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Palladium-catalyzed alkynylselenation of acetylenedicarboxylates leading to enyne selenides and application to synthesis of multisubstituted aryl selenides

Takenori Mitamura, Akiya Ogawa *

Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Nakaku, Sakai, Osaka 599-8531, Japan

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ABSTRACT

Upon treatment of a mixture of alkynyl selenides and acetylenedicarboxylates with $Pd(OAc)_2/P(o\text{-tol})_3/K_2CO_3/H_2O$-catalytic system, the alkynylselenation of acetylenedicarboxylates takes place to give the corresponding alkynylvinyl selenides. Furthermore, alkynyl selenides undergo the intermolecular [2+2+2] cycloaddition reaction in the presence of $PdCl_2(PPh_3)_2$ as a catalyst, affording the corresponding multisubstituted aryl selenides selectively.

Organoselenium compounds are focused on a material chemistry, biology, and organic synthesis, because of their unique reactivities, properties, and biological activities, and therefore, the development of the convenient methods for the preparation of organoselenium compounds is one of the important topics.[1] Transition-metal-catalyzed methods are expected to be one of the powerful tools for the selective construction of organoselenium compounds.[2] Recently, the transition-metal-catalyzed reactions of organochalcogen compounds is extended: for example, the selective addition to alkynes based on the catalytic activation of Ch—Ch,[3] Ch—H,[4] Ch—E,[5] and Ch—C[6] bonds has been discovered in last two decades (Ch = S, Se; E = B, Si, Ge, Sn, P, etc.; C = C(O)R, allyl, CN).[7] Although characteristic reactivities and synthetic utilities of organosulfur compounds by the combination of transition metal catalysts have been disclosed, the research area of transition-metal-catalyzed reactions of organoselenium compounds is still remained undeveloped. During the course of our studies, we focused on alkynyl selenides,[8,9] which have a *sp*C–Se bond, and examined the reactions in the presence of transition metal complexes for the purpose of the development of novel transition-metal-catalyzed reactions of organoselenium compounds.

We first examined the palladium-catalyzed reaction of alkynyl selenide **1a** with diethyl acetylenedicarboxylate (**2a**) in toluene upon heating at 115 °C for 16 h (Table 1). When the reaction was performed in the presence of $Pd(PPh_3)_4$, a novel alkynylselenation of **2a** occurred, affording the corresponding alkynylvinyl selenide **3a** in 9% yield (entry 1).[10] Thus, we screened palladium complexes and additives such as phosphines. When $Pd(OAc)_2$ was used along with $P(o\text{-Tol})_3$, K_2CO_3, and H_2O in this reaction, the yield of the desired alkynylselenation increased to 42% (entry 2).[11] Other phosphines such as $P(p\text{-Tol})_3$, $P(OMe)_3$, P^nBu_3, PCy_3, and DPPE (entries 3—7), and other palladium complexes such as $Pd(OAc)_2$ and $Pd(dba)_2$ (entries 8 and 9) were less effective for this alkynylselenation. In contrast, the use of $PdCl_2$ as a catalyst produced a selenide **4a** bearing multisubstituted aryl group (entry 10).[12] The structure of the product **4a** was determined by X-ray crystal analysis, as shown in Figure 1. This product **4a** was generated most probably via a $PdCl_2$-catalyzed [2+2+2] cycloaddition of **1a** with 2 equivalents of **2a**.[13,14] In addition, when $PdCl_2(PPh_3)_2$ and $PdCl_2(PhCN)_2$ were employed for the reaction of **1a** with **2a**, the yields of **4a** increased (entries 11 and 12). $NiCl_2(PPh_3)_2$ and $RhCl(PPh_3)_3$ indicated poor efficiency for the alkynylselenation and the [2+2+2] cycloaddition of alkynyl selenide (entries 13 and 14).

We next examined the palladium-catalyzed reactions of alkynyl selenides with acetylenedicarboxylates by use of $Pd(OAc)_2/P(o\text{-Tol})_3/K_2CO_3/H_2O$ catalytic system. The results of the alkynylselenation of **2** with several alkynyl selenides **1** are summarized in Table 2. Similar conditions could be employed with aryl substituted alkynyl selenides **1b** and **1c**, and alkyl substituted alkynyl selenide **1d** successfully (entries 3—5). When the phenyl group of **1a** was replaced by other aryl groups, the corresponding alkynylvinyl selenides **3e** and **3f** were obtained in similar yields (entries 6 and 7). The ORTEP diagram of **3f** (*Z* isomer) is shown in Figure 2. The stereochemistry of vinyl unit is unambiguously determined. In the

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* Corresponding author. Tel./fax: +81 72 254 9290.
E-mail address: ogawa@chem.osakafu-u.ac.jp (A. Ogawa).

