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A Palladium-Catalyzed Regio- and Stereoselective Four-Component Coupling Reaction

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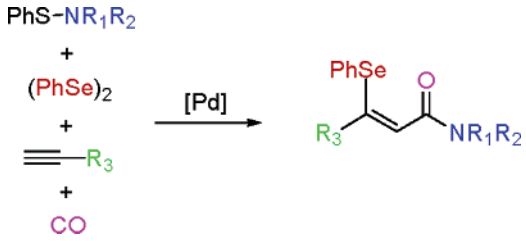

$Pd(PPh_3)_4$ catalytically assembles sulfenamide, alkyne, carbon monoxide, and diphenyl diselenide regio- and stereoselectively in a one-pot four-component coupling reaction to yield (*Z*)-β-selenyl acrylamides. The reaction proceeds in good to excellent yields (60−95%) and is tolerant of a range of functional groups on both the nitrogen of the sulfenamide and the alkyne. Moderate selectivities ranging from 4:1 to 7:1 β-selenyl to β-sulfenyl acrylamide have been observed despite the initial concentration of 2:1 selenium to sulfur in the reaction. The chalcogeno selectivity was found to depend directly on CO pressure; increased pressure decreased selectivity for selenium over sulfur.

Introduction

The development of one-pot multicomponent coupling reactions has provided a rapid and elegant means for the preparation of complex molecular architectures from simple and diverse building blocks.[1−3] The attraction to the synthetic chemist lies in the multitude of advantages that include higher yields than almost any sequential synthesis to the same target, a single purification step, and easy adaptation to combinatorial synthetic schemes.[4−6] Well-known examples include the Ugi four-component reaction,[7] as well as the Hantzsch,[8] Biginelli,[9] Mannich,[10] Passerini,[11] and Bucherer−Bergs[12] three-component reactions. These assembly processes have several common aspects that enhance their utility including (1) high selectivity for the synthesis of one isomeric form of a single product, (2) tolerance of structural diversity on one or more of the reagents, and (3) the formation of at least one C−C bond.

As previously communicated, we have developed a new palladium-mediated four-component coupling reaction for the synthesis of β-selenyl acrylamides (Scheme 1).[13] This reaction satisfies the above-mentioned criteria in that it produces high yields of a single regio- and stereoisomer, there is considerable diversity available in both the alkyne and sulfenamide ($PhS-NR_2$) reagents, and one C−C bond as well as two C-heteroatom bonds (C−N, C−Se) is formed. In addition, the reaction yields a product with two reactive functionalities available for subsequent modification: an α,β-unsaturated amide and a vinylic pseudohalide group, PhSe−.[14] It should be noted

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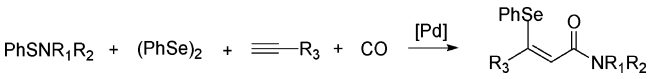
SCHEME 1



that few multicomponent couplings give products with more than one reactive functionality and, although metal-catalyzed multicomponent coupling reactions[1,2,15] are well-known, they are generally limited to three components with the corresponding four-component reactions[16] being far more rare.

An unusual pair of heteroatom delivery agents are used in our system, PhS−NR_2 and $(PhSe)_2$. Sulfenamides represent an alternative to the traditional NR_2 delivery agents, namely, amines and silylamines. Despite the need for their preparation, sulfenamides are easily synthesized in one step from commercially available starting materials, and neither they nor their starting materials are noxious.[17] Although not commonly encountered, sulfenamides have found some synthetic utility. For example, Kuniyasu and co-workers found them to be quite useful in the production of thiocarbamates in the palladium-catalyzed azathiolation of carbon monoxide,[18a] and more recently, Kondo and co-workers have prepared polyfunctionalized alkenes via the ruthenium-mediated addition of sulfenamides to alkynes.[18b] In addition, a specific class of sulfenamide, 4′-nitrobenzenesulfenanalide (NBSA), has been found to be an effective reagent for the amidino- and amidosulfenylation,[19] aminosulfenylation,[20,21] and bromosulfenylation[22] of alkenes. The introduction of the PhSe group is more highly precedented using the easily handled $(PhSe)_2$.[23] The PhSe−SePh bond is easily cleaved by palladium, and it is known that Pd−SePh groups are capable of migratory insertion, a key reaction in our system.[15h] It is important to note that the reactions mixtures do not contain significant quantities of thiols or selenols and, therefore, are not particularly odiferous.

To the best of our knowledge, no simple or general methodology exists for the synthesis of the β-selenyl acrylamides despite the wealth of knowledge regarding the preparation and reactivity of the corresponding vinyl chalcogenides.[14e,23,24] The most common preparation of β-selenyl acrylamides involves the initial synthesis of β-functionalized acrylates from the hydrochalcogenation of preformed alkynoic esters. The acrylamide derivatives are then prepared in subsequent steps by simple condensation methods. This approach, though effective, requires several steps and generally involves the use of the noxious chalcogenols.[25]

Recently, new methodology for the preparation of the related β-sulfenyl acrylates and β-telluryl acrylamides has been reported.[26,27] The former has been prepared via the palladium-catalyzed thioesterification of alkynes and the latter via the photoinduced group-transfer radical addition of tellurylcarbamates to aromatic acetylenes. Neither has yet been extended to include β-selenyl acrylamides. Other less common methods for the preparation of β-chalcogenyl acrylamides exist but are limited by low yield, substrate specificity, and α rather than β substitution of the chalcogen.[15e,25,28]

In this paper, we present a full study of the β-selenyl acrylamide-forming reaction, including reactant generality, mechanism, and the selective partitioning of selenium and sulfur in the reaction products. The effect of two- and three-component side reactions on the overall formation of the β-selenyl acrylamides is also considered.

Results and Discussion

The reaction of *S*-phenyl-*N*-dimethyl sulfenamide, $PhSNMe_2$ (**1**), with 1-pentyne, CO, and diphenyl diselenide (**2**) was catalyzed by 4.0% $Pd(PPh_3)_4$ (**3**) in benzene at 85 °C for 168 h to yield the β-selenyl acrylamide (*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide (**4**) in 84% isolated yield based on sulfenamide (Scheme 2). As

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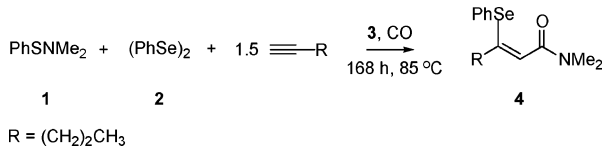
SCHEME 2



previously reported,[13] the reaction proceeded with 100% regiospecificity for placing selenium in the β-position and 100% stereoselectivity for yielding only the *Z* isomer as determined by both ^{1}H NMR and NOE difference spectroscopy.

Optimization experiments were carried out to determine the ideal catalyst and solvent system for the reaction. For aliphatic alkynes, $Pd(PPh_3)_4$ was identified as the only active catalyst as Pd_2dba_3, $(dppf)_2PdCl_2$, $(PPh_3)_2PdCl_2$, $(AsPh_3)_2PdCl_2$, $Pd(OAc)_2$, $PdCl_2$, $Pt(PPh_3)_4$, and $ClRh(PPh_3)_3$ produced only trace or no β-selenyl acrylamide. Interestingly, for phenyl acetylene, only $(PPh_3)_2PdCl_2$ was found to be active;[29] the use of $Pd(PPh_3)_4$, $(AsPh_3)_2PdCl_2$, and $(dppf)_2PdCl_2$ resulted in trace or no β-selenyl acrylamide product. Benzene was found to be the solvent of choice, but only a moderate decrease in yield was observed in toluene, acetonitrile, and methylene chloride.

The best yields of acrylamide were obtained at 150−170 h of reaction at 80−85 °C in the presence of 3−5% of palladium with an optimal stoichiometry of 1 equiv of sulfenamide and diphenyl diselenide to 1.5 equiv of alkyne. The long reaction times were found to be necessary to obtain the highest yields of β-selenyl acrylamide as, for example, an increase in isolated yield of 55−84% was observed upon increasing the reaction time from 68 to 168 h for the preparation of acrylamide **4**. Attempts to reduce the reaction time by either increasing temperature or CO pressure resulted in a decreased yield of β-selenyl acrylamide with a concomitant increase in undesired byproducts.

As can be seen in Table 1, the reaction can deliver a variety of NR_2 groups to the product. Both simple dialkyl- and allyl-functionalized sulfenamides, $PhSNEt_2$ (**5**) and PhSN(allyl)Me (**6**), were found to react with 1-pentyne to give β-selenyl acrylamides in 70 and 82% isolated yields, respectively (entries 7 and 14). An increase in catalyst loading to 8% palladium was necessary for reactions with benzyl- and diallyl-functionalized sulfenamides, PhSN(Bn)Me (**7**) and $PhSN(allyl)_2$ (**8**), to obtain excellent GC yields of acrylamide, 95 and 85% in the case of 1-pentyne, respectively (entries 11 and 15). *N*-benzyl-functionalized sulfenamides can be used with a lower catalyst loading, but such reactions were observed to proceed in lower yields in some cases (entries 12 and 13). Not surprisingly, neither a primary sulfenamide, PhSN(H)Me (**9**), nor a sterically encumbered sulfenamide, $PhSN(^iPr)_2$ (**10**), yielded acrylamide (entries 16 and 17) as both have been reported to be inactive toward the related palladium-catalyzed azathiolation of CO.[18] Attempts to prepare a primary β-selenyl acrylamide via TMS protection of a sulfenamide also failed; couplings attempted with PhSN(Bn)TMS (**11**) resulted in a complex mixture of products (entry 18).

