Studies on Transition Metal-Catalyzed Cleavage of Carbon-Chalcogen Bonds and Addition to Unsaturated Hydrocarbons

Masashi Toyofuku

Osaka University

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（遷移金属触媒を用いる炭素－カルコゲン結合の切断と

不飽和炭化水素類への付加反応に関する研究）

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Preface

The study described in this thesis has been carried out (2003-2009) under the direction of Professor Nobuaki Kambe at Department of Applied Chemistry, Graduate School of Engineering, Osaka University. The objective of this thesis is concerned with studies on construction of various carbon skeletons via cleavage of carbon-chalcogen bonds and addition to unsaturated hydrocarbons using palladium and platinum catalysts.

Department of Applied Chemistry
Graduate School of Engineering, Osaka University
Suita, Osaka, Japan
January, 2009

Masashi Toyofuku

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Chapter 4 Palladium(0)-Catalyzed Intramolecular Cyclization of Carbamothioates and –selenoates Having an Allene Moiety

General Introduction

Transition metal-catalyzed addition of heteroatom-containing compounds to unsaturated hydrocarbons has been well-exploited as one of the most straightforward methods for the introduction of heteroatom functionality to organic molecules.[1,2] In the presence of appropriate transition metal catalyst, hydrogen-heteroatom or heteroatom-heteroatom bonds such as H-SiR_3 and R_2B-BR_2 are activated and added smoothly to unsaturated hydrocarbons.[1] Recently, addition involving cleavage of carbon-heteroatom bonds has been attracted great interest.[2] This reaction proceeds with the concomitant formation of new carbon-heteroatom and carbon-carbon bonds. As the represented examples, our group has developed platinum(0)-catalyzed intermolecular decarbonylative addition of thiol or selenol esters to alkynes giving functionalized vinylchalcogenides.[3,4] Oxidative addition of carbon-chalcogen (sulfur or selenium) bonds of thiol or selenol esters to Pt(0) species should be an initial step in this catalytic system.

In the field of synthetic chemistry, transition metal-catalyzed reaction initiated by oxidative addition of carbon-chalcogen bonds has been less remarked than the reaction using carbon-halogen bonds.[5] While the oxidative addition of carbon-chalcogen bonds is faster than the corresponding carbon-halogen bonds,[6] the oxidative adducts, "*C*-M-*Y*" complexes (*C* = carbon group, *Y* = chalcogen group, M = transition metal) are less stable (i.e. more reactive) than that of the corresponding "*C*-M-X" complexes (X = halogen).[7] From this point of view, organochalcogenides may have great potential as substrates for various catalytic reactions.

This thesis describes on group 10 metal-catalyzed construction of various carbon skeletons via the cleavage of carbon-chalcogen bonds and addition to alkynes and allenes. In chapter 1, palladium(0)-catalyzed intramolecular cyclization of carbamothioates and -selenoates having an alkyne moiety is disclosed. In chapter 2, platinum(0)-catalyzed intramolecular cyclization of vinyl sulfides and selenides having an alkyne moiety is described. In chapter 3, palladium(0)-catalyzed addition of selenol esters to allenes leading to regioselective formation of allyl selenides is discussed. Finally, palladium(0)-catalyzed intramolecular cyclization of carbamothioates and -selenoates having an allene moiety is developed in chapter 4.

References and Notes

[1] For recent reviews, see: (a) *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley: Zürich, 2001. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435. (c) Han, L. –B.; Tanaka, M. *Chem. Commun.* **1999**, 395. (d) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (e) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205. (f) Ogawa, A. *J. Organomet. Chem.* **2000**, *611*, 463. (g) Kuniyasu, H.; Kurosawa, H. *Chem. Eur. –J.* **2002**, *8*, 2660. (h) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (i) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320.

[2] (a) Tanaka, M.; Hua, R. *Pure Appl. Chem.* **2002**, *74*, 181. (b) Hua, R. *Acta Phys. –Chim. Sin.* **2004**, *20*, 989. (c) Kuniyasu, H.; Kambe, N. *Chem. Lett.* **2006**, *35*, 1320.

[3] (a) Sugoh, K.; Kuniyasu, H.; Sugae, T.; Ohtaka, A.; Takai, Y.; Tanaka, A.; Machino, C.; Kambe, N.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 5108. (b) Hirai, T.; Kuniyasu, H.; Kato, H.; Kurata, Y.; Kambe, N. *Org. Lett.* **2003**, *5*, 3871. (c) Yamashita, F.; Kuniyasu, H.; Terao, J.; Kambe, N. *Org. Lett.* **2008**, *10*, 101. (d) For related studies, see ref 2c.

[4] For other type reactions, see: (a) Choi, N.; Kabe, Y.; Ando, W. *Tetrahedron Lett.* **1991**, *32*, 4573. (b) Hua, R.; Takeda, H.; Onozawa, S.; Abe, Y.; Tanaka, M. *J. Am. Chem. Soc.* **2001**, *123*, 2899. (c) Kamiya, I.; Kawakami, J.; Yano, S.; Nomoto, A.; Ogawa, A. *Organometallics* **2006**, *25*, 3562. (d) Hua, R.; Takeda, H.; Onozawa, S.; Abe, Y.; Tanaka, M. *Org. Lett.* **2007**, *9*, 263. (e) Yamashita, K.; Takeda, H.; Kashiwabara, T.; Hua, R.; Shimada, S.; Tanaka, M. *Tetrahedron Lett.* **2007**, *48*, 6655.