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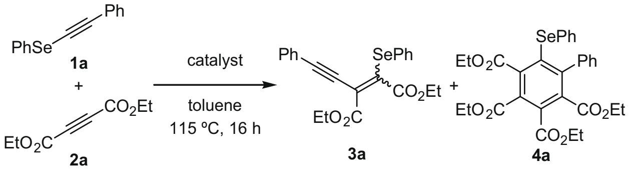
Table 1
Screening of palladium catalysts[a]



Entry	Catalyst	Yield of **3a**[b] (%)	Yield of **4a**[b] (%)
1[c]	$Pd(PPh_3)_4$	9	ND
2[d,e]	$Pd(OAc)_2/P(o\text{-}Tol)_3$	42 (36)	Trace
3[c,d]	$Pd(OAc)_2/P(p\text{-}Tol)_3$	ND	Trace
4[c,d]	$Pd(OAc)_2/P(OMe)_3$	ND	Trace
5[d,g]	$Pd(OAc)_2/P^nBu_3$	24	Trace
6[c,d]	$Pd(OAc)_2/PCy_3$	6	Trace
7[c,d,f]	$Pd(OAc)_2$/DPPE	13	14
8[e]	$Pd(OAc)_2$	8	9
9[e]	$Pd(dba)_2$	Trace	7
10[e,g]	$PdCl_2$	5	58
11[g]	$PdCl_2(PPh_3)_2$	5	81 (70)
12[g]	$PdCl_2(PhCN)_2$	8	64 (61)
13[c,g]	$NiCl_2(PPh_3)_2$	ND	ND
14[c,g]	$RhCl(PPh_3)_3$	7	ND

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (2 equiv), catalyst (10 mol %), toluene (1 mL), 115 °C, 16 h.

[b] Yields were determined by GC, and values in parenthesis are isolated yield.

[c] The starting material **1a** was recovered mainly.

[d] Phosphine ligand (30 mol %), K_2CO_3 (20 mol %), and H_2O (ca. 1 mmol) were added.

[e] The fragmentation products of **1a**, for example, diphenyl diselenide, were obtained.

[f] DPPE (20 mol %) was used as phosphine.

[g] Compound **2a** (3 equiv) was employed.

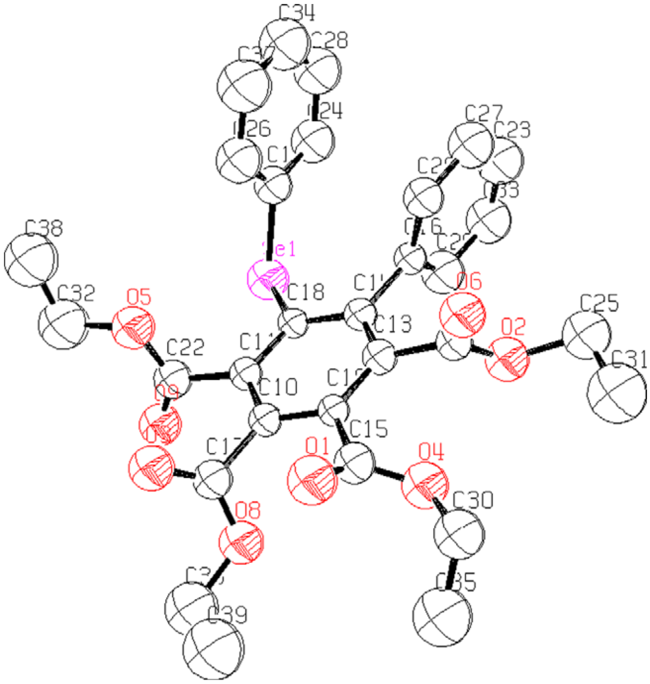
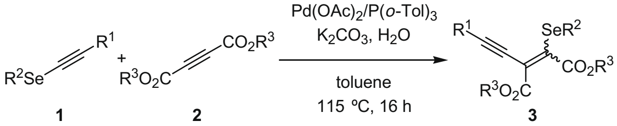


Figure 1. ORTEP diagram of **4a**.

cases of other alkynes such as ethyl propiolate, phenylacetylene, ethyl 2-butynorate, and ethyl phenylpropiolate, no desired product was obtained, and instead, oligomerization of alkynes and fragmentation of alkynyl selenide took place.

