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The Regio- and Stereoselective One-Pot Catalytic Preparation of β-Selenyl Acrylamides

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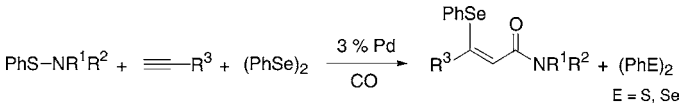
ABSTRACT



$Pd(PPh_3)_4$ is found to catalytically assemble sulfenamides, terminal aliphatic alkynes, carbon monoxide, and diphenyl diselenides regio- and stereoselectively in a single-pot reaction to produce good yields of β-selenyl acrylamides.

Transition-metal-catalyzed heteroatom functionalization of unsaturated substrates with the chalcogenides has recently become of interest due to the many useful transformations available to the resulting vinyl chalcogenides.[1] Various transition-metal-catalyzed chalcogenide−element additions of Y−G compounds (Y = S, Se, Te; G = H, Si, Ge, B, P, S, Se) to alkenes, alkynes, isocyanides, and CO have been developed,[2] but reactions in which G = N have only one example in the azathiolation of carbon monoxide.[3] Herein, we report a new palladium-catalyzed regio- and stereoselective chalcogenide−element addition (Y = Se, G = N) to terminal alkynes in the presence of carbon monoxide to give β-selenyl acrylamides.

Despite the extensive chemistry of the vinyl chalcogenides,[1a,b,4] there exists neither a general nor a simple methodology for preparing β-selenyl acrylamides. Most commonly, β-functionalized acrylate precursors are synthesized from the hydrochalcogenation of preformed alkynoic esters,[5] and the amide derivatives are then prepared in subsequent steps by condensation methods.[6] This approach, though effective, requires the independent preparation of the alkynoic ester and generally involves the use of the noxious chalcogenols. Recently, β-telluryl acrylamides have been accessed by the photoinduced group transfer radical addition of tellurylcarbamates to acetylenes.[7] This process is limited to electron deficient aryl acetylenes and results in a mixture of both *E* and *Z* isomers. Although a variety of other methods exist for making vinyl chalcogenide derivatives of acryloyl moieties, many are specific for α-substitution, are low yielding, or are limited to specific substrates.[5,8]

We have discovered a new, versatile route to β-selenyl acrylamides involving the one-pot assembly of four components. The reaction of *S*-phenyl-*N*-dimethylsulfenamide,

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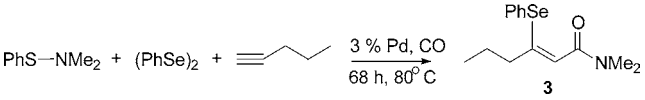
$PhSNMe_2$ **(1a)**, with 1-pentyne, CO, and diphenyl diselenide (**2a**) was catalyzed by 2.5% $Pd(PPh_3)_4$ in benzene at 80 °C for 68 h. The β-selenyl acrylamide, (*Z*)-3-phenylselenylhex-2-enoic acid dimethylamide (**3**), was produced in 70% GC yield (55% isolated) with 100% regiospecificity for the β position and 100% stereoselectivity for the *Z* isomer as determined by both ^{1}H NMR and NOE difference spectrometry. The only active catalyst identified was $Pd(PPh_3)_4$; $Pt(PPh_3)_4$, $PdCl_2$, $(AsPh_3)_2PdCl_2$, and $ClRh(PPh_3)_3$ produced trace or no β-selenyl acrylamide under similar conditions. Benzene, toluene, and acetonitrile were found to be acceptable solvents, but significant inhibition in methylene chloride was observed (Table 1).

Table 1. Effects of Catalyst and Solvent on the Synthesis of β-Selenyl Acrylamides

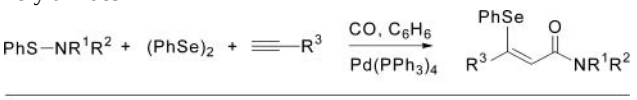


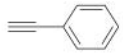
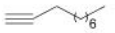
entry	catalyst	solvent	GC yield, %
1	$Pd(PPh_3)_4$	C_6H_6	70
2	$Pd(PPh_3)_4$	$C_6H_5CH_3$	53
3	$Pd(PPh_3)_4$	CH_3CN	60
4	$Pd(PPh_3)_4$	CH_2Cl_2	48
5	$Pt(PPh_3)_4$	C_6H_6	trace
6	$PdCl_2$	C_6H_6	0
7	$(AsPh_3)_2PdCl_2$	C_6H_6	0
8	$ClRh(PPh_3)_3$	C_6H_6	0

The highest yields were obtained at 50−60 h and 80−85 °C with the exception of reactions involving *S*-phenyl-*N*-diallylsulfenamide, $PhSN(allyl)_2$ (**1e**) (entry 10, Table 2). The optimal stoichiometry was found to be 1 equiv of sulfenamide and diphenyl diselenide to 1.5 equiv of alkyne and 3−5% palladium.