[5] Organochalcogenides have been used as pseudo-halides in some catalytic reaction. For recent examples, see: (a) Silveira, C. C.; Braga, A. L.; Vieira, A. S.; Zeni, G *J. Org. Chem.* **2003**, *68*, 662. (b) Itami, K.; Higashi, S.; Mineno, M.; Yoshida, J. *Org. Lett.* **2005**, *7*, 1219. (c) Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 15734.

[6] For oxidative addition of aryl telluride and aryl iodide to Pd(0), see: Han, L. –B.; Choi, N.; Tanaka, M. *J. Am. Chem. Soc.* **1997**, *119*, 1795. We have also disclosed oxidative addition of thiol ester or vinyl selenide to Pt(0) proceeded faster than the corresponding acid chloride or vinyl bromide, respectively (unpublished data).

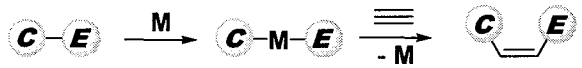
[7] The acyl-Pt-SAr complex was converted to the corresponding acyl-Pt-Cl complex quantitatively by the reaction with the acid chloride (unpublished data). Similar ligand exchange reaction was reported. See ref [6].

Chapter 1

Palladium(0)-Catalyzed Intramolecular Cyclization of Carbamothioates and –selenoates Having an Alkyne Moiety

1-1 Introduction

Transition metal-catalyzed 1,2-addition of typical element compounds to carbon-carbon unsaturated bonds involving cleavage of σ-bonds such as R_3Si-H, R_2B-BR_2 and RSe-P(O)(OR')$_2$ has attracted great interest in organic and organometallic chemistry.[1] In this field, simultaneous addition of carbon and heteroatom units (represented by "*C*" and "*E*", respectively) to alkynes via oxidative addition of "*C-E*" bonds to metal catalysts (**M**) is one of the most important transformations (Scheme 1), and has the following two features: i) simultaneous formation of new carbon-carbon and carbon-heteroatom bonds, ii) cis-selective constructing multi-functionalized alkenes.



E = Cl, Si, Sn, B, S, Se, *etc.*

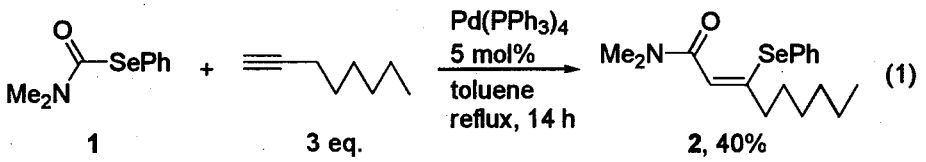
Scheme 1. Addition of *C-E* bonds to alkynes catalyzed by **M**

Although intermolecular process has been well explored by many research groups including us,[2,3] the corresponding intramolecular process is not studied very well. Suginome and co-workers reported Ni and Pd-catalyzed intramolecular cyanosilylation and cyanoboration of alkynes to give sila- or boracycles, which are good precursors of various vinyl cyanides.[4] Gandon, Aubert and co-workers reported Co-catalyzed intramolecular arylsilylation of alkynes to form silicon-containing polycyclic frameworks.[5] These reports can be regarded as new synthetic methods for novel heterocycles. As pioneering studies on construction of carbocycles, Zhang and co-workers developed Rh-catalyzed intramolecular allylchlorination of alkynes.[6] Echavarren and co-workers also found Pd-catalyzed intramolecular allylstannylation of alkynes.[7] Both authors only showed the cyclization to five-membered rings by using allylic heteroatom compounds as starting materials.

This chapter discusses on palladium(0)-catalyzed intramolecular acylchalcogenation of alkynes which is a new strategy for the construction of lactams and cycloalkanones having an exo methylene moiety[8].

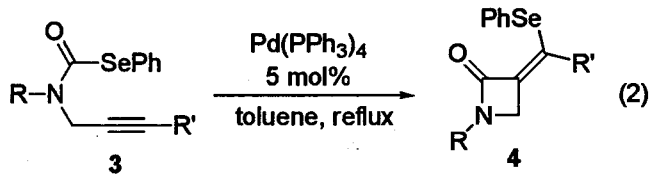
1-2 Results and Discussion

In the course of our studies on transition metal catalyzed reaction of organosulfides and –selenides with alkynes,[9] we have found $Pd(PPh_3)_4$ catalyzed carbamoselenation of 1-octyne with a carbamoselenoate, $Me_2NC(O)$-SePh (**1**). When toluene (0.3 mL) containing **1** (0.5 mmol), 1-octyne (1.5 mmol) and $Pd(PPh_3)_4$ (5 mol%) was heated at reflux for 14 h, β-seleno acrylamide **2** was isolated in 40% yield (eq 1).[10]



Meyer and Knapton developed $Pd(PPh_3)_4$ catalyzed intermolecular four-components coupling reaction using alkynes, sulfenamides, diselenides and carbon monoxide to give β-seleno acrylamides.[11] They also claimed that carbamothiolation of 1-pentyne with a carbamothioate, $Me_2NC(O)$-SPh, was sluggish (<5%) in the presence of $Pd(PPh_3)_4$.