With respect to a variety of functionalized alkynes, the reaction proceeded in good to excellent yields (Table 1). Simple aliphatic alkynes such as 1-pentyne and 1-decyne reacted to yield acrylamide as well as alkynes substituted with cyano, halogen, ester, and dialkylamine functionalities. Internal alkynes as well as hydroxy-substituted alkynes were found to be unreactive (entries 6 and 4). Propargyl alcohols have been reported to undergo intramolecular lactonization under similar conditions, but no lactone product was observed upon workup of the reaction involving 5-hydroxy-1-pentyne.[15o] Notably, phenyl acetylene was found to be unreactive for acrylamide formation with catalyst **3** but was partially converted to acrylamide in low yield with $(PPh_3)_2PdCl_2$ (entry 5). In addition, the conjugated alkyne, 3-methyl-butyn-3-ene, was also found to be unreactive under Pd(0) catalysis but was observed in trace quantities under $(PPh_3)_2PdCl_2$ catalysis (entry 10).

One of the more surprising aspects of this reaction is that sulfenamide proved to be a better source of the NR_2 group than the more traditional sources, simple amines and silylamines. Both diethylamine (**29**) and *N*,*N*-dimethyltrimethylsilylamine (**30**) were found to produce β-selenyl acrylamide under typical reaction conditions but in significantly reduced yields relative to sulfenamide (Table 2).

Mechanism. Coupling the mechanistic work on the reactivity of transition metals with diaryl dichalcogenides published by others with our own observations, it seems reasonable to propose that the formation of β-selenyl acrylamides proceeds according to the following catalytic cycle (Figure 1).[13,15h,o,18,30,31] The loss of phosphine to give a coordinatively unsaturated Pd species is followed by oxidative addition (I) of diphenyl diselenide to generate a Pd(II) diselenolate species that stereoselectively inserts alkyne via *cis*-selenopalladation (II) to yield a vinyl palladium selenolate. Selective CO insertion into the palladium−carbon bond (III) gives a transient palladium−acyl intermediate that can then react with sulfenamide via σ-bond metathesis (IV) to yield β-selenyl acrylamide and a mixed palladium thiolate selenolate species. The catalyst can then re-enter the cycle either by reductive elimination (V) or by direct insertion of alkyne (VI) into either the Pd−SPh or Pd−SePh bond.

As this reaction involves the assembly of four components, we were particularly interested in determining the degree to which two- and three-component side reactions were contributing to the overall reaction mixture and if any of the resulting byproducts were, in fact, mechanistically relevant. As such, a detailed analysis of the reaction mixture resulting from the preparation of acrylamide **4** was undertaken. Although acrylamide **4** was isolated in 84% yield based on sulfenamide, it was found to comprise only 47.5% of the final reaction mixture. A complete

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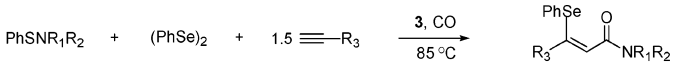
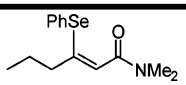
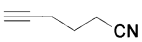
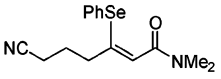
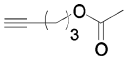
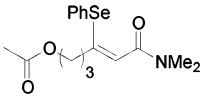
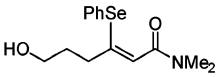
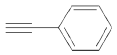
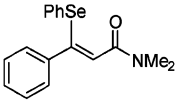
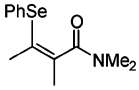
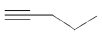
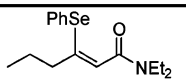
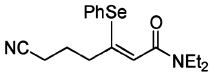
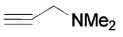
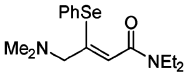
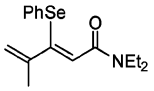
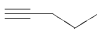
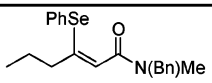
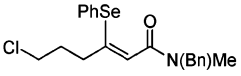
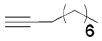
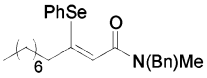
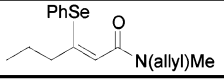
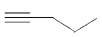
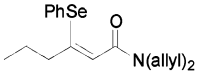
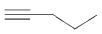
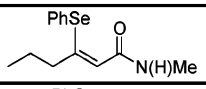
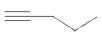
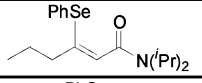
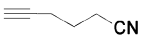
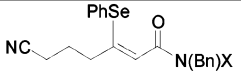
(31) Although it is likely that some of the catalytically active metal complexes are binuclear, we have not specifically addressed this question and thus represent all metal species as monomeric. For discussions regarding nuclearity in palladium-catalyzed Se−Se bond additions to alkynes see: Ananikov, V. P.; Beletskaya, I. P.; Aleksandrov, G. G.; Eremenko, I. L. *Organometallics* **2003**, *22*, 1414.

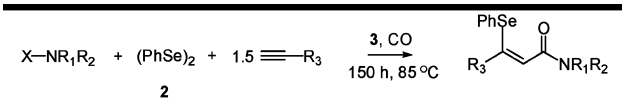
TABLE 1. Palladium-Catalyzed Preparation of β-Selenyl Acrylamides



entry	PhS—NR_1R_2	—R_3	product	compound	yield,%
1	PhS—NMe_2			**4**	84
2				**12**	70
3				**13**	72
4				**14**	0
5				**15**	30[a]
6				**16**	0
7	PhS—NEt_2			**17**	70
8				**18**	80
9				**19**	85[b]
10				**20**	trace[a]
11	PhS—N(Bn)Me			**21**	95[b,c]
12				**22**	60
13				**23**	60
14	PhS—N(allyl)Me			**24**	82
15	PhS—$N(allyl)_2$			**25**	85[b,c]
16	PhS—N(Me)H			**26**	0
17	PhS—$N(^iPr)_2$			**27**	0
18	PhS—N(Bn)TMS		 X = TMS, SPh	**28a,b**	trace

[a] $(PPh_3)_2PdCl_2$. [b] GC yield. [c] 8% $Pd(PPh_3)_4$.

TABLE 2. Effect of the NR_2 Source on the Preparation of β-Selenyl Acrylamides



entry	X-NR_1R_2	—R_3	product	yield, %[a]
1	$PhSNEt_2$ **5**		**18**	85
2	$HNEt_2$ **29**		**18**	40
3	$TMSNMe_2$ **30**		**12**	40

[a] GC yield.

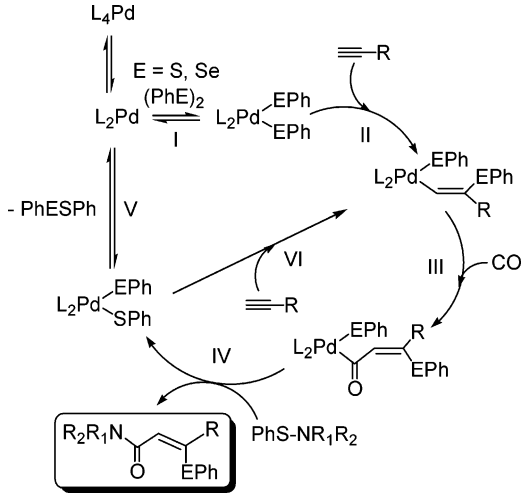
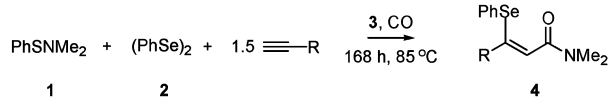


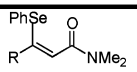
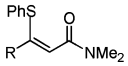
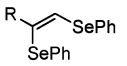
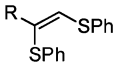
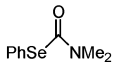
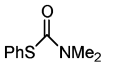
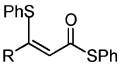
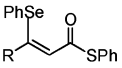
FIGURE 1. Initially proposed catalytic cycle.

analysis of all products is presented in Table 3. Before discussing the byproducts arising from the two- and three-component reactions, it must be emphasized that, since under the reaction conditions all three diaryl dichalcogenides are present (**2**, **31**, and **32**), one might expect that *all* classes of products would be present as both S and Se derivatives. Particularly important to the understanding of the reaction mechanism is not only the presence of the sulfur analogue (**33**) of the major product **4** but also the relative ratio of these two products. Selectivity is discussed later in the paper.

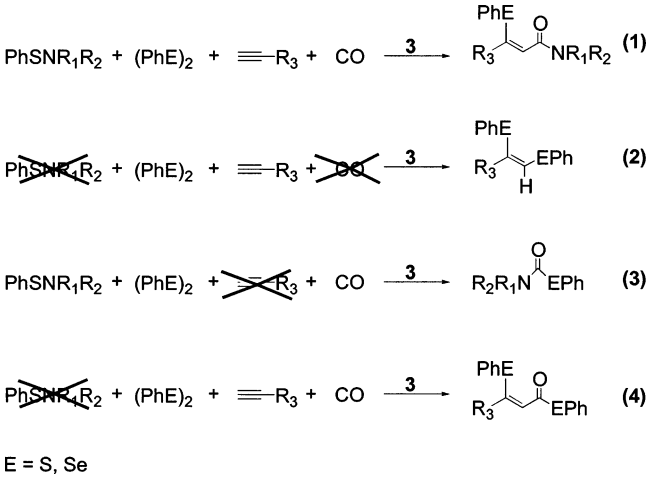
Not surprisingly, evidence was found for the two- and three-component side reactions shown in Scheme 3. These reactions have been reported and studied extensively by Kuniyasu, Ogawa, Sonoda, and Kurosawa.[15h,18] Byproducts **34** and **35** are indicative of simple dichalcogenation of alkyne (eq 2, Scheme 3). The presence of byproducts **36** and **37** is consistent with azaselenolation and azathiolation of CO (eq 3, Scheme 3). The byproducts (**38**, **39**) present in the largest quantities are those resulting from the carbonylative addition of the diaryl dichalcogenides to alkyne (eq 4, Scheme 3). Although these two byproducts comprise nearly 20% of the reaction mixture, it must be remembered that sulfenamide is the limiting reagent under our optimized reaction conditions