Table 2
The palladium-catalyzed alkynylselenation with alkynyl selenides[a,b]



Entry	**1**	R^1	R^2	**2**	R^3	**3**	Yield[c] (%)	[*E*/*Z*][d]
1	**1a**	C_6H_5–	C_6H_5–	**2a**	Et-	**3a**	42 (36)	81/19
2	**1a**	C_6H_5–	C_6H_5–	**2b**	Me-	**3a′**	40 (33)	86/14
3	**1b**	4-Me-C_6H_4–	C_6H_5–	**2a**	Et-	**3b**	40 (34)	79/21
4	**1c**	4-NC-C_6H_4–	C_6H_5–	**2a**	Et-	**3c**	42 (38)	82/18
5	**1d**	$CH_3(CH_2)_3$–	C_6H_5–	**2a**	Et-	**3d**	37 (31)	77/23
6	**1e**	C_6H_5–	4-Me-C_6H_4–	**2a**	Et-	**3e**	39 (36)	75/25
7	**1f**	C_6H_5–	4-Cl-C_6H_4–	**2a**	Et-	**3f**	43 (36)	58/42

[a] Reaction conditions: **1** (0.2 mmol), **2** (2 equiv), $Pd(OAc)_2$ (10 mol %), P(*o*-tol)$_3$ (30 mol %), K_2CO_3 (20 mol %), toluene (1 mL), H_2O (ca. 1 mmol), 115 °C, 16 h.

[b] Formally, 1,2-addition products of benzeneselenol or diphenyl diselenide to **2** were also obtained as byproducts.

[c] Yields were determined by ^1H NMR and values in parenthesis are isolated yield.

[d] Determined by ^1H NMR.

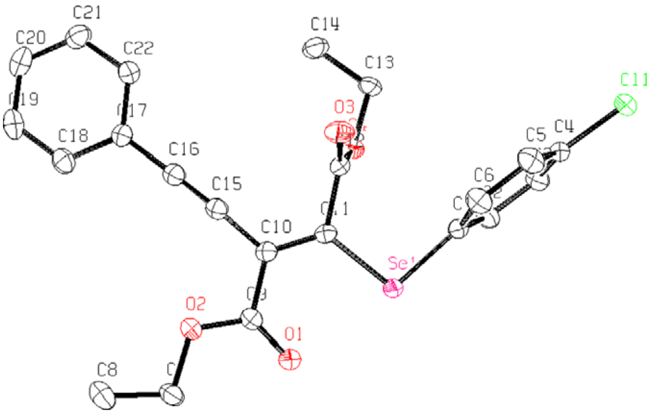
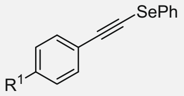
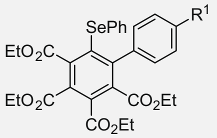
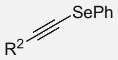
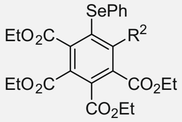
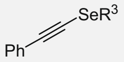
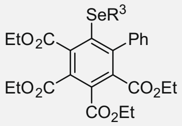


Figure 2. ORTEP diagram of **3f** (*Z* isomer).

Table 3 represents the scope and limitation of the palladium-catalyzed [2+2+2] cycloaddition of various alkynyl selenides **1** with **2**. Dimethyl acetylenedicarboxylate (**2b**) could be also employed for this cycloaddition (entry 2). Several functionalities such as methyl, pentyl, methoxy, chloro, and cyano substituents were tolerant of this reaction condition, forming the corresponding selenides **4** in good yields (entries 3–7). Similar conditions can be employed with **1d** having aliphatic alkynyl group and **1j** having trimethylsilyl group (entries 8 and 9). In contrast, the reaction of **1k** and **1l** bearing ester or methoxymethyl groups provided the corresponding selenides **4k** and **4l**, respectively, in lower yields (entries 10 and 11), and **1m** having amino group did not afford **4m** (entry 12). Alkynyl selenides having substituted aryl and aliphatic seleno groups underwent the desired cycloaddition reactions, producing **4n**, **4e**, **4f**, **4o**, and **4p** in good yields (entries 13–17). In addition, this [2+2+2] cycloaddition could be employed with alkynyl sulfide **5a**, affording the corresponding sulfide **6a** successfully (Eq. 1). When the reaction was carried out using diphenylacetylene, ethyl 2-butynolate, ethyl phenylpropiolate, 4-phenyl-3-butyn-2-one, ethyl propiolate, and phenylacetylene, oligomerization of alkynes and fragmentation of alkynyl selenide proceeded predominantly.