The result of eq 1 led us to perform the reaction of carbamoselenoates **3** having a propargyl group on the N atom aiming to construct α-alkylidene-β-lactam framework, a core structure of several antibiotics and various synthetic intermediates (eq 2). When *Se*-phenyl *N*-methyl-*N*-prop-2-ynyl carbamoselenoate **3a** (0.4 mmol) was treated with $Pd(PPh_3)_4$ (5 mol%) in toluene (2.0 mL) at reflux, the corresponding α-alkylidene-β-lactam **4a** was formed in 74% yield with excellent regio- and stereoselectivity (Tabel 1, run 1).



Tabel 1. Intramolecular Cyclization of **3** to Form **4** (eq 2)

run	**3**	R	R'	**4**, isolated yield[a]	*E/Z*
1	**3a**	Me	H	**4a**, 74%	0/100
2[b]	**3a**	Me	H	**4a**, 81%	0/100
3[c]	**3b**	^{n}Bu	H	**4b**, 60% (85%)	2/98
4	**3c**	Bn	H	**4c**, 59% (84%)	3/97
5[c]	**3d**	Bn	Et	**4d**, 88% (94%)	3/97
6[d]	**3e**	Me	4-ClC_6H_4	**4e**, 76%	11/89

Condition: **3** (0.4 mmol), $Pd(PPh_3)_4$ (5 mol%), toluene (2.0 mL), relux, 1 h. [a]Numbers in parantheses are NMR yields. [b] $Pd(PPh_3)_4$ (1 mol%). [c]Toluene (0.5 mL). [d]Toluene (4.0 mL), 20 h.

Other examined transition metal complexes such as $Pd(dba)_2$, $Pd(OAc)_2$, $Pd(PPh_3)_2Cl_2$, $Pt(PPh_3)_4$, $Ni(COD)_2$, $Ni(PPh_3)_4$, and $RhCl(CO)(PPh_3)_3$ were ineffective. PCy_3 and dppe were not appropriate ligands. The results using several carbamoselenoates are also summarized in Table 1. β-Lactam **4a** was obtained in 81% yield even when the amount of $Pd(PPh_3)_4$ was reduced to 1 mol% (run 2). Bulkier alkyl substituents on nitrogen, e.g. *n*-butyl or benzyl, did not affect the reaction (runs 3 and 4). In contrast to the fact that internal alkynes are sluggish in oxycarbonylthiolation reactions,[2t] carbamoselenoates **3d** and **3e** having an internal alkyne moiety undergo intramolecular carbamoselenation to afford the desired β-lactams **4d** and **4e** in good yields (runs 5 and 6), respectively. The structures of products were confirmed by either NOE experiments or X-ray analysis, and the *E/Z* ratios were determined by ^{1}H NMR. The ORTEP diagram of *Z*-**4e** is shown in Figure 1.

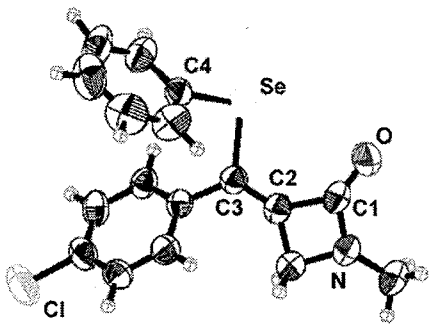
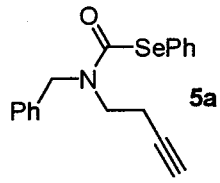
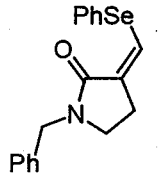
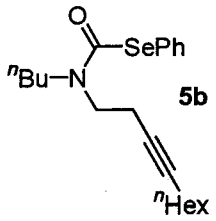
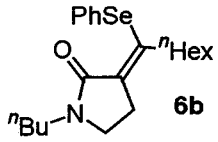
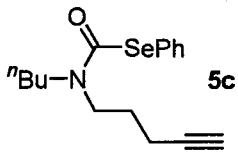
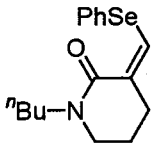
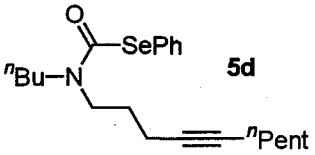
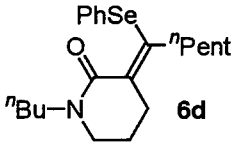
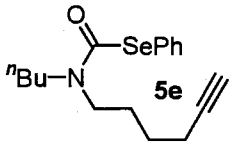
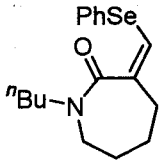
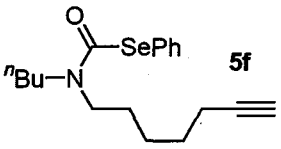
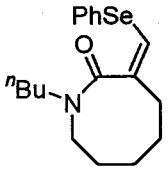