TABLE 3. Complete Product Distribution for the Four-Component Coupling Reaction



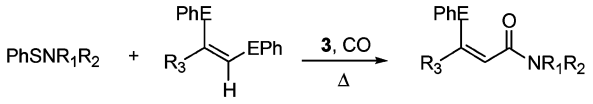
PhSe-SePh		PhS-SPh	PhSe-SPh
17.0%	47.5%	0.3%	trace
2	**4**	**31**	**32**
			
6.8%	2.7%	trace	3.4%
33	**34**	**35**	**36**
			SePPh3
0.1%	10.3%	11.1%	trace
37	**38**	**39**	**40**
PhSePh			
trace			
41			

SCHEME 3



and that the reactions described by eqs 2 and 4 will continue to occur after all sulfenamide has been consumed. As a result, compounds **38** and **39** are expected byproducts even in high-yielding reactions. Trace selenium triphenyl phosphine (**40**) and diphenyl selenide (**41**) were also observed in the final reaction mixture with the latter most likely arising from the aryl-group exchange between phosphine and diphenyl diselenide.[32]

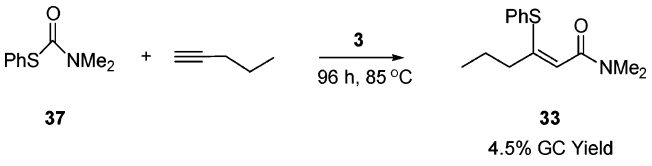
TABLE 4. Reactivity of Dichalcogenated Byproducts Toward Acrylamide Formation



PhSNR$_1$R$_2$	PhE / R$_3$ / EPh / H	% Pd	product	yield, %[a]
PhSNMe$_2$	E = Se R$_3$ = (CH$_2$)$_2$CH$_3$	5	**4**	0
1	**34**			
PhSNMe$_2$	E = S R$_3$ = (CH$_2$)$_2$CH$_3$	5	**33**	0
1	**35**			
PhSNEt$_2$	E = Se R$_3$ = (CH$_2$)$_3$CN	50	**18**	0
5	**42**			

[a] GC yield.

SCHEME 4



37 **33**

4.5% GC Yield

Given that the two- and three-component byproducts were present in the reaction mixtures, we thought it important to determine if any of them could be intermediates in the production of the four-component product. Both selenium and sulfur addition products **34** and **35** were prepared and reacted under 0.5 atm of initial CO pressure with sulfenamide **1** in the presence of catalytic amounts of palladium to determine if the products of dichalcogenation (eq 2, Scheme 3) lay along the reaction pathway towards acrylamide formation. GC analysis of the final reaction mixtures showed no acrylamide products, even in the presence of 50% catalyst **3** (Table 4). It can be concluded then that the formation of addition products such as **34** and **35** is essentially irreversible and that they do not contribute to acrylamide formation.

With respect to the reactivity of the two-component products arising from azathiolation and azaselenolation toward acrylamide formation (Scheme 3, eq 3), we have found that a small percentage of thiocarbamate **37** can be converted to β-sulfenyl acrylamide **33** upon reaction with alkyne in the presence of catalytic amounts of catalyst **3** (Scheme 4). On the basis of this finding, it seems likely then that selenocarbamate **36** is also active to a small degree for producing β-selenyl acrylamide **4**. The most likely explanation is that the chalcogenocarbamates can oxidatively re-add to palladium, insert alkyne, and reductively eliminate to give the four-component product. A radical-type mechanism similar to the one encountered in the photoinduced preparation of β-telluryl acrylamides can be envisioned, but is unlikely because only the *Z* isomer of the four-component product is produced.[27]

SCHEME 5

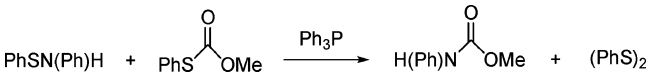
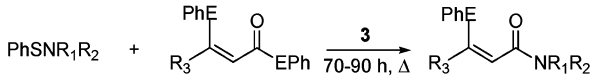


TABLE 5. Reactivity of the Carbonylative Addition Byproducts Toward Acrylamide Formation



PhS-NR$_1$R$_2$	PhE / O / R$_3$ / EPh	% Pd	product	yield, %[a]
PhSNMe$_2$	E = Se R$_3$ = (CH$_2$)$_2$CH$_3$	4	**4**	100
1	**43**			
PhSNEt$_2$	E = Se R$_3$ = (CH$_2$)$_2$CH$_3$	0	**17**	100
5	**43**			
PhSNEt$_2$	E = S R$_3$ = (CH$_2$)$_3$CN	0	**45**	100
5	**44**			

[a] GC yield.

The final class of byproducts, those that arise from the carbonylative addition of the dichalcogenides to the alkyne (eq 4, Scheme 3), do appear to have a potentially significant role in the overall four-component reaction. We suspected that this might be the case based on the previously reported reactivity of sulfenamides with thioesters (Scheme 5).[33]

Selenium carbonylative addition product (**43**) was prepared and reacted with sulfenamides **1** and **5** in the presence and absence of catalyst **3**. In all cases, complete conversion to the β-selenyl acrylamides **4** and **17** was observed. In addition, the reaction of sulfenamide **5** with the cyano-functionalized sulfur carbonylative addition product (**44**) also yielded β-sulfenyl acrylamide (**45**) quantitatively in the absence of catalyst **3** (Table 5). It can be concluded then that the reaction of the carbonylative addition byproducts with sulfenamide is facile and a contributing factor to the production of acrylamide in the reaction.

On the basis of these mechanistic studies, we propose the following revision of the catalytic cycle (Figure 2). We have added steps VII and VIII to acknowledge the fact that significant product formation may arise from this alternative pathway. The key factor, which we have not been able to determine unequivocally, is the relative rates of reductive elimination (VII) of the palladium−acyl intermediate vs the proposed σ-bond metathesis (IV) of sulfenamide with the palladium−acyl intermediate. We have chosen not to include the pathway that involves the initial formation of selenocarbamate (eq 3, Scheme 3) since the low yields obtained under the control conditions (Scheme 4) suggest that this is not a significant pathway in the overall four-component reaction.

(32) Jones, W. D.; Reynolds, K. A.; Sperry, C. K.; Lachicotte, R. J.; Godleski, S. A.; Valente, R. R. *Organometallics* **2000**, *19*, 1661.

(33) Parfenov, E. A.; Fomin, V. A. *Zh. Obshch. Khim.* **1981**, *51*, 1129.

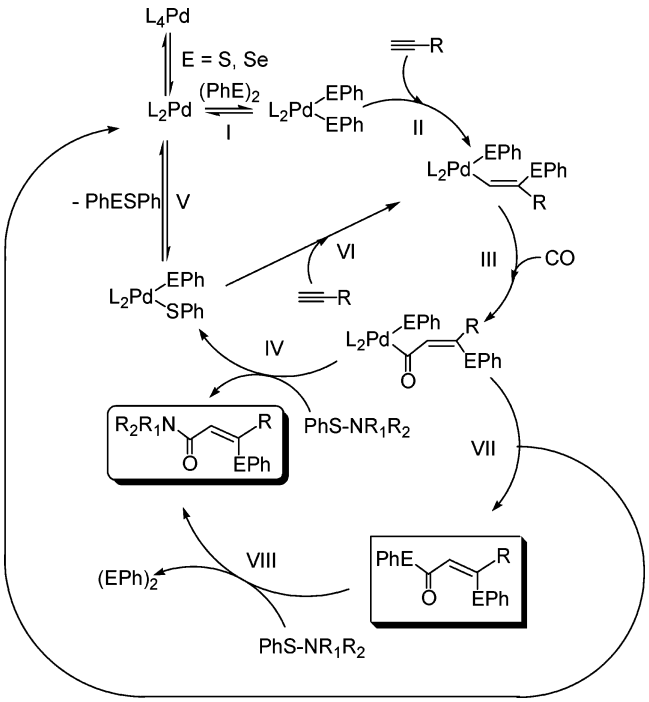


FIGURE 2. Revised catalytic cycle.

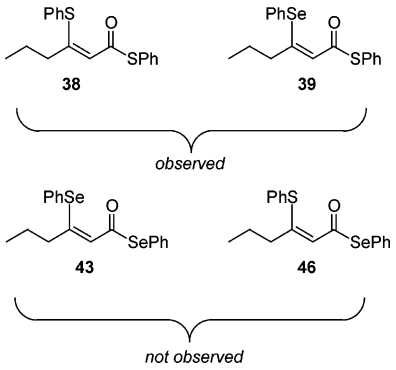


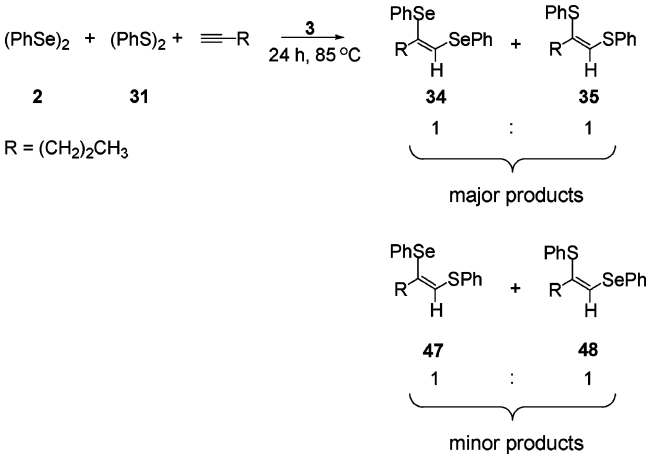
FIGURE 3. Potential carbonylative addition byproducts.

Selectivity. One of the more fascinating aspects of the reaction is the selective formation of β-selenyl acrylamide over β-sulfenyl acrylamide. Analysis of several reaction mixtures arising from the synthesis of β-selenyl acrylamide **4** yielded selectivities ranging from 4:1 to 7:1 selenium to sulfur acrylamide product **33**. Significantly, these observed selectivities were much larger than we expected on the basis of the initial 2:1 ratio of selenium to sulfur in the reaction mixture.

