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Palladium(II) Acetate in Pyridine as an Effective Catalyst for Highly Regioselective Hydroselenation of Alkynes

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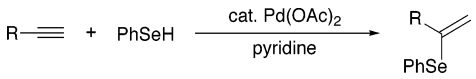
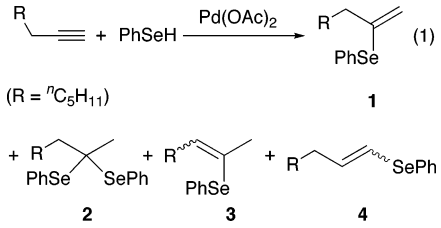
Received July 24, 2004



A highly regioselective hydroselenation of terminal alkynes with benzeneselenol can be achieved by the combination of palladium acetate and pyridine, providing the corresponding terminal alkenes, (i.e., 2-phenylseleno-1-alkenes) as a sole product. In this hydroselenation, pyridine may act as a suitable ligand for active palladium intermediates.

Recently, organosulfur compounds have been employed as substrates for transition-metal-catalyzed reactions and several synthetically useful reactions of them have been developed in the presence of transion matal catalysts.[1] In contrast, the transition-metal-catalyzed reactions of organoselenium compounds have been scarcely investigated, probably because the higher affinity of selenium to transition metal catalysts may extensively decrease the catalytic activity in the reactions of selenium compounds.[2] In 1992, we reported the first example of transition-metal-catalyzed addition reactions of benzeneselenol to terminal alkynes, in which palladium complexes such as $Pd(OAc)_2$, $PdCl_2$, $PdCl_2(PPh_3)_2$, $PdCl_2(PhCN)_2$, and $Pd(PPh_3)_4$ are used as the catalyst.[2m] However, the product selectivity of hydroselenation is not adequate in comparison with the corresponding palladium-catalyzed hydrothiolation of terminal alkynes with benzenethiol, which provides the terminal alkenes (i.e., 2-phenylthio-1-alkenes), as a sole product (cat. $Pd(OAc)_2$, THF, 67 °C).[3]

In THF, this $Pd(OAc)_2$-catalyzed hydroselenation of terminal alkynes with benzeneselenol provides 2-phenylseleno-1-alkene (**1**) as the major product, but the reaction is accompanied by the formation of further addition product (**2**) of PhSeH to vinylic selenide, double bond isomerization product (**3**), and 1-phenylseleno-1-alkene (**4**) as byproducts (eq 1, and entry 1 in Table 1).



The product selectivity is somewhat increased by using benzene as the solvent; however, byproducts **2**−**4** are still formed similarly (entry 2, in Table 1). Thus, much effort has been invested to improve the selectivity and efficiency for this hydroselenation and we have successfully found that *palladium acetate in pyridine* attains an excellent product selectivity in the hydroselenation of alkynes with benzeneselenol: 2-phenylseleno-1-alkene (**1**) was obtained as a sole product (entry 5 in Table 1). On the other hand, the reaction in the absence of catalyst did not proceed efficiently (entry 6 in Table 1).

TABLE 1. Influence of Solvents on Hydroselenation[a]

			yield, %[b]			
entry	solvent	temp, °C	**1**	**2**	**3**	**4**
1	THF	67	46	15	10	5
2	benzene	80	62	13	7	<3
3	toluene	100	23	29	34	0
4	pyridine	80	47	0	0	0
5	pyridine	100	77	0	0	0
6[c]	pyridine	100	3	0	0	0

[a] Reaction conditions: $Pd(OAc)_2$ (2 mol %), 1-octyne (1.0 mmol), solvent (0.5 mL), PhSeH (1.0 mmol), 15 h. [b] Determined by ^1H NMR. [c] In the absence of catalyst.

Table 2 represents the results of the $Pd(OAc)_2$-catalyzed hydroselenation of various terminal alkynes.

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10.1021/jo048727j CCC: $30.25
Published on Web 12/17/2004

TABLE 2. Hydroselenation of Terminal Alkynes[a]

entry	acetylene	product	yield, %[b]
1	$^nC_6H_{13}$—	$^nC_6H_{13}$(PhSe)	quant (quant)
2	NC	NC, PhSe	93
3	HO	HO, PhSe	89 (85)
4	Ph	Ph, PhSe	76 (67)
5		PhSe	53
6	HO	HO, PhSe	71[c]
7	MeO	MeO, PhSe	56[d]

[a] Reaction conditions: $Pd(OAc)_2$ (2 mol %), alkyne (1.0 mmol), PhSeH (1.0−1.1 mmol), pyridine (0.5 mL), 15 h, 100 °C. [b] NMR (isolated) yield. [c] $HOCH_2CH{=}CHSePh$ was obtained in 12% yield (E/Z = 42/58) as a byproduct. [d] *p*-MeO-C_6H_4-CH=CHSePh was obtained in 38% yield (Z>95%) as a byproduct.

Substituted aliphatic alkynes gave the corresponding hydroselenation products in high to excellent yields regioselectively (entries 1−6). Exceptionally, in the case of propargylic alcohol, regioisomer (3-phenylseleno-2-propene-1-ol) was also obtained as a byproduct (entry 6).[4]

In general, the radical addition of PhSeH to aliphatic alkynes requires longer reaction time under neutral conditions in the presence of a very small amount of air contamination or upon irradiation with room light. Contrary to this, similar radical addition to aryl-substituted alkynes proceeds faster.[5] For example, the radical addition of PhSeH to 1-hexyne requires a long reaction time (240 h) affording 1-(phenylseleno)-1-hexene in 45% yield, whereas the additon to ethynylbenzene is accomplished within 5 min in the presence of a trace amount of oxygen contamination, which provides 2-(phenylseleno)styrene exclusively. With these facts in hand, the result that the $Pd(OAc)_2$-catalyzed hydroselenation of 1-ethynyl-4-methoxybenzene provides the corresponding 2-phenylseleno-substituted terminal alkene as the major product (56%) is noteworthy (entry 7).