Figure 1. ORTEP diagram of *Z*-**4e**

Table 2. Intramolecular Cyclization of **5** to Form **6**

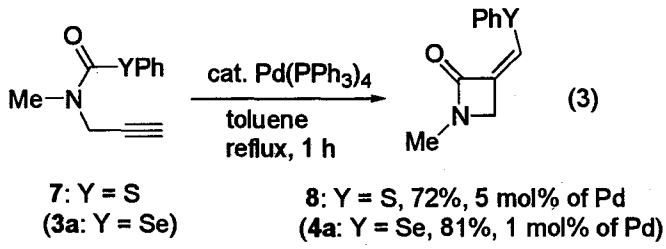
run	carbamoselenoates **5**	lactams **6**	time, h	Isolated Yield	*E/Z*
1	 **5a**	 **6a**	2	70%	0/100
2	 **5b**	 **6b**	2	90%	0/100
3	 **5c**	 **6c**	1	75%	0/100
4	 **5d**	 **6d**	1	90%	0/100
5	 **5e**	 **6e**	12	74%[b] (12%)[a]	0/100
6	 **5f**	 **6f**	12	30%[c]	0/100

Condition: **5** (0.4 mmol), $Pd(PPh_3)_4$ (5 mol%), toluene (0.5 mL), relux. [a]1 h, NMR yield. [b]Toluene (2.0 mL), 12 h. [c]Xylene (2.0 mL), reflux, 12 h.

The bond angle (°) of C3-Se-C4 was 97.8, and torsion angles of Se-C3-C2-C1and C4-Se-C3-C2 were -0.6 and -146, respectively. The atoms of O, C1, C2, C3 and Se are in

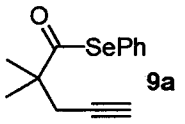
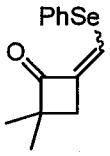
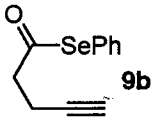
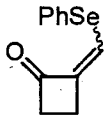
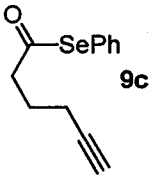
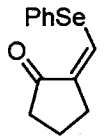
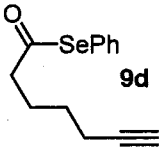
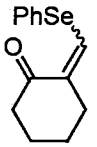
coplanar alignment. These structural features do not conflict the results obtained by DFT calculations as described later. Since non-bonding distance between O-Se (3.45 Å) was slightly longer than the sum of van der Waals radii of O and Se (3.42 Å), there is no intramolecular interaction between carbonyl oxygen and selenium atom.[12]

The developed strategy was applied successfully to the synthesis of larger α-alkylidenelactams. When a carbamoselenote **5a** having a 3-butynyl group on the N atom was treated under similar conditions, α-alkylidene-γ-lactam **6a** was obtained in 70% isolated yield with perfect regio- and stereoselectivity (Table 2, run 1). γ-Lactam **6b** and δ-lactams **6c**, **d** were also readily formed from corresponding carbamoselenoates **5b-d** (runs 2-4). Although the reaction of carbamoselenate **5e** having a 5-hexynyl group was slower, seven-membered lactam **6e** was also obtained in 74% yield after 12 h (run 5). In the case of **5f** having a 6-heptynyl group, eight-membered lactam **6f** was also prepared albeit in a low yield (run 6). Under similar conditions, a nine-membered lactam was not obtained. The structures of products were confirmed by NOE experiments. Next, we examined the reaction of carbamothioate **7** aim to synthesize α-alkylidene-β-lactam **8** having sulfur functional group (eq 3). Although it was reported that intermolecular reaction gave a carbamothiolation product in a low yield,[11b] intramolecular carbamothiolation took place efficiently to give **8** in 72% yield.



This intramolecular cyclization strategy can be applied to the synthesis of four- to six-membered cycloalkanones. In the first trial, we disclosed that intramolecular acylselenation of selenol ester **9a** proceeded to give cyclobutanone **10a** in 74% yield with *E*/*Z* ratio of 26/74 (Table 3, run 2). Then we found that when the reaction time was shortened to 10 min or the reaction was conducted at lower concentration **10a** was obtained in higher yields and selectivity (runs 1 and 3). For these results, isomarization of *Z*-**10a** may occur via the further reaction of *Z*-**10a** with Pd(0) species.[13] As anticipated the reaction of selenolester **9b** not having two methyl groups was slow (runs 4 and 5). Although cyclopentanone **10c** was formed quantitatively with perfect stereoselectivity under similar conditions as run 1 (run 6), formaition of six-membered ring was slow (runs 7 and 8).

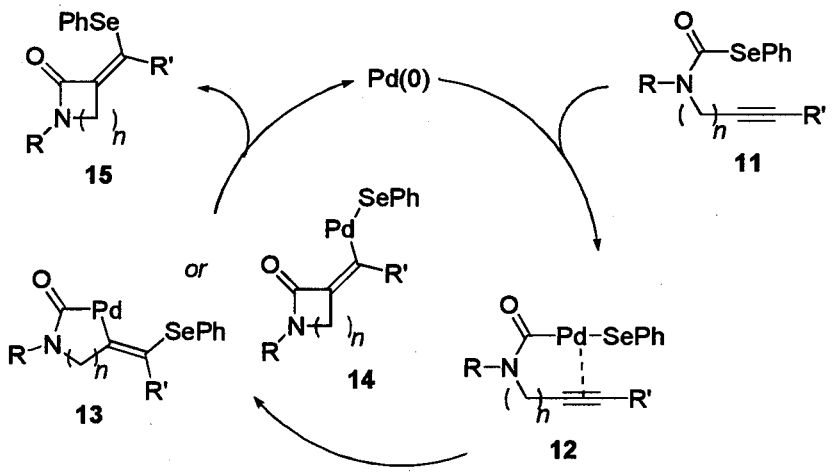
Table 3. Intramolecular Cyclization of **9** to Form **10**