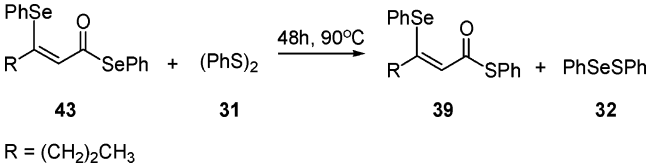
We have determined that the observed selectivity is *not* due to a difference in the insertion rate of alkyne into the Pd−SePh and Pd−SPh bonds. We had initially suspected this possibility as it would be consistent with our observation that, while the reaction mixture contained the mixed chalcogeno-carbonylative addition product **39**, we never observed the reverse-substituted regioisomer (**46**) (Figure 3). Such a distribution of products would be expected if alkyne preferentially inserted into Pd−SePh whenever the catalyst bore both SePh and SPh groups.

To address this question of selective selenopalladation versus thiopalladation of the alkyne, a competition

SCHEME 6



SCHEME 7



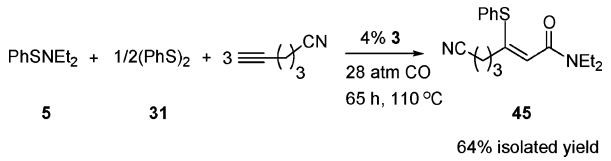
experiment involving the reaction of stoichiometric amounts of 1-pentyne, diphenyl diselenide, and diphenyl disulfide in the presence of catalytic palladium was conducted for 1 day at 85 °C (Scheme 6). GC analysis of the final reaction mixture showed that the all-selenium and -sulfur dichalcogenated products, **34** and **35**, were formed in a 1:1 ratio. Small amounts of the mixed selenium and sulfur addition products, (**47**) and (**48**), were also observed, again in a 1:1 ratio. These results strongly indicate that there is no kinetic preference for alkyne insertion into Pd−SePh over Pd−SPh.

We have identified an alternative explanation for the absence of the mixed carbonylative addition regioisomer **46**. It appears that the selenium carbonylative addition products such as **43** are preferentially converted into their corresponding thioesters in the presence of diphenyl disulfide. For example, the mixed byproduct **39** can be produced in amounts similar to those encountered in the preparation of β-selenyl acrylamide **4** by the simple reaction of diphenyl disulfide with the selenium carbonylative addition product **43** (Scheme 7). This reaction also explains the absence of derivative **43**, which to this point was not satisfactorily accounted for on the basis of our revised mechanistic proposal (Figure 2).

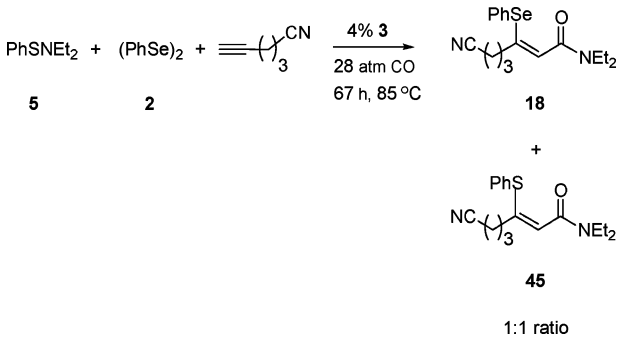
An intriguing result relevant to the discussion of selectivity was obtained when attempts were made to extend the methodology to give the related β-sulfenyl acrylamides. Surprisingly, we found that the acrylamide products could not be produced in significant yield by repeating the reactions with added diphenyl disulfide in place of diphenyl diselenide. Only upon increasing the initial CO pressure from 0.5 to 28 atm and by adding excess alkyne were we able to obtain good yields of β-sulfenyl acrylamide relative to sulfenamide (Scheme 8).

This unexpected difference in reactivity between sulfur and selenium led us to examine the potential effect of

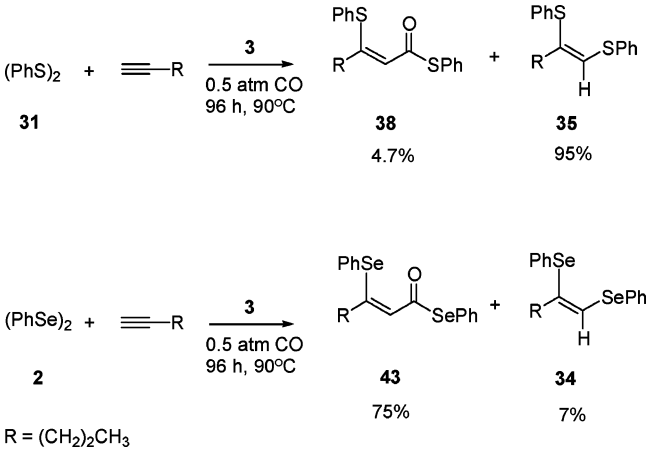
SCHEME 8



SCHEME 9



SCHEME 10

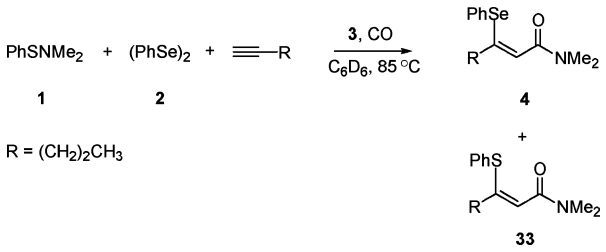


CO pressure on acrylamide reaction selectivity. *Increasing the CO pressure in reactions that previously gave at least 4:1 selectivity for β-selenyl acrylamides to β-sulfenyl acrylamides resulted in a complete loss of selectivity* (Scheme 9). Presumably, at this higher pressure, the CO insertion step ceases to be rate determining, and therefore, any inherent rate differences between the Se and S derivatives become irrelevant to product distribution.

It seemed logical to hypothesize that the variation between the sulfur and selenium acrylamide-forming reactions at low CO pressure could be due to the differential activity of the chalcogens toward carbonylative addition. This idea was tested further by examining the carbonylative addition of diphenyl disulfide and diphenyl diselenide to 1-pentyne under conditions similar to those of the acrylamide-producing reactions (Scheme 10). The carbonylative addition of diphenyl disulfide to 1-pentyne was found to produce a near-quantitative yield of only the simple addition product **35**; only trace amounts of the carbonylative addition product **38** were present. In contrast, the selenium carbonylative addition product **43** was the major product obtained with only small amounts of the addition product **34** present under the same reaction conditions. It thus appears that the carbonylative addition of diphenyl disulfide to the alkyne is less

FIGURE 4. Potential chelation of the vinyl selenoether intermediates.

SCHEME 11



favored than the corresponding carbonylative addition of diphenyl diselenide at low CO pressure.

We believe that the difference in rates likely corresponds to the differences in chelation strengths of the seleno- and sulfidoethers. Selenoethers exhibit much higher binding constants to mid-valent metals than sulfidoethers because of both selenium's lower electronegativity and its larger, more diffuse valence orbitals. Thus, selenium is more likely to bind to palladium to form a four-membered- and/or a five-membered-ring chelate than is sulfur (Figure 4).[34] Chelation may facilitate the rate of formation of carbonylated product either by creating a crowded coordination sphere or by inhibiting the deinsertion of CO. In any case, the seleno-favoring effect must be significant, given that the vinyl sulfidoether would ordinarily be expected to be faster at migratory insertion on the basis of simple nucleophilicity arguments. Negative hyperconjugation with selenium would be expected to more effectively delocalize the negative charge on the anionic vinyl ligand, disfavoring migration to CO relative to the sulfur analogue.[35]

Finally, in addition to the effect of CO pressure on determining reaction selectivity, the concentrations of both diphenyl disulfide and diphenyl diselenide in the reaction mixture should also play an important role as the concentration of diphenyl disulfide is expected to increase and the concentration of diphenyl diselenide is expected to decrease with reaction time. To address this effect of chalcogen concentration, a detailed ^{1}H NMR experiment in which the concentrations of both selenium- and sulfur-containing acrylamides **4** and **33** were measured as a function of time (Scheme 11). As expected, the best selectivity for the formation of **4** over **33** was observed early in the reaction, but this selectivity was observed to decrease slowly over time as the reaction progressed to consume sulfenamide **1** and, consequently, produce diphenyl disulfide and acrylamide **33**.

On the basis of our findings, we believe that two major factors contribute to the observed selective formation of β-selenyl acrylamides over β-sulfenyl acrylamides are (1)

(34) Levason, W.; Orchard, S. D.; Reid, G. *Coord. Chem. Rev.* **2002**, *225*, 159.
(35) Mo, Y.; Schleyer, P. v. R.; Wu, W.; Lin, M.; Zhang, Q.; Gao, J. *J. Phys. Chem. A* **2003**, *107*, 10011.

an initially small concentration of diphenyl disulfide (or PhS−SePh) and (2) the favorable insertion of CO into vinyl β-selenoethers relative to vinyl β-sulfidoethers at low CO pressure.

Conclusions

In conclusion, we have developed a high-yielding method for the formation of regio- and stereodefined β-selenyl and β-sulfenyl acrylamides via a palladium-catalyzed four-component coupling reaction in which one C−C bond and two carbon−heteroatom bonds are formed. From a synthetic standpoint, the reaction exhibits excellent tolerance for a wide variety of substituents on both the nitrogen of the sulfenamide and alkyne. In addition, the versatility of the chalcogens as pseudo-halides coupled with the presence of the α,β-unsaturated amide functionality makes the β-chalcogenyl acrylamides synthetically attractive targets.[14]

Experimental Section

***S*-Phenyl-*N*-dimethyl-sulfenamide (1):** ^{1}H NMR (300 MHz, C_6D_6) δ 2.53 (s, 6 H), 6.93−7.37 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 48.3, 127.1, 128.8, 129.9, 137.2; MS (EI) *m/z* 153 (M^+), 138, 109, 77, 65.

