economic: in most cases, all the starting materials are consumed to produce the target compounds with no side products being observed.

To summarize, a new, efficient, atom-economic, three-component reaction between alkenes, secondary phosphanes, and elemental selenium to give previously unknown diselenophosphinic esters has been discovered and elaborated. The results contribute to the fundamental chemistry of organic phosphanes, elemental selenium, and alkenes, as well as to the synthesis of organoselenophosphorus compounds via multi-component reactions. Diselenophosphinic esters represent promising building blocks, potential precursors of drugs, and active iniferters (RAFT-agents).

Acknowledgments

This work was supported by the Russian Foundation for Basic Research (Grant No: 11-03-92003-HHC_a) and the President of the Russian Federation [programs for the support of leading scientific schools (Grant NSh-3230.2010.3) and young Russian scientists (Grant MK-629-2010.3)].

Supplementary data

Supplementary data (general remarks, experimental procedures, and characterization data for compounds **10a**–**i**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.10.094.

References and notes

1. For recent examples of the synthesis of salts of diselenophosphinic acids, see: (a) Davies, R. P.; Martinelli, M. G. *Inorg. Chem.* **2002**, *41*, 348–352; (b) Davies, R. P.; Francis, C. V.; Jurd, A. P. S.; Martinelli, M. G.; White, A. J. P.; Williams, D. J. *Inorg. Chem.* **2004**, *43*, 4802–4804; (c) Hua, G.; Zhang, Q.; Li, Y.; Slawin, A. M. Z.; Woollins, J. D. *Tetrahedron* **2009**, *65*, 6074–6082; (d) Davies, R. P.; Martinelli, M. G.; Patel, L.; White, A. J. P. *Inorg. Chem.* **2010**, *49*, 4626–4631.
2. For the application of heavy metal diselenophosphinates as single-source precursors of remarkable nanomaterials, see: (a) Nguyen, C. Q.; Afzaal, M.; Malik, M. A.; Helliwell, M.; Raftery, J.; O'Brien, P. *J. Organomet. Chem.* **2007**, *692*, 2669–2677; (b) Kawai, T.; Hasegawa, Y.; Adachi, T. U.S. Patent WO 2007/102271, 2007; *Chem. Abstr.* **2007**, *147*, 368034.; (c) Panneerselvam, A.; Nguyen, C. Q.; Waters, J.; Malik, M. A.; O'Brien, P.; Raftery, J.; Helliwell, M. *Dalton Trans.* **2008**, 4499–4506; (d) Hasegawa, Y.; Adachi, T.; Tanaka, A.; Afzaal, M.; O'Brien, P.; Doi, T.; Hinatsu, Y.; Fujita, K.; Tanaka, K.; Kawai, T. *J. Am. Chem. Soc.* **2008**, *130*, 5710–5717; (e) Maneeprakorn, W.; Nguyen, C. Q.; Malik, M. A.; O'Brien, P.; Raftery, J. *Dalton Trans.* **2009**, 2103–2108; (f) Panneerselvam, A.; Nguyen, C. Q.; Malik, M. A.; O'Brien, P.; Raftery, J. *J. Mater. Chem.* **2009**, *19*, 419–427; (g) Tanaka, C. Q.; Adachi, T.; Hasegawa, Y.; Kawai, T. *J. Alloy. Compd.* **2009**, *488*, 538–540; (h) Maneeprakorn, W.; Malik, M. A.; O'Brien, P. *J. Mater. Chem.* **2010**, *20*, 2329–2335; (i) Cossairt, B. M.; Owen, J. S. *Chem. Mater.* **2011**, *23*, 3114–3119.
3. (a) Kimura, T.; Murai, T. *J. Org. Chem.* **2005**, *70*, 952–959; (b) Kimura, T.; Murai, T.; Mizuhata, N. *Heteroatom. Chem.* **2005**, *16*, 185–191; (c) Moon, J.; Nam, H.; Kim, S.; Ryu, J.; Han, C.; Lee, C.; Lee, S. *Tetrahedron Lett.* **2008**, *49*, 5137–5140; (d) Song, E.; Jo, Y.; Bae, G.; Oh, I.-K.; Jung, H. M.; Lee, S. *Bull. Korean Chem. Soc.* **2009**, *30*, 2129–2131; (e) Artem'ev, A. V.; Chernysheva, N. A.; Gusarova, N. K.; Malysheva, S. F.; Yas'ko, S. V.; Albanov, A. I.; Trofimov, B. A. *Synthesis* **2011**, 1309–1313.
4. For very recent publications on advances on the synthesis of salts of diselenophosphinic acids, see: (a) Trofimov, B. A.; Artem'ev, A. V.; Malysheva, S. F.; Gusarova, N. K. *J. Organomet. Chem.* **2009**, *694*, 4116–4120; (b) Trofimov, B. A.; Artem'ev, A. V.; Gusarova, N. K.; Malysheva, S. F.; Fedorov, S. V.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A. *Synthesis* **2009**, 3332–3338; (c) Artem'ev, A. V.; Malysheva, S. F.; Gusarova, N. K.; Trofimov, B. A. *Synthesis* **2010**, 2463–2467; (d) Artem'ev, A. V.; Malysheva, S. F.; Gusarova, N. K.; Belogorlova, N. A.; Trofimov, B. A. *Synthesis* **2010**, 1777–1780; (e) Artem'ev, A. V.; Gusarova, N. K.; Malysheva, S. F.; Trofimov, B. A. *Russ. Chem. Bull.* **2010**, *59*, 1671; (f) Artem'ev, A. V.; Gusarova, N. K.; Malysheva, S. F.; Kraikivskii, P. B.; Belogorlova, N. A.; Trofimov, B. A. *Synthesis* **2010**, 3724–3730; (g) Gusarova, N. K.; Artem'ev, A. V.; Malysheva, S. F.; Fedorov, S. V.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A.; Trofimov, B. A. *Tetrahedron Lett.* **2010**, *51*, 1840–1843.