run	selenolesters **9**	cycloalkanones **10**	concentration, M	time	NMR Yield[a]	*E*/*Z*[b]
1	 **9a**	 **10a**	0.8	10 min	90%	8/92
2	**9a**	**10a**	0.8	1 h	74% (58%)[c]	26/74
3	**9a**	**10a**	0.08	12 h	99%	7/93
4	 **9b**	 **10b**	0.8	10 min	trace	-/-
5	**9b**	**10b**	0.2	12 h	33% (15%)	36/64
6	 **9c**	 **10c**	0.8	10 min	99% (82%)	0/100
7	 **9d**	 **10d**	0.8	10 min	27%	0/100
8	**9d**	**10d**	0.2	12 h	51% (42%)	15/85

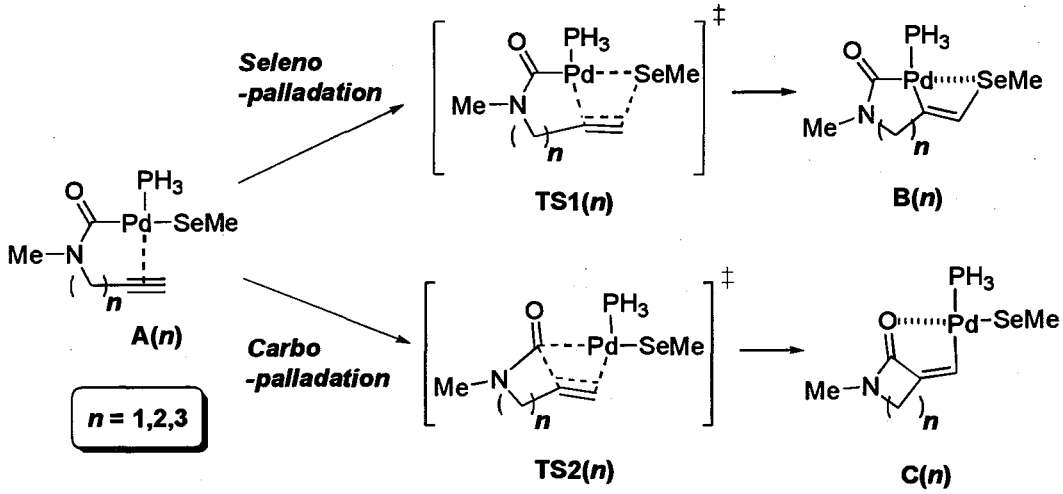
Condition: **9** (0.4 mmol), $Pd(PPh_3)_4$ (5 mol%), toluene, relux. [a]Numbers in parentheses are isolated yields. [b]Determined by crude ^1H NMR. Isomerization of *Z*-isomer to *E* occured under purification of **10a** and **10b**. [c]PhSePh was also isolated in 19% yield.

Plausible reaction pathways for α-alkylidenelactams **15** are depicted in Scheme 2. The present transformation will be initiated by oxidative addition of NC(O)-Se bond of **11** to Pd(0) prior to or after coordination of the internal C-C triple bond to Pd to give **12**. Subsequently the alkyne inserts into the Pd-Se bond, *selenopalladation*, to afford the palladacycle **13** or inserts into the NC(O)-Pd bond of **12**, *carbopalladation*, to form the selenolate complex

("*vinyl*-Pd-SePh") **14**. These two mechanisms, *selenopalladation* and *carbopalladation*, need to be considered due to the following facts. As for *selenopalladation*, insertion of alkynes into metal-chalcogen bond of the complexes having a ***C*-M-*Y*** unit (**M** = Pd or Pt, ***Y*** = sulfur or selenium groups) prior to C-C bond-forming reductive elimination was already proposed in several catalytic systems. [2t, v, n, 3b-f, h] In addition, we found recently the definitive evidence for the insertion of alkynes into Pt-SAr bonds by stoichiometric reactions.[14] As for *carbopalladation*, Grigg and co-workers reported Pd-catalyzed tandem cyclization-anion capture processes of carbamoyl chlorides, $R_2NC(O)$-Cl, having a terminal alkynyl group on the N atom.[15, 16] The authors proposed an intramolecular cyclization mechanism via insertion of alkyne moiety into the $R_2N(O)C$-Pd bond to form "*vinyl*-Pd-Cl" species. Furthermore, some studies on the Pd catalyzed reactions revealed facile C-S or C-Se bond-forming reductive elimination from Pd(II) complexes.[17] Reductive elimination leads to the cyclized products **15** and regenerates the Pd(0) species. To estimate which pathway, *selenopalladation* or *carbopalladation*, is more plausible for alkyne insertion step, DFT calculations were conducted on the model structures (n = 1,2,3) shown in Scheme 3.