***S*-Phenyl-*N*-diethyl-sulfenamide (5):** ^{1}H NMR (300 MHz, C_6D_6) δ 1.08 (t, J = 7.0 *Hz*, 6 H), 2.79 (q, J = 7.0 Hz, 4 H), 6.92−7.35 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.8, 53.4, 125.0, 125.5, 128.8, 142.1; MS (EI) *m/z* 181 (M^+), 166, 109, 77, 65.

***S*-Phenyl-*N*-allyl-*N*-methyl-sulfenamide (6):** ^{1}H NMR (300 MHz, C_6D_6) δ 2.59 (s, 3), 3.34 (d, J = 6.4 Hz, 2 H), 4.98 (m, 2 H), 5.79 (dtd, J = 10.0, 7.0, 2.4 Hz, 1 H), 6.93−7.36 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 45.2, 63.3, 117.1, 126.4, 127.6, 128.7, 135.4; MS (EI) *m/z* 179 (M^+), 138, 109, 77, 65.

***S*-Phenyl-*N*-benzyl-*N*-methyl-sulfenamide (7):** ^{1}H NMR (300 MHz, C_6D_6) δ 2.51 (s, 3 H), 3.87 (s, 2 H), 6.95−7.35 (m, 10 H); ^{13}C NMR (75 MHz, C_6D_6) δ 45.2, 65.1, 127.0, 128.6, 128.7, 128.9, 138.2, 138.8; MS (EI) *m/z* 229 (M^+), 138, 109, 91, 77, 65.

***S*-Phenyl-*N*-diallyl-sulfenamide (8):** ^{1}H NMR (300 MHz, C_6D_6) δ 3.44 (d, J = 6.4 Hz, 4 H), 5.04 (m, 4 H), 5.83 (dtd, J = 10.5, 6.4, 2.6 Hz, 2 H), 6.92−7.35 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 60.9, 117.5, 126.1, 128.9, 135.6, 140.6; MS (EI) *m/z* 205 (M^+), 164, 109, 77, 65, 41.

***S*-Phenyl-*N*-methyl-sulfenamide (9):** ^{1}H NMR (300 MHz, C_6D_6) δ 2.24 (br s, 1 H), 2.42 (d, J = 17.4 Hz, 3 H), 6.93−7.35 (m, 5); ^{13}C NMR (75 MHz, C_6D_6) δ 38.4, 123.8, 125.2, 128.8, 129.1, 141.7; MS (EI) *m/z* 139 (M^+), 124, 109, 97, 65.

***S*-Phenyl-*N*-diisopropyl-sulfenamide (10):** ^{1}H NMR (300 MHz, C_6D_6) δ 1.07 (d, J = 6.4 Hz, 12 H), 3.12 (hpt, J = 6.5 Hz, 2 H), 6.89−7.36 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 21.9, 55.8, 122.1, 124.4, 128.6, 146.4; MS (EI) *m/z* 209 (M^+), 194, 152, 109, 77, 65.

***S*-Phenyl-*N*-trimethylsilyl-*N*-benzyl-sulfenamide (11):** ^{1}H NMR (300 MHz, C_6D_6) δ 0.80 (s, 9 H), 3.55 (s, 2 H), 7.07−7.19 (m, 10 H); MS (EI) *m/z* 215 (M^+ − TMS), 109, 91 (base), 77, 65, 51.

***(Z)*-1,2-Bis(phenylseleno)-1-pentene (34):** ^{1}H NMR (300 MHz, C_6D_6) δ 0.69 (t, J = 7.3 Hz, 3 H), 1.41 (m, $J_1 = J_2$ = *7.4 Hz*, 2 H), 2.14 (t, J = 7.2 Hz, 2 H), 6.86−7.75 (m, 11 H); MS (EI) *m/z* 382 (M^+), 314, 183, 157, 143, 129, 115, 91, 77 (base), 65.

***(Z)*-1,2-Bis(phenylthio)-1-pentene (35):** ^{1}H NMR (300 MHz, C_6D_6) δ 0.70 (t, J = 7.3 Hz, 3 H), 1.43 (m, $J_1 = J_2$ = *7.4 Hz*, 2 H), 2.10 (t, J = 7.5 Hz, 2 H), 6.49 (s, 1 H), 6.85−7.73 (m, 10 H); MS (EI) *m/z* 286 (M^+) (base), 177, 167, 147, 135, 109, 91, 77, 65.

6-Cyano-(*Z*)-1,2-bis(phenylseleno)-1-pentene (42): ^{1}H NMR (300 MHz, C_6D_6) δ 0.97 (m, $J_1 = J_2$ = *7.0 Hz*, 2 H), 1.51 (t, J = 7.0 Hz, 2 H), 1.98 (t, J = 7.0 Hz, 2 H), 6.88−7.88 (m, 11 H); MS (EI) *m/z* 407 (M^+), 314, 250, 233, 157, 129, 115, 77 (base).

***(Z)*-1,3-Bis(phenylthio)-2-hexen-1-one (38):** ^{1}H NMR (300 MHz, C_6D_6) δ 0.46 (t, J = *7.3 Hz*, 3 H), 1.09 (m, $J_1 = J_2$ = *7.6 Hz*, 2 H), 1.81 (t, J = 7.4 Hz, 2 H), 6.22 (s, 1 H), 6.83−7.73 (m, 10 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.3, 22.8, 38.4, 117.9, 127.2, 128.7, 129.1, 129.2, 129.3, 135.1, 135.9, 137.4, 160.9, 183.5; MS (EI) *m/z* 314 (M^+), 205 (base), 176, 109, 91, 77, 65.

***(Z)*-1,3-Bis(phenylseleno)-2-hexen-1-one (43):** ^{1}H NMR (300 MHz, C_6D_6) δ 0.43 (t, J = 7.3 Hz, 3 H), 1.06 (m, $J_1 = J_2$ = *7.6 Hz*, 2 H), 1.84 (t, J = 7.5 Hz, 2 H), 6.53 (s, 1 H), 6.86−7.76 (m, 10 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.3, 23.2, 39.6, 122.6, 129.6, 131.3, 132.5, 133.1, 133.3, 133.5, 136.2, 137.5, 162.2, 186.3; MS (EI) *m/z* 253 (M^+ − SePh) (base), 157, 91, 77, 65.

6-Cyano-(*Z*)-1,3-bis(phenylthio)-2-hexen-1-one (44): ^{1}H NMR (300 MHz, C_6D_6) δ 0.95 (m, $J_1 = J_2$ = *6.9 Hz*, 2 H), 1.20 (t, J = 6.9 Hz, 2 H), 1.76 (t, J = 6.8 Hz, 2 H), 6.07 (s, 1 H), 6.90−7.73 (m, 10 H); MS (EI) *m/z* 230 (M^+ − SPh)(base), 189, 109, 77, 65, 51.

***N*-Dimethyl Phenyl Selenocarbamate (36).** To a glass bomb in a nitrogen-filled glovebox were added sulfenamide **1** (43.0 mg, 0.28 mmol), $(PhSe)_2$ **2** (64.0 mg, 0.20 mmol), 5.5% chlorocarbonylbis(triphenylphosphine) rhodium (8.0 mg, 11.0 μmol), and benzene (4.0 mL). The reaction was charged with 0.5 atm of CO gas and heated for 64 h at 85 °C with stirring. The resultant solution was degassed, filtered through Celite, and reduced in vacuo. The crude reaction mixture was partially purified via column chromatography using 5% ethyl acetate/hexanes and methanol to yield *N*-dimethyl phenyl selenocarbamate (**36**). ^{1}H NMR (300 MHz, C_6D_6) δ 2.44 (br s, 6 H), 6.83−7.75 (m, 5 H); MS (EI) *m/z* (M^+), 229, 157, 77, 72 (base), 65.

***N*-Dimethyl Phenyl Thiocarbamate (37).** According to the method of Kuniyasu et al.,[18] to a stainless steel reaction vessel with glass insert in a nitrogen-filled glovebox were added sulfenamide **1** (40.0 mg, 0.26 mmol), 5.6% catalyst **3** (13.0 mg, 11.2 μmol), and pyridine (2 mL). The reaction was charged with 28 atm of CO gas and heated for 24 h at 90 °C with stirring. The resultant solution was degassed, filtered through Celite, and reduced in vacuo. The crude reaction mixture was purified by column chromatography using hexanes and methanol to yield the red oil (**37**) (38.0 mg, 0.21 mmol) in 80% yield: ^{1}H NMR (300 MHz, C_6D_6) δ 2.27 (br s, 6 H), 6.83−7.75 (m, 5 H); MS (EI) *m/z* 181 (M^+), 109, 77, 72 (base), 65.