To get insight into the role of pyridine in this catalytic reaction, we examined the catalytic hydroselenation by using pyridine (or its derivatives) as ligands in toluene (Table 3). When the $Pd(OAc)_2$-catalyzed reaction of 1-octyne with PhSeH in toluene was conducted by employing 40 mol % of pyridine, the corresponding 2-(phenylseleno)-1-octene was successfully obtained in moderate yield with high product selectivity (entry 2). In this reaction, the use of a bidentate ligand such as 2,2′-bipyridyl (20 mol %) in place of pyridine led to the increase in the yield of the desired vinyl selenide with excellent regioselectivity (entries 3−5). These results strongly suggest that pyridine acts as a suitable ligand for an active palladium intermediate.[6]

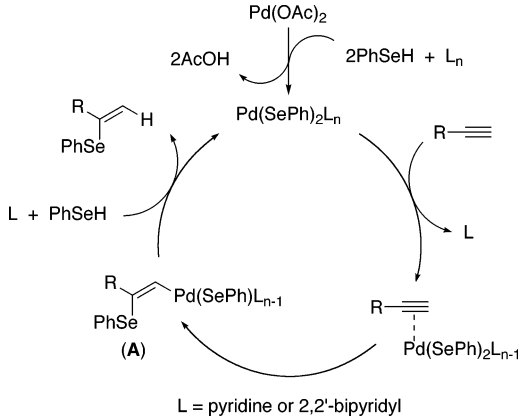
TABLE 3. Catalytic Hydroselenation with Pyridine or 2,2′-Bipyridyl

$^nC_6H_{13}$— + PhSeH $\xrightarrow[\text{solvent}]{Pd(OAc)_2}$ $^nC_6H_{13}$(PhSe)

entry	solvent	time, h	additive, mol %	yield, %[a]
1	pyridine	15	none	77
2	toluene	15	pyridine (40)	38
3	toluene	15	2,2′-bipyridyl (20)	63
4	toluene	10	2,2′-bipyridyl (20)	60
5	toluene	10	2,2′-bipyridyl (40)	63

[a] Determined by ^1H NMR.

SCHEME 1. A Possible Pathway for the Pd(II)-Catalyzed Hydroselenation



Although the elucidation of the precise mechanism requires further detailed investigations, Scheme 1 shows a possible reaction pathway, which includes the following: (1) ligand exchange of the acetate group with the PhSe group to give an $Pd(SePh)_2L_n$ as an active catalyst and AcOH; (2) coordination of alkyne to the palladium selenide species; (3) *syn*-selenopalladation of alkyne to form *β-cis*-(phenylseleno)vinylpalladium intermediate (**A**); (4) the protonolysis of the vinylpalladium intermediate with PhSeH to provide 2-phenylseleno-1-alkene with regeneration of the catalyst.

In general, the reductive elimination process of *vic*-bis(phenylseleno)alkene from the vinylpalladium intermediate (**A**) complex takes place smoothly in the presence of phosphine ligands.[2j,7] In this hydroselenation, however, there is no phosphine ligand so that the reductive elimination may be difficult. Consequently, the hydroselenation product is obtained by trapping with PhSeH.

(4) Although the reason 2-phenyl-2-propenols were formed as byproducts in the case of propargylic alcohols is unclear, the coordination of the propargylic oxygen to palladium may contribute to the formation of the regioisomers (2-phenylseleno-2-propenol).

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(6) In the absence of pyridine, palladium selenide ($Pd(SePh)_2$) molecules as key species for this hydroselenation of alkynes easily react with each other by the coordination of the selenide ligand to the other palladium center to form polymerized complex, which is insoluble in usual organic solvents and loses the catalytic activation. Therefore, pyridine might inhibit the polymerization and protect the catalyst from the poisoning.

In summary, we have developed the highly regioselective hydroselenation of terminal alkenes by the combination of $Pd(OAc)_2$ and pyridine. Pyridine (or 2,2′-bipyridyl) acts as a useful ligand for this reaction, and may prevent catalyst poisoning by inhibiting the polymerization of the palladium selenide catalysts. This catalytic system provides a useful method for the transition-metal-catalyzed reactions of organoselenium compounds.

Experimental Section

General Procedure for the Hydroselenation. Into a two-necked flask equipped with a reflux condenser and a magnetic stirring bar were placed palladium acetate (4.5 mg, 0.02 mmol), pyridine (0.5 mL), alkyne (1.0 mmol), and benzeneselenol (106−115 μL, 1.0−1.1 mmol) under N_2 atmosphere. The mixture was heated at 100 °C with stirring for 15 h. After the reaction was complete, the resulting catalyst was removed by filtration through Celite, and the filtrate was evaporated under reduced pressure. The purification of the products was performed by preparative TLC (PTLC) on Wakogel B-5F silica gel with a mixed solvent of hexane/ethyl acetate as an eluent.

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) (No. 14044063, Exploitation of Multi-Element Cyclic Molecules) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. We acknowledge the analytical section of Osaka University for elemental analyses.

Supporting Information Available: Analytical and spectral data and representative ^1H NMR sprectra for the $Pd(OAc)_2$-catalyzed hydroselenation of 1-octyne in THF and pyridine. This material is available free of charge via the Internet at http://pubs.acs.org.

JO048727J

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