Scheme 2. Plausible Reaction Pathways for α-Alkylidenelactam **15**



Scheme 3. Computational Models for Alkyne Insertion Processes

A(*n*), **B(*n*)** and **C(*n*)** are model compounds for alkyne-coordinated complex **12**, palladacycle **13** and selenolate complex **14**, respectively (see, Scheme 2). **TS1(*n*)** and **TS2(*n*)** are transition state models from **A(*n*)** to **B(*n*)** and **C(*n*)**, respectively. Calculations were carried out using the Gaussian 03 set of programs with the B3LYP functional, the 6-31+G(d) basis set for all nonmetallic atoms (H, C, O, N, P) and the LANL2DZ basis set for Pd and Se. Calculated energies of optimized **TS1(*n*)**, **TS2(*n*)**, **B(*n*)**, **C(*n*)** relative to **A(*n*)** are shown in Table 4.

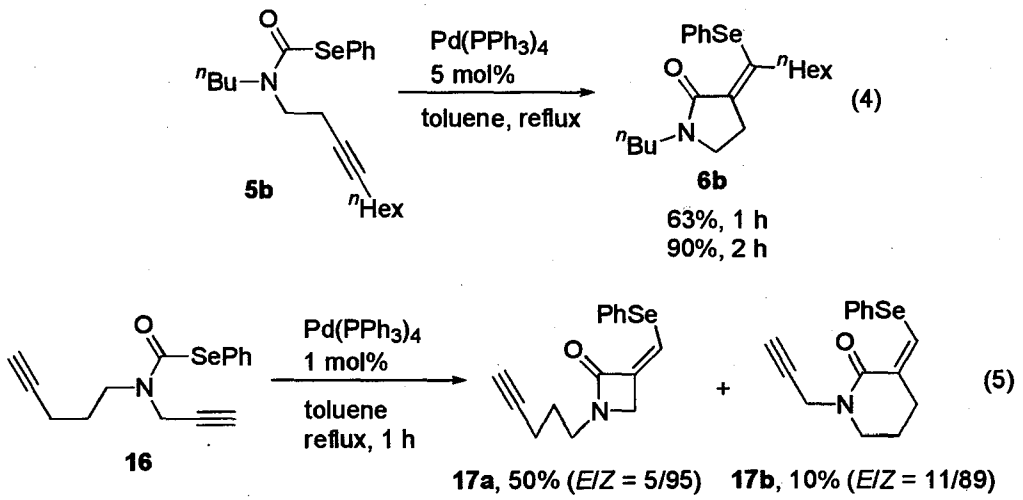
Table 4. Calculated Energies[a] of Optimized **TS1(*n*)**, **TS2(*n*)**, **B(*n*)** and **C(*n*)**

n	TS1(*n*)	TS2(*n*)	B(*n*)	C(*n*)
1	+7.7	+20.9	-14.0	-8.4
2	+10.4	+15.5	-10.8	-36.1
3	+10.0	+13.5	-9.6	-38.8

[a]Gibbs free energies (kcal/mol) relative to optimized **A(*n*)** at 298.15 K, gas-phase (1 atm).

TS1(*n*) were more stable than **TS2(*n*)** in all cases of *n* values which were carried out. These results indicate that *selenopalladation* (from **A(*n*)** to **B(*n*)**) is more kinetically favored pathway than *carbopalladation* (from **A(*n*)** to **C(*n*)**) for the formation of four-, five-, and six-membered lactams. In this reaction system, four-membered lactam formation is faster than those of five- and six-membered lactams. Although cyclizations of **4d** and **6d** were completed within 1 h (Table 1, run 5 and Table 2, run 4), cyclization of **6b** was not finished in 1 h (eq 4). When carbamoselenoate **16** having both 2-propynyl and 4-pentynyl groups on the N atom was

employed, four-membered lactam **17a** was obtained predominantly over six-memebred lactam **17b** (eq 5).



These experimental findings do not conflict with the theoretical results shown in Table 4: relative energy of **TS1(1)** (+7.7 kcal/mol) is lower than **TS1(2)** (+10.4 kcal/mol) and **TS1(3)** (+10.0 kcal/mol). Ball-and-stick models of **A(*n*)**, **TS1(*n*)** and **B(*n*)** are shown in Figure 2. Numeric values in parentheses identify calculated torsion angles (°) of Se-Pd-C-C'. Remarkably, these angles of **A(1)** (2.483) and **TS(1)** (6.051) are much smaller than the corresponding **A(2)** (39.726), **A(3)** (22.081), **TS1(2)** (22.081), and **TS1(3)** (23.412). Se, O, N, C and C' atoms are in almost coplanar alignment in cases of **A(1)**, **TS1(1)** and **B(1)**. This alignment was also confirmed in the crystal structure of *Z*-**4e** (Figure 1). Since the axis of C≡C prefers to be parallel to the coordination plane of the metal before migratory insertion occurs,[18] **A(1)** may be more smoothly converted to **B(1)** through **TS(1)** than **A(2)** and **A(3)**. The axis of C≡C is conformationally fixed to be parallel to the coordination plane of Pd by the amide plane (N(O=)C) and one methylene chain in **A(1)** and **TS(1)**. Four-membered ring construction by reductive elimination of C_{sp2}-C_{sp2} unit from five membered palladacycle intermediate such as **B(1)** or **13** has been proposed.[19] In conclusion, rapid generation of five-membered palladacycle via *thio-* or *selenopalladation* of an alkyne moiety may be a key to the effective construction of strained four-membered ring skeletons in this catalytic system.