5. For a recent review describing the chemistry and applications of diselenophosphinates, see Artem'ev, A. V.; Malysheva, S. F.; Gusarova, N. K.; Trofimov, B. A. *Org. Prep. Proc. Int.* **2011**, *43*, 381–449.
6. For the synthesis of heavy metal diselenophosphinate complexes, see: (a) Müller, A.; Christophliemk, P.; Rao, V. V. K. *Chem. Ber.* **1971**, *104*, 1905–1914; (b) Müller, A.; Rao, V. V. K.; Christophliemk, P. *J. Inorg. Nucl. Chem.* **1974**, *36*, 472–475; (c) Nguyen, C. Q.; Adeogun, A.; Afzaal, M.; Malik, M. A.; O'Brien, P. *Chem. Commun.* **2006**, 2182–2184; (d) Lobana, T. S.; Wang, J.-C.; Liu, C. W. *Coord. Chem. Rev.* **2007**, *251*, 91–110; (e) Artem'ev, A. V.; Malysheva, S. F.; Gusarova, N. K.; Trofimov, B. A. *Russ. J. Gen. Chem.* **2011**, *81*, 1449–1452.
7. (a) Mel'nikov, N. N.; Novozhilov, K. V.; Pylova, T. N. *The Pesticide*, Chemistry, Moscow, **1980**.; (b) Matolcsy, G.; Nadasy, M.; Andriska, V. *Pesticide Chemistry*; Elsevier: Budapest, 1988; (c) Edmundson, R. S. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; Ter- and quinque-valent phosphorus acids and their derivatives; Wiley: New York, 1996; Vol. 4, pp 397–494; (d) Haiduc, I. *J. Organomet. Chem.* **2001**, *623*, 29–42.
8. (a) *Selenium in Nutrition: Revised Edition*, National Academy Press, Washington, **1983**.; (b) Parker, J. N.; Parker, P. M. *Selenium: A Medical Dictionary, Bibliography, and Annotated: Research Guide to Internet References*; Icon Group International: San Diego, 2004; (c) Reilly, C. *Selenium in Food and Health*; Springer: New York, 2006; (d)*Selenium: Its Molecular Biology and Role in Human Health*; Hatfield, D. L., Berry, M. J., Gladyshev, V. N., Eds., 2nd ed.; Springer: New York, 2006.
9. *General procedure for the synthesis of diselenophosphinic esters* ***10a–i***: To a solution of secondary phosphane **1**–**3** (1.0 mmol) in 1,4-dioxane (8 mL) were added consecutively alkene **4**–**9** (1.2 mmol) and powdered grey selenium (0.158 g, 2.0 mmol) at ambient temperature under argon. The suspension was stirred until dissolution of the selenium (ca. 3 h) at 85 °C to give a yellowish transparent solution. The solvent was removed under reduced pressure (1 Torr, 50–60 °C) and the residue purified by flash chromatography (neutral alumina, hexane) to give diselenophosphinate **10a**–**c**,**e**–**i** in 85–95% yield. Diselenophosphinate **10d** was isolated by column chromatography (neutral alumina, toluene) in 54% yield.
10. Artem'ev, A. V.; Gusarova, N. K.; Malysheva, S. F.; Ushakov, I. A.; Trofimov, B. A. *Tetrahedron Lett.* **2010**, *51*, 2141–2143.
11. For reviews on the availability of secondary phosphines, see: (a) Trofimov, B. A.; Arbuzova, S. N.; Gusarova, N. K. *Russ. Chem. Rev.* **1999**, *68*, 215–228; (b) Trofimov, B. A.; Gusarova, N. K. *Mendeleev Commun.* **2009**, *19*, 295–302.
12. *Three-component reaction between bis(2-phenethyl)phosphane selenide, elemental selenium and styrene*: To a solution of bis(2-phenethyl)phosphane selenide (0.321 g, 1.0 mmol) in 1,4-dioxane (8 mL) were added consecutively styrene (0.115 g, 1.2 mmol) and powdered grey selenium (0.079 g, 1.0 mmol) at ambient temperature under argon. The suspension was stirred until dissolution of the selenium (ca. 3 h) at 85 °C to give a yellowish transparent solution. The solvent was removed under reduced pressure (1 Torr, 50–60 °C) and the residue purified by flash chromatography (neutral alumina, hexane) to give diselenophosphinate **10a** in 86% yield.