Moderate 4:1 selectivity for the formation of the β-selenyl acrylamide **3** over the β-sulfenyl acrylamide (**4**) (Scheme 1) was observed. This ratio represents a 2-fold increase in what would be expected based on the initial ratio of 2:1 Se/S. Several minor byproducts were observed by GC−MS and ^{1}H and ^{13}C NMR spectroscopy. The identities of these species were confirmed by comparison to independently prepared standards and their amounts quantified by gas chromatography (Scheme 1). Thiocarbamate (**5a**) and selenylcarbamate (**5b**) were the expected byproducts of the competing azathiolation and azaselenylation of carbon monoxide.[3] The presence of (*Z*)-1,3-(phenylthio)-2-penten-1-one (**6a**), 3-phenylselenyl-hex-2-enoic acid *S*-phenyl ester (**6b**), and (*Z*)-1,2,-bis(phenylseleno)-1-pentene (**7**) in the reaction mixture was also anticipated as they are known to arise from the palladium catalyzed addition and carbonylative addition of the diaryl chalcogenides (**2a**, **2b, 2c**) to 1-pentyne.[2g] Furthermore, diphenyl selenide (**8**) formation during the course of the reaction is indicative of aryl group exchange between phosphine and diphenyl diselenide.[9] All of the above-described

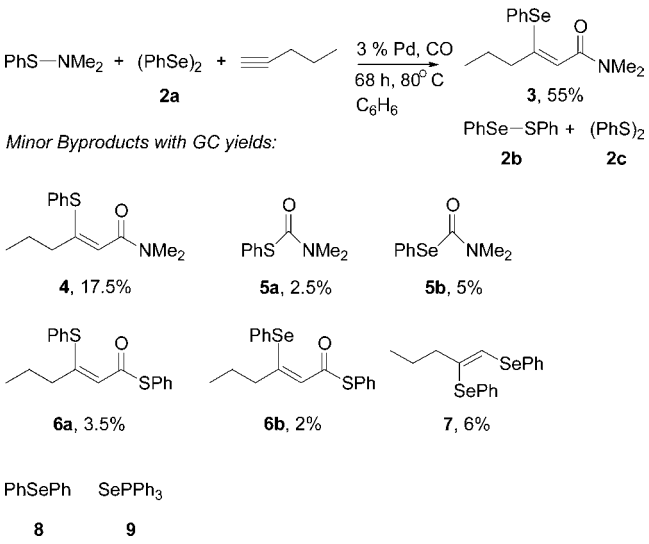
Table 2. Palladium-Catalyzed Synthesis of Various β-Selenyl Acrylamides



entry	PhS—NR^1R^2	—R^3	yield, %	product	*E/Z*
1	PhS—NMe_2		55	**3**	0/100
2			0	—	—
3			0	—	—
4			0	—	—
5	PhS—N(Bz)Me		45	**10**	0/100
6			60	**11**	0/100
7			60	**12**	0/100
8	PhS—NEt_2		55	**13**	0/100
9	PhS—N(Me)(allyl)		61[a]	**14**	0/100
10	PhS—N(allyl)$_2$		60	**15**	0/100
11	PhS—N(H)Me		0	—	—
12	PhS—N(cyclopropyl)$_2$		0	—	—

[a] GC yield.

Scheme 1



byproducts were easily separated from the β-selenyl acrylamide via column chromatography.

Reactions with various sulfenamides and alkynes are summarized in Table 2. Extending the reaction to include

different, more sensitive functionalities on the nitrogen of the sulfenamide was successful with little to no change in the reaction yield. *S*-Phenyl-*N*-benzyl-*N*-methyl sulfenamide, PhS−N(Bz)Me (**1b**), was found to react in 60% yield with 1-decyne (entry 7) and 45% with 1-pentyne (entry 5). *S*-Phenyl-*N*-allyl-*N*-methylsulfenamide, PhSN(allyl)Me (**1d**), and S-phenyl-*N*-diallylsulfenamide **1e** were found to react with 1-pentyne in 61 and 60% yields, respectively (entries 9 and 10). Higher temperatures, 105 °C, and higher catalyst loading were found to be necessary to obtain good yields with S-phenyl-*N*-diallylsulfenamide and 1-pentyne.

Not surprisingly, *S*-phenyl-*N*-methylsulfenamide, PhSN(H)Me (**1f**) (entry 11), produced no acrylamide due most likely to the formation of palladium hydrides via the direct interaction of the sulfenamide N−H bond with the palladium center. *S*-Phenyl-*N*-diisopropyl sulfenamide, PhSN(^{i}Pr)$_2$ (**1g**), was apparently too sterically encumbered substrate for the reaction (entry 12).

With respect to alkyne, the reaction tolerates terminal aliphatic alkynes of differing chain length as well as halogen substitution. Internal alkynes (entry 4), phenyl acetylenes (entry 2), and acetylenes with hydroxy (entry 3) substituents did not serve as acceptable substrates, however. The lack of tolerance for phenyl and hydroxyl groups markedly differs from the behavior exhibited by the palladium catalyzed carbonylative addition of diaryl chalcogenides to terminal acetylenes.[2g]

Although we are still conducting mechanistic studies, initial data suggest that the overall catalytic cycle involves initial insertion of alkyne into a Pd−SePh bond, followed by CO insertion and σ−bond metathesis with the sulfenamide to give the β-selenyl acrylamide and a Pd−SPh containing inorganic compound. The recycling of the palladium thiolate back to a palladium selenolate is of particular interest and is the subject of ongoing experiments. An alternative mechanism can be envisioned with the first step toward product formation being direct oxidative addition of sulfenamide to Pd(0), but this path can be ruled out based on previous observations by others on the related azathiolation of carbon monoxide.[3] Finally, we are searching for explanations for the moderate selectivity for Se over S incorporation. Although some evidence suggests that there may be a slight preference for alkyne insertion into Pd−SePh over Pd−SPh, we have not yet ruled out the simple explanation that Pd−SPh concentrations do not become significant until late in the reaction.

In conclusion, we have successfully developed a novel catalytic process for the regio- and stereoselective synthesis of a variety of β-selenyl acrylamides. These compounds are of great synthetic interest as the vinyl selenides are easily manipulated by a variety of reactions.[1] Future work in this area is underway to elucidate the exact mechanism and to extend this methodology to the preparation of sulfenyl and telluryl acrylamides.

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Supporting Information Available: Experimental procedures and characterization data for β-selenyl acrylamides **3** and **10**−**15**. Characterization data for sulfenamides **1a**−**g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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