***(Z)*-3-Phenylselenyl-hex-2-enoic Acid Dimethylamide (4).** To a glass bomb in a nitrogen-filled glovebox were added $(PhSe)_2$ **2** (63.0 mg, 0.20 mmol), sulfenamide **1** (29.0 mg, 0.19 mmol), 1-pentyne (30.0 μL, 0.30 mmol), 4.5% catalyst **3** (10.0 mg, 8.6 μmol), and benzene (1.5 mL). The reaction was charged with 0.5 atm of CO gas and heated for 168 h at 85 °C with stirring. The resultant orange solution was degassed, filtered through Celite, and reduced in vacuo to yield a red, viscous oil. The crude reaction mixture was purified via column chromatography using 5% ethyl acetate/hexanes, 20% ethyl acetate/hexanes, ethyl acetate to yield the orange oil (*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide (**4**) (47.5 mg, 0.16 mmol) in 84% yield. The following percentages of byproducts in the final reaction mixture were determined by GC using the internal standards method (hexamethylbenzene) and were identified either by comparison to independently prepared standards or by isolation from column chromatography: $(PhSe)_2$ **2**, 17.0%; (*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide **4**, 47.5%; $(PhS)_2$ **31**, 0.3%; PhS−SePh **32**, trace; (*Z*)-3-phenylsulfenyl-hex-2-enoic acid dimethylamide **33**, 6.8%; (*Z*)-1,2-bis-(phenylseleno)-1-pentene **34**, 2.7%; (*Z*)-1,2-bis(phenylthio)-1-pentene **35**, trace; *N*-dimethyl phenyl selenocarbamate **36**, 3.4%; *N*-dimethyl phenyl thiocarbamate **37**, 0.1%; (*Z*)-1,3-bis-

(phenylthio)-2-hexen-1-one **38**, 10.3%; 3-phenylselenyl-hex-2-enoic acid *S*-phenyl ester **39**, 11.1%; $SePPh_3$ **40**, trace; PhSePh **41**, trace. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). **4:** ^{1}H NMR (300 MHz, C_6D_6) δ 0.61 (t, J = 7.3 Hz, 3 H), 1.34 (m, $J_1 = J_2 = 7.5$ *Hz*, 2 H), 2.16 (t, J = 7.4 Hz, 2 H), 2.31 (s, 3 H), 2.69 (s, 3 H), 6.29 (s, 1 H), 6.92−7.62 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.4, 23.5, 34.9, 36.5, 40.1, 114.3, 128.5, 128.9, 130.6, 137.7, 157.5, 166.6; IR (NaCl) 3070, 2887, 2325, 1960, 1815, 1633 (C=O), 1438, 1034, 674 cm^{-1}; MS (EI) *m*/*z* 297 (M^+), 253, 157, 140 (base), 72. HRMS calcd for $C_{14}H_{19}NOSe$ 297.063927, found 297.063185. Anal. calcd for $C_{14}H_{19}NOSe$: C, 56.55; H, 6.39; N, 4.71. Found: C, 56.90; H, 6.44; N, 4.67. **33:** ^{1}H NMR (300 MHz, C_6D_6) δ 0.65 (t, J = 7.4 Hz, 3 H), 1.36 (m, $J_1 = J_2 = 7.4$ *Hz*, 2 H), 2.03 (t, J = 7.3 Hz, 2 H), 2.44 (s, 3 H), 2.71 (s, 3 H), 5.98 (s, 1 H), 6.90−7.42 (m, 5 H); MS (EI) *m*/*z* 249 (M^+), 205, 176, 140 (base), 109, 72. **39**: ^{1}H NMR (300 MHz, C_6D_6) δ 0.45 (t, J = 7.3 Hz, 2 H), 1.10 (m, $J_1 = J_2 = 7.5$ *Hz*, 2 H), 1.92 (t, J = 7.4 Hz, 2 H), 6.55 (s, 1 H), 6.89−7.56 (m, 10 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.3, 23.5, 39.7, 120.1, 127.4, 128.8, 129.1, 129.4, 131.2, 133.3, 135.9, 137.1, 163.0, 184.7; MS (EI) *m*/*z* 362 (M^+), 253 (base), 157, 109, 91, 77, 65.

6-Cyano-(*Z*)-3-phenylselenyl-hex-2-enoic Acid Dimethylamide (12). Following the general procedure, with the exception of heating for only 115 h, 6-cyano-(*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide (**12**) (45.0 mg, 0.14 mmol) was prepared in 70% yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 1.15 (m, $J_1 = J_2 = 7.2$ *Hz*, 2 H), 1.34 (t, J = 7.0 Hz, 2 H), 2.15 (t, J = 7.2 Hz, 2 H), 2.36 (s, 3 H), 2.68 (s, 3 H), 6.34 (s, 1 H), 6.93−7.07 (m, 3 H), 7.46−7.48 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 15.3, 25.0, 34.9, 36.3, 36.6, 116.0, 119.0, 129.2, 130.0, 137.3, 154.3, 166.3; MS (EI) *m*/*z* 322 (M^+), 278, 165 (base), 157, 77, 72. HRMS calcd for $C_{15}H_{18}N_2OSe$ 322.058553, found 322.058434.

Acetic Acid 5-Dimethylcarbamoyl-(*Z*)-4-phenylselenyl-pent-4-enyl Ester (13). Following the general procedure, with the exception of heating for only 115 h, acetic acid 5-dimethylcarbamoyl-(*Z*)-4-phenylselenyl-pent-4-enyl ester (**13**) (53.3 mg, 0.15 mmol) was prepared in 72% yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 1.54 (m, $J_1 = J_2 = 7.1$ *Hz*, 2 H), 1.58 (s, 3 H), 2.21 (t, J = 7.3 Hz, 2 H), 2.35 (s, 3 H), 2.68 (s, 3 H), 3.73 (t, J = 6.4 Hz, 2 H), 6.33 (s, 1 H), 6.93−6.99 (m, 3 H), 7.55−7.57 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.5, 29.3, 34.6, 35.0, 36.5, 63.1, 114.8, 129.0, 130.3, 137.7, 156.3, 166.6, 170.0; MS (EI) *m*/*z* 355 (M^+), 269, 198 (base), 157, 138, 111, 72, 43. HRMS calcd for $C_{16}H_{21}NO_3Se$ 355.069892, found 355.068664.

6-Hydroxy-(*Z*)-3-phenylselenyl-hex-2-enoic Acid Dimethylamide (14). Following the general procedure, with the exception of heating for only 50 h, the formation of 6-hydroxy-(*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide (**14**) was not detected by GC−MS.

***N,N*-Dimethyl-3-phenyl-3-phenylselenyl Acrylamide (15).** Following the general procedure, with the exception of using 6.0% $(PPh_3)_2PdCl_2$, *N,N*-dimethyl-3-phenyl-3-phenylselenyl-acrylamide (**15**) (12.0 mg, 0.04 mmol) was prepared in 30% yield. The *E*/*Z* ratio was determined by ^{1}H NMR spectroscopy (*E*/*Z* = 100). ^{1}H NMR (300 MHz, C_6D_6) δ 2.34 (s, 3 H), 2.70 (s, 3 H), 6.48 (s, 1 H), 6.74−7.27 (m, 10 H); MS (EI) *m*/*z* 331 (M^+), 287, 254, 157, 72 (base).

(*Z*)-2-Methyl-3-phenylselenyl-but-2-enoic Acid Dimethylamide (16). Following the general procedure, with the exception of heating for only 50 h, the formation of (*Z*)-2-methyl-3-phenylselenyl-but-2-enoic acid dimethylamide (**16**) was not detected by GC−MS.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Diethylamide (17). Following the general procedure, with the exception of heating for 140 h, (*Z*)-3-phenylselenyl-hex-2-enoic acid diethylamide (**17**) (46.0 mg, 0.14 mmol) was prepared in 70% yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 0.59 (t, J = 7.3 Hz, 3 H), 0.77 (br s, 3 H), 0.99 (br s, 3 H), 1.33 (m, $J_1 = J_2 = 7.3$ *Hz*, 2 H), 2.18 (t, J = 7.0 Hz, 2 H), 2.84 (br s, 2 H), 3.26 (br s, 2 H), 6.37 (s, 1 H), 6.94−7.00 (m, 3 H), 7.61−7.63 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.4, 13.6, 14.8, 23.6, 40.1, 40.7, 42.1, 114.0, 128.5, 128.9, 130.8, 137.8, 157.8, 166.0; MS (EI) *m*/*z* 325 (M^+), 253, 168 (base), 157, 100. HRMS calcd for $C_{16}H_{23}NOSe$ 325.094576, found 325.094485.

6-Cyano-(*Z*)-3-phenylselenyl-hex-2-enoic Acid Diethylamide (18). Following the general procedure, 6-cyano-(*Z*)-3-phenylselenyl-hex-2-enoic acid diethylamide (**18**) (55.0 mg, 0.16 mmol) was prepared in 80% yield. The *E*/*Z* ratio was determined by ^{1}H NMR and NOE difference spectroscopy (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 0.83 (t, J = 6.9 Hz, 3 H), 0.98 (t, J = 6.9 Hz, 3 H), 1.09 (m, $J_1 = J_2 = 7.0$ *Hz*, 2 H), 1.30 (t, J = 7.0 Hz, 2 H), 2.17 (t, J = 7.1 Hz, 2 H), 2.85 (q, J = 6.9 Hz, 2 H), 3.24 (q, J = 6.9 Hz, 2 H), 6.41 (s, 1 H), 6.90−7.03 (m, 3 H), 7.45−7.47 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.5, 14.8, 15.2, 24.8, 36.2, 40.7, 42.1, 115.9, 118.9, 129.1, 130.2, 137.4, 154.5, 165.5; MS (EI) *m*/*z* 350 (M^+), 278, 193 (base), 157, 77, 72. HRMS calcd for $C_{17}H_{22}N_2OSe$ 350.089092, found 350.089734.

4-Dimethylamino-(*Z*)-3-phenylselenyl-hex-2-enoic Acid Diethylamide (19). Following the general procedure, 4-(dimethylamino)-(*Z*)-3-phenylselenyl-hex-2-enoic acid diethylamide (**19**) was prepared in 85% GC yield. The *E*/*Z* ratio was determined by ^{1}H NMR (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 0.79 (t, J = 6.7 Hz, 3 H), 0.99 (t, J = 6.7 Hz, 3 H), 1.87 (s, 6 H), 2.35 (s, 1 H), 2.68 (s, 1 H), 2.90 (q, 2 H), 3.27 (q, 2 H), 6.87 (s, 1 H) 6.90−7.08 (m, 3 H), 7.68−7.77 (m, 2 H); MS (EI) *m*/*z* 340 (M^+), 219, 183, 157, 82, 72, 58 (base).