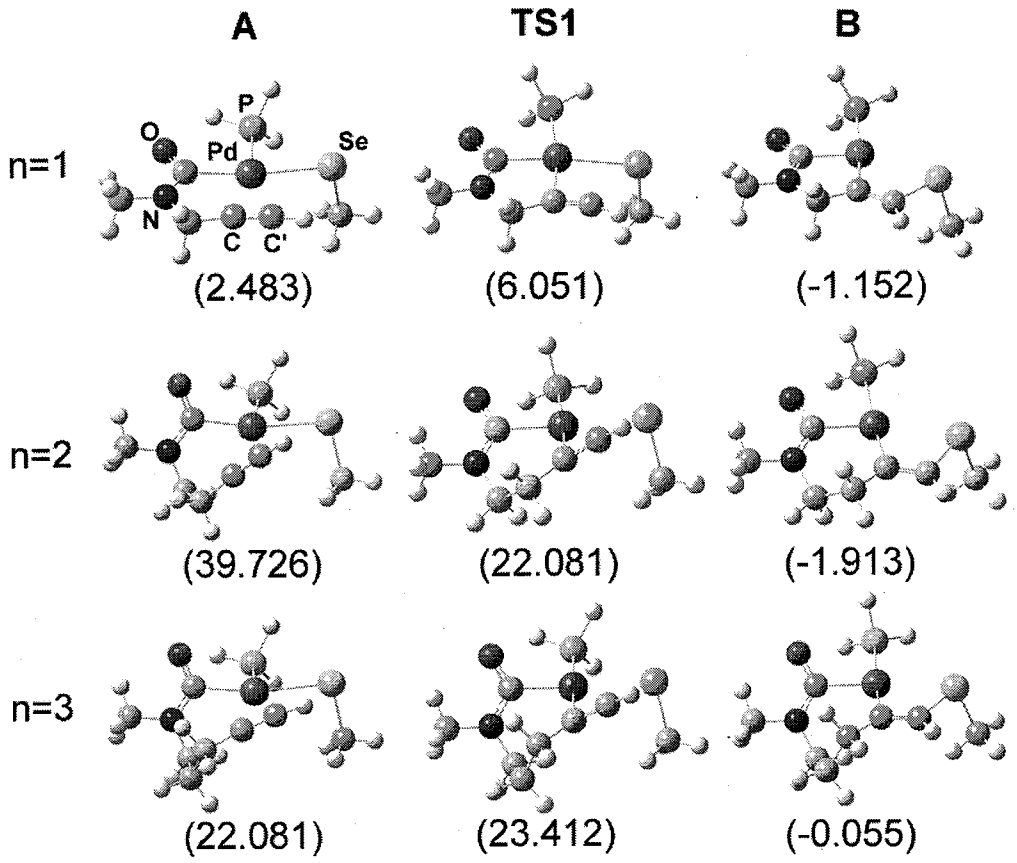
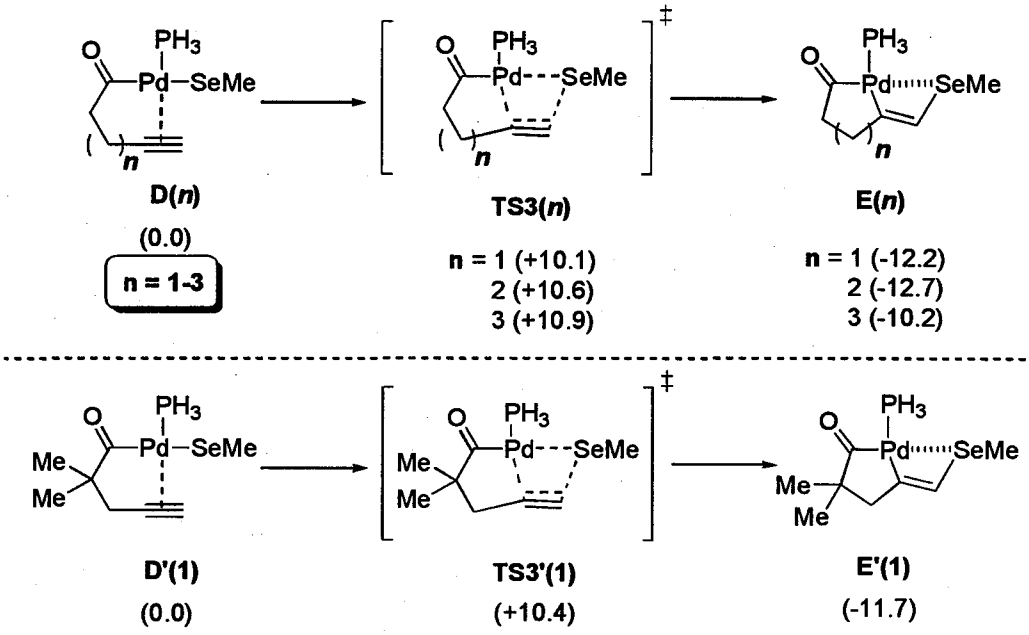


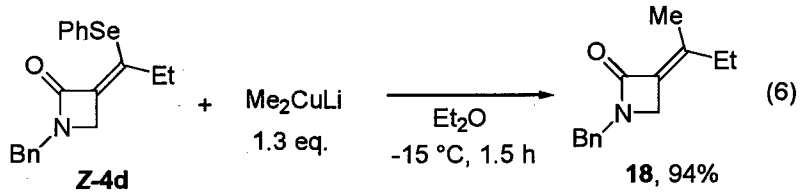
Figure 2. Ball-and-stick models of optimized **A(*n*)**, **TS1(*n*)** and **B(*n*)**. Numeric values in parentheses identify torsion angles of Se-Pd-C-C'.