Table 3
The palladium-catalyzed [2+2+2] cycloaddition of alkynyl selenide[a,b]

Entry	Alkynyl selenide		Product	Yield[c] (%)
				
1	**1a**	R^1 = H–	**4a**	70
2[d]	**1a**	H–	**4a′**	60
3	**1b**	Me-	**4b**	64
4	**1g**	^{n}Pen-	**4g**	68
5	**1h**	MeO-	**4h**	58
6	**1i**	Cl-	**4i**	71
7	**1c**	NC-	**4c**	52
				
8	**1d**	R^2 = ^{n}Bu-	**4d**	54
9	**1j**	TMS-	**4j**	42
10[e]	**1k**	EtO_2C–	**4k**	26
11[e]	**1l**	$MeOCH_2$–	**4l**	24
12[e]	**1m**	Me_2NCH_2–	**4m**	ND
				
13	**1n**	R^3 = 4-MeO-C_6H_4–	**4n**	72
14	**1e**	4-Me-C_6H_4–	**4e**	63
15	**1f**	4-Cl-C_6H_4–	**4f**	60
16	**1o**	4-F-C_6H_4–	**4o**	59
17	**1p**	Et-	**4p**	85

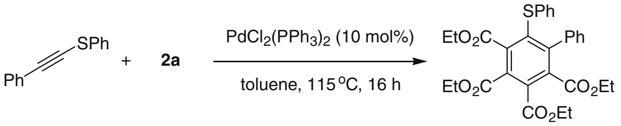
[a] Reaction conditions: **1** (0.2 mmol), **2a** (3 equiv), $PdCl_2(PPh_3)_2$ (10 mol %), toluene (1 mL), 115 °C, 16 h.

[b] The corresponding diselenide and/or monoselenide were obtained as byproducts.

[c] Isolated yield.

[d] Dimethyl acetylenedicarboxylate (**2b**, 3 equiv) was used in place of **2a**.

[e] Instead of the desired reaction, [2+2+2] cycloaddition of three molecules of **2a** took place predominantly, and the starting material **1** was recovered unchanged.



5a 3 equiv **6a**, 40% (1)

In summary, we have developed a new palladium-catalyzed reaction of alkynyl selenides with acetylenedicarboxylates. Alkynylselenation of acetylenedicarboxylates with alkynyl selenides has been attained by use of $Pd(OAc)_2/P(o\text{-Tol})_3/K_2CO_3/H_2O$-catalytic system, leading to alkynylvinyl selenides. In contrast, the treatment of alkynyl selenides with $PdCl_2(PPh_3)_2$ catalyst in the presence of acetylenedicarboxylates, has been found to afford multisubstituted aryl selenides selectively via the [2+2+2] cycloaddition reaction.

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Supplementary data

Supplementary data (general experimental procedure and characterization date for alkynylselenation products, [2+2+2] cycloaddition products, and new alkynyl selenides) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.125.

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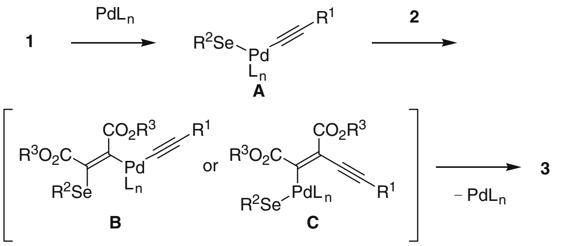
11. A plausible pathway for the palladium-catalyzed alkynylselenation may include the following steps (Eq. 2): (1) the oxidative addition of **1** into Pd complex to form palladium selenide species **A**; (2) the sequential selenopalladation or alkynylpalladation of **2**; (3) the reductive elimination of alkynylvinyl selenide **3** with regeneration of the Pd catalyst.



(2)

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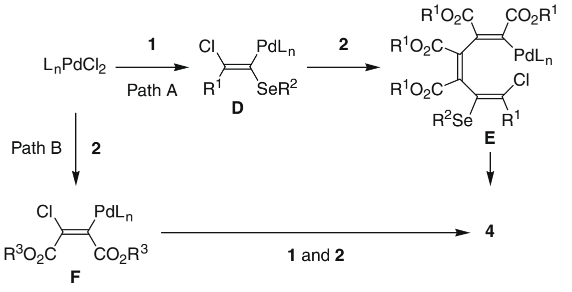
13. $PdCl_2$-catalyzed [2+2+2] cycloaddition reactions of acetylenes proceed via chloropalladation of acetylenes, see: *Metal Catalyzed Cascade Reactions*; Müller, T. J. J., Ed.; Springer: Berlin, 2006; Vol. 19.
14. The palladium-catalyzed [2+2+2] cycloaddition of alkynyl selenides may proceed via the following pathways (Eq. 3): path A involves chloropalladation of **1**, sequential insertion of two molecules of **2**, and intramolecular cyclization to form **4** with recovery of the Pd catalyst; path B includes chloropalladation of **2**, insertion of **1** and **2**, and intramolecular cyclization to give **4** with elimination of the Pd catalyst.



(3)