(*Z*)-4-Methyl-3-phenylselenyl-penta-2,4-dienoic Acid Diethylamide (20). Following the general procedure, with the exception of using 6.0% $(PPh_3)_2PdCl_2$, (*Z*)-4-methyl-3-phenylselenyl-penta-2,4-dienoic acid diethylamide (**20**) was detected in trace amounts by GC and GC−MS.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Methylbenzylamide (21). Following the general procedure, with the exception of running in the presence of 8% catalyst **3**, (*Z*)-3-phenylselenyl-hex-2-enoic acid methylbenzylamide (**21**) was prepared in 95% GC yield. The *E*/*Z* ratio was determined by ^{1}H NMR (*E*/*Z* = 0/100). Two distinct rotamers were observed by ^{1}H and ^{13}C NMR at room temperature. ^{1}H NMR (300 MHz, C_6D_6) δ 0.49 (t, J = 7.1 Hz, 3 H), 0.60 (t, J = 7.0 Hz, 3 H), 1.34 (m, 4 H), 2.07 (t, J = 7.1 Hz, 2 H), 2.19 (t, J = 7.2 Hz, 2 H), 2.39 (s, 3 H), 2.81 (s, 3 H), 4.06 (s, 2 H), 4.51 (s, 2 H), 6.35 (s, 1 H), 6.42 (s, 1 H), 6.95−7.69 (m, 20 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.3, 13.4, 23.5, 23.6, 33.6, 34.2, 39.9, 40.2, 50.8, 53.2, 113.9, 130.5, 132.3, 132.4, 134.5, 137.7, 138.4, 158.9, 159.1, 166.8, 167.2; MS (EI) *m*/*z* 373 (M^+), 296, 253, 216 (base), 157, 120, 91, 77, 65.

6-Chloro-(*Z*)-3-phenylselenyl-hex-2-enoic Acid Benzylmethylamide (22). Following the general procedure,[13] with the exception of heating for 64 h at 78 °C, 6-chloro-(*Z*)-3-phenylselanyl-hex-2-enoic acid benzylmethylamide (**22**) (50.0 mg, 0.12 mmol) was prepared in 60% yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). Two distinct rotamers were observed by ^{1}H and ^{13}C NMR at room temperature. ^{1}H NMR (300 MHz, C_6D_6) δ 1.44 (m, $J_1 = J_2 = 7.5$ *Hz*, 2 H), 1.54 (m, $J_1 = J_2 = 7.1$ *Hz*, 2 H), 2.19 (t, J = 7.0 Hz, 2 H), 2.30 (t, J = 7.3 Hz, 2 H), 2.38 (s, 3 H), 2.80 (m, 5 H), 2.91 (t, J = 7.0 Hz, 2 H), 4.05 (s, 2 H), 4.50 (s, 2 H), 6.38 (s, 1 H), 6.46 (s, 1 H), 6.94−7.55 (m, 20 H); ^{13}C NMR (75 MHz, C_6D_6) δ 32.2, 32.4, 33.7, 34.2, 34.9, 35.1, 43.4, 43.7, 50.8, 53.3, 115.1, 115.2, 126.6, 130.1, 137.5, 138.2, 156.5, 156.8, 166.5, 167.1; MS (EI) *m*/*z* 407 (M^+), 287, 250 (base), 157, 91, 77, 65. HRMS calcd for $C_{20}H_{22}NOClSe$ 407.057262, found 407.055513.

(*Z*)-3-Phenylselenyl-undec-2-enoic Acid Benzylmethylamide (23). Following the general procedure,[13] with the exception of heating for 64 h at 78 °C, (*Z*)-3-phenylselenyl-undec-2-enoic acid benzylmethylamide (**23**) (50.5 mg, 0.11

mmol) was prepared in 60% yield. The *E*/*Z* ratio was determined by ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). Two distinct rotamers were observed by ^{1}H and ^{13}C NMR at room temperature. The rotamers were resolved into one species at 350 K. ^{1}H NMR (300 MHz, C_6D_6) δ 0.87 (t, J = 6.9 Hz, 6 H), 1.03−1.40 (m, 24 H), 2.19 (t, J = 7.1 Hz, 2 H), 2.28 (t, J = 7.3 Hz, 2 H), 2.41 (s, 3 H), 2.81 (s, 3 H), 4.09 (s, 2 H), 4.52 (s, 2 H), 6.42 (s, 1 H), 6.48 (s, 1 H), 6.94−7.73 (m, 20 H); ^{13}C NMR (75 MHz, d_8-tol) δ 14.4, 23.1, 29.6, 30.5, 30.7, 32.3, 33.6, 34.2, 38.3, 38.5, 50.8, 53.4, 113.6, 113.7, 130.7, 131.6, 132.3, 132.5, 133.6, 133.9, 134.6, 135.0, 138.5, 159.2, 159.6, 167.1, 167.7; MS (EI) *m*/*z* 443 (M^+), 323, 286 (base), 157, 120, 91, 77, 65.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Allylmethylamide (24). Following the general procedure, with the exception of heating for 126 h, (*Z*)-3-phenylselenyl-hex-2-enoic acid allylmethylamide (**24**) (57.0 mg, 0.18 mmol) was prepared in 82% yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). Two distinct rotamers were observed by ^{1}H and ^{13}C NMR at room temperature. ^{1}H NMR (300 MHz, C_6D_6) δ 0.59 (m, 6 H), 1.22 (br s, 4 H), 2.16 (m, 4 H), 2.45 (s, 3 H), 2.78 (s, 3 H), 3.40 (m, 2 H), 3.92 (m, 2 H), 4.91 (m, 4 H), 5.40 (m, 1 H), 5.60 (m, 1 H), 6.35 (s, 2 H), 6.88−6.99 (m, 6 H), 7.58−7.62 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6) 13.4, 23.6, 33.5, 34.2, 40.1, 50.0, 52.0, 114.0, 116.0, 116.9, 130.5, 133.5, 134.1, 137.8, 158.0, 158.6, 166.4, 166.9; MS (EI) *m*/*z* 323 (M^+), 253, 166 (base), 157, 77, 41. HRMS calcd for $C_{16}H_{21}NOSe$ 323.079852, found 323.078835.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Diallylamide (25). Following the general procedure, with the exception of running in the presence of 10% catalyst **3**, (*Z*)-3-phenylselenyl-hex-2-enoic acid diallylamide (**25**) was prepared in 85% GC yield. The *E*/*Z* ratio was determined by NOE difference and ^{1}H NMR spectroscopy (*E*/*Z* = 0/100). ^{1}H NMR (300 MHz, C_6D_6) δ 0.57 (t, J = 7.3 Hz, 3 H), 1.31 (m, $J_1 = J_2 = 7.4$ *Hz*, 2 H), 2.15 (t, J = 7.4 Hz, 2 H), 3.55 (s, 2 H), 4.00 (d, J = 5.3 Hz, 2 H), 4.94 (m, 4 H), 5.44 (m, 1 H), 5.73 (m, 1 H), 6.38 (s, 1 H), 6.95−7.81 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.4, 21.4, 23.5, 40.1, 48.4, 49.1, 113.8, 116.1, 117.1, 130.5, 131.7, 132.3, 133.5, 133.9, 137.8, 159.2, 166.7; MS (EI) *m*/*z* 349 (M^+), 272, 253, 192 (base), 157, 77, 41. HRMS calcd for $C_{18}H_{23}NOSe$ 349.093142, found 349.094485.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Methylamide (26). Following the general procedure, with the exception of heating for only 70 h, the formation of (*Z*)-3-phenylselenyl-hex-2-enoic acid methylamide (**26**) was not detected by GC−MS.

(*Z*)-3-Phenylselenyl-hex-2-enoic Acid Diisopropylamide (27). Following the general procedure, with the exception of heating for only 50 h, the formation of (*Z*)-3-phenylselenyl-hex-2-enoic acid diisopropylamide (**27**) was not detected by GC−MS.

6-Cyano-3-phenylselenyl-hex-2-enoic Acid Phenylsulfanylethylamide (28a) and 6-Cyano-3-phenylselenyl-hex-2-enoic Acid Trimethylsilylamineethylamide (28b). Following the general procedure, the formation of 6-cyano-3-phenylselenyl-hex-2-enoic acid phenylsulfanylethylamide (**28a**) and 6-cyano-3-phenylselenyl-hex-2-enoic acid trimethylsilylamineethylamide (**28b**) was observed by GC−MS. **28a:** MS (EI) *m*/*z* 384 (M^+ − SPh), 278, 227, 157, 91, 77, 65, 51. **28b:** MS (EI) *m*/*z* 384 (M^+ − TMS), 342, 278, 227, 157, 91, 77, 65, 51.

The Preparation of Acrylamide 18 from Amine 29. To a glass bomb in a nitrogen-filled glovebox were added $(PhSe)_2$ **2** (65.0 mg, 0.21 mmol), 5-cyano-1-pentyne (32.0 μL, 0.30 mmol), 4.7% of catalyst **3** (11.5 mg, 9.9 μmol), and benzene (2.5 mL). The glass bomb was sealed, transferred to a vacuum line, and placed under nitrogen where amine **29** (21 μL, 0.2 mmol) was added. The reaction was charged with 0.5 atm of CO gas and heated for 138 h at 90 °C with stirring. The resultant solution was degassed, filtered through Celite, and analyzed by GC and GC−MS. The GC yield of 6-cyano-(*Z*)-3-phenylselenyl-hex-2-enoic acid diethylamide **18** was determined to be 40%.

The Preparation of Acrylamide 12 from Amine 30. Following the procedure stated above, 6-cyano-(*Z*)-3-phenylselenyl-hex-2-enoic acid dimethylamide **12** was prepared in 40% GC yield.