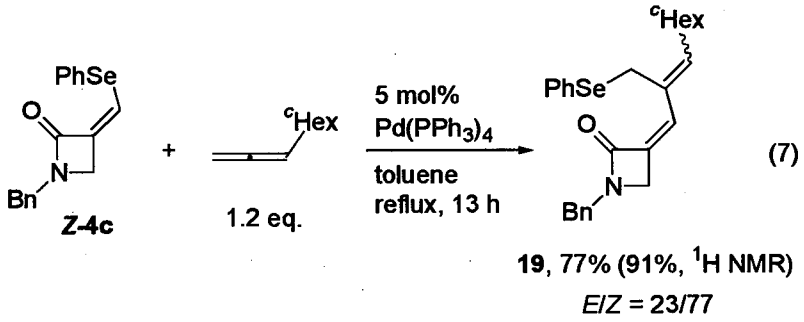
Scheme 4. Computational Models for Alkyne Insertion Step for **9** (Table 4)

Acylselenation of alkynes may proceed via similar pathways shown in Scheme 2; however, the order of cyclization efficiency of four- to six-membered cyclic ketones was different from that of the corresponding lactams. Thus, DFT calculations of *selenopalladation* step were conducted on the model compounds (n = 1-3) shown in Scheme 4. Calculated energies of optimized **TS3(*n*)** and **E(*n*)** relative to **D(*n*)** and **TS3'(1)** and **E'(1)** relative to **D'(1)** are shown in parentheses. Difference of cyclization efficiencies of **9c** to **9d** and **9a** to **9b** may not be arisen in alkyne insertion step. From calculation results and the geminal dialkyl effect[20] seen in the reaction of **9a**, alkyne coordination step may be rate determining in intramolecular acylselenation of alkynes.

Since vinyl selenides having an electron withdrawing group at β-position are known to undergo cross-coupling reaction with dialkylcuprates,[21] *Z*-**4d** was subjected to react with Me_2CuLi, giving rise to **18** with compleate retention of the configuration (eq 6).

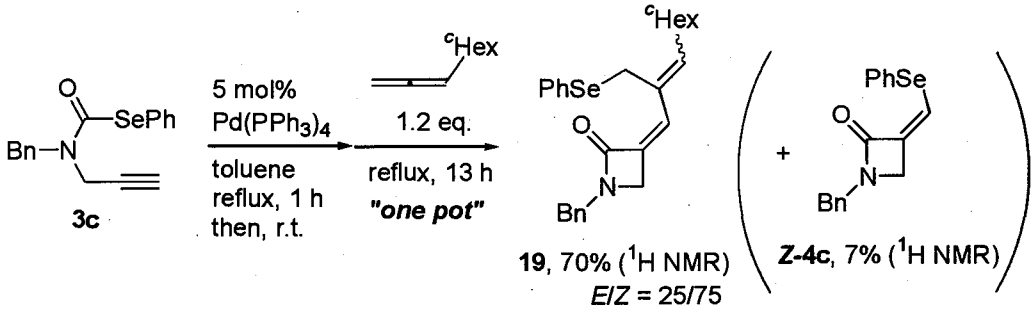


When *Z*-**4c** was allowed to react with 1.2 equiv of cyclohexylallene in the presence of $Pd(PPh_3)_4$, allyl selenide **19** was obtained in high yield with perfect regioselectivity (eq 7).



On the contrary, the reaction of **6c** (Table 2) with cyclohexylallene under similar conditions did not afford the expected adduct. Judging from IR absorption of carbonyl groups in **4c** (1720 cm^{-1}) and **6c** (1634 cm^{-1}) as well as ORPET diagram of **4c**, carbonyl oxygen of **6c** coordinates to selenium, where as no interaction was found in **4c**. Therefore, coordination of allenes to the oxidative adduct may be retarded by carbonyl coordination. Then we examined the one-pot

reaction of **3c** with cyclohexylallene in the presence of $Pd(PPh_3)_4$ catalyst. When cyclohexyallene was added after the reaction of **3c** with $Pd(PPh_3)_4$ under toluene reflux for 1 h, sequential vinylselenation of cyclohexylallene proceeded to give allyl selenide **19** (eq 8).



(8)

1-3 Conclusions

$Pd(PPh_3)_4$-catalyzed intramolecular carbamoselenation of alkynes to form α-alkylidene-β-lactams was described in detail. This reaction can be successfully applied to carbamothiolation and to the synthesis of five- to seven-membered lactams and four- to six-membered cyclic ketones. This is a rare reaction that four-membered ring formation is faster than five- and six-membered rings.[