The Attempted Preparation of Acrylamide 4 from Bis-(arylseleno)-1-alkene 34 and Sulfenamide 1. To a glass bomb in a nitrogen-filled glovebox were added bis(phenylseleno)-1-alkene **34** (45.8 mg, 0.12 mmol), sulfenamide **1** (19.1 mg, 0.12 mmol), 9.0% of catalyst **3** (12.5 mg, 10.8 μmol), and benzene (2.5 mL). The reaction was charged with 0.5 atm of CO gas and heated for 72 h at 90 °C with stirring. The resultant solution was degassed, filtered through Celite, and analyzed by GC and GC−MS. Acrylamide **4** was not detected.

The Attempted Preparation of Acrylamide 33 from Bis(phenylthio)-1-alkene 35 and Sulfenamide 1. Following the general procedure stated above, the formation of acrylamide **33** was not detected.

The Attempted Preparation of Acrylamide 18 from Bis(phenylseleno)-1-alkene 42 and Sulfenamide 5 in the Presence of Substoichiometric Pd. Following the general procedure, with the exception of heating for 144 h in the presence of 50% catalyst **3**, the formation of acrylamide **18** was not detected.

The Preparation of Acrylamide 33 from Thiocarbamate 37 and 1-Pentyne. To a glass bomb in a nitrogen-filled glovebox were added thiocarbamate **37** (38.0 mg, 0.21 mmol), 1-pentyne (20 μL, 0.20 mmol), 5% of catalyst **3**, and benzene (2.0 mL). The reaction was heated for 96 h at 85 °C with stirring. The resultant solution was filtered through Celite and analyzed by GC−MS and GC. A 4.5% GC yield of acrylamide **33** was observed.

The Preparation of Acrylamide 4 from Phenylseleno-2-alken-1-one 43 and Sulfenamide 1 in the Presence of Catalytic Pd. To a glass bomb in a nitrogen-filled glovebox were added phenylseleno-2-alkenone **43** (73.8 mg, 0.18 mmol), sulfenamide **1** (28.0 mg, 0.18 mmol), 4.0% of catalyst **3** (8.3 mg, 7.2 μmol), and benzene (2.5 mL). The reaction was heated for 96 h at 75 °C with stirring. The reaction was filtered through Celite and analyzed by GC−MS and GC. A 100% GC yield of acrylamide **4** was observed.

The Preparation of Acrylamide 17 from Phenylseleno-2-alken-1-one 43 and Sulfenamide 5 in the Absence of Catalyst. To a glass bomb in a nitrogen-filled glovebox were added phenylseleno-2-alkenone **43** (74.0 mg, 0.18 mmol), sulfenamide **5** (33.0 mg, 0.18 mmol), and benzene (2.5 mL). The reaction was heated for 96 h at 75 °C with stirring. The reaction was filtered through Celite and analyzed by GC−MS and GC. A 100% GC yield of acrylamide **17** was observed.

The Preparation of Acrylamide 45 from Phenylthio-2-alken-1-one 44 and Sulfenamide 5 in the Absence of Catalyst. To a glass bomb in a nitrogen-filled glovebox were added phenylthio-2-alken-1-one **44** (27.6 mg, 0.12 mmol), sulfenamide **5** (23.0 mg, 0.12 mmol), and benzene (2.5 mL). The reaction was heated for 70 h at 90 °C with stirring. The resultant orange solution was filtered through Celite and reduced in vacuo to yield a viscous oil. GC analysis showed the yield of acrylamide (**45**) to be 100%. The crude reaction mixture was purified via column chromatography using 5% ethyl acetate/hexanes, 20% ethyl acetate/hexanes, and ethyl acetate to yield the orange oil 6-cyano-(*Z*)-3-phenylsulfenyl-hex-2-enoic acid diethylamide **45** (37.0 mg, 0.11 mmol) in 92% yield. ^{1}H NMR (300 MHz, C_6D_6) δ 0.82 (t, J = 6.7 Hz, 3 H), 1.01 (t, J = 6.7 Hz, 3 H), 1.12 (m, $J_1 = J_2 = 7.0$ *Hz*, 2 H), 1.33 (t, J = 7.0 Hz, 2 H), 2.00 (t, J = 7.0 Hz, 2 H), 2.91 (q, J = 6.9 Hz, 2 H), 3.27 (q, J = 6.8 Hz, 2 H), 6.07 (s, 1 H), 6.90−6.93 (m, 3 H), 7.28−7.30 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 13.4, 14.7, 15.2, 24.0, 34.9, 39.9, 42.3, 118.9, 121.3, 129.2, 133.4, 134.1, 146.2, 165.0; MS (EI) *m*/*z* 302 (M^+), 230, 193 (base), 109, 100, 77, 65, 51.

The Palladium-Catalyzed Reaction of 1-Pentyne with $(PhS)_2$ and $(PhSe)_2$. To a glass bomb in a nitrogen-filled glovebox were added $(PhS)_2$ **31** (65.4 mg, 0.30 mmol), $(PhSe)_2$

2 (94.2 mg, 0.30 mmol), 1-pentyne (30.0 μL, 0.30 mmol), 4.5% of catalyst **3** (17.0 mg, 14.7 μmol), and benzene (3 mL). The reaction was heated for 24 h at 90 °C with stirring. The resultant solution was filtered through Celite and analyzed by GC−MS and GC. (*Z*)-1,2-Bis(phenylseleno)-1-pentene **34** and (*Z*)-1,2-bis(phenylthio)-1-pentene **35** were both detected in 27.0% GC yield. (*Z*)-1-phenylthio-2-phenylseleno-1-pentene (**47**) and (Z)-1-phenylseleno-2-phenylthio-1-pentene (**48**) were also observed in 17 and 20% yields, respectively, by GC.

The Reaction of Phenylseleno-2-hexen-1-one 43 with $(PhS)_2$. To a glass bomb were added phenylseleno-2-hexen-1-one **43** (61.5 mg, 0.15 mmol), $(PhS)_2$ **31** (34.5 mg, 0.16 mmol), and benzene (2 mL). The reaction was heated for 48 h at 90 °C with stirring. The reaction was filtered through Celite and analyzed by GC−MS and GC. A 5.3% GC yield of 3-phenylselenyl-hex-2-enoic acid *S*-phenyl ester **39** (0.008 mmol) was observed. Trace amounts of diaryl dichalcogenide **32** were also observed.

6-Cyano-(*Z*)-3-phenylsulfenyl-hex-2-enoic Acid Diethylamide (45). To a stainless steel reaction vessel with glass insert in a nitrogen-filled glovebox were added $(PhS)_2$ **31** (13.0 mg, 0.06 mmol), sulfenamide **5** (18.5 mg, 0.11 mmol), 5-cyano-1-pentyne (32.0 μL, 0.30 mmol), 4.0% of catalyst **3** (5.0 mg, 4.3 μmol), and benzene (2.0 mL). The reaction was charged with 28 atm of CO gas and heated for 65 h at 110 °C with stirring. The resultant solution was degassed, filtered through Celite, and reduced in vacuo to yield a viscous oil. The crude reaction mixture was purified via column chromatography using 5% ethyl acetate/hexanes, 20% ethyl acetate/hexanes, and ethyl acetate to yield the orange oil 6-cyano-(*Z*)- 3-phenylsulfenyl-hex-2-enoic acid diethylamide **45** (20.0 mg, 0.07 mmol) in 64% yield. Spectral data match those obtained in prior experiments.

The High-Pressure Preparation of Acrylamides 18 and 45 from 5-Cyano-1-pentyne and Sulfenamide 5. To a stainless steel reaction vessel with glass insert in a nitrogen-filled glovebox were added $(PhSe)_2$ **2** (63.0 mg, 0.20 mmol), sulfenamide **5** (36.7 mg, 0.20 mmol), 5-cyano-1-pentyne (32.0 μL, 0.30 mmol), 4.9% of catalyst **3** (11.5 mg, 9.9 μmol), and xylenes (2.5 mL). The reaction was charged with 28 atm of CO gas and heated for 67 h at 85 °C with stirring. The resultant solution was degassed, filtered through Celite, and analyzed by GC. A 25% GC yield of both acrylamides **18** and **45** was observed.

The Comparative Carbonylative Additions of $(PhS)_2$ and $(PhSe)_2$ to 1-pentyne. (a) To a glass bomb in a nitrogen-filled glovebox were added $(PhS)_2$ **31** (43.0 mg, 0.20 mmol), 1-pentyne (25.0 μL, 0.25 mmol), 6.2% of catalyst **3** (14.5 mg, 12.5 μmol), and benzene (2.0 mL). The reaction was charged with 0.5 atm of CO gas and heated for 94 h at 90 °C with stirring. The resultant solution was degassed, filtered through Celite, and analyzed by GC−MS and GC. Phenylthio-2-hexen-1-one **38** and bis(phenylthio)-1-pentene **35** were detected in GC yields of 4.7 and 95%, respectively. (b) Following the general procedure stated above, phenylseleno-2-hexen-1-one **43** and bis(phenylseleno)-1-pentene **34** were detected in GC yields of 75 and 7%, respectively.

The ^1H NMR Analysis of Reaction Selectivity. To a screw-top NMR tube in a nitrogen-filled glovebox were added 0.1 mL of a 0.0203 M C_6D_6 solution of sulfenamide **1**, 0.1 mL of a 0.02 M C_6D_6 solution of $(PhSe)_2$ **2**, 0.15 mL of a 0.02 M C_6D_6 solution of 1-pentyne, 0.1 mL of a 0.01 M C_6D_6 solution of catalyst **3**, and 0.1 mL of a 0.115 M C_6D_6 solution of anisole standard. The reaction was charged with CO gas and heated to 80 °C. The reaction was monitored by ^1H NMR every 24 h for 6 days. Integrated areas were used to determine the relative amounts of both selenium and sulfur acrylamide products **4** and **33**. The product ratio of **4**:**33** after 3 h reaction and every 24 h is as follows: 100:1, 6:1, 4.5:1, 3.3:1, 3.2:1, 4:1, 3.5:1.

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Supporting Information Available: General procedures, including the synthesis of sulfenamides. This material is available free of charge via the Internet at http://pubs.acs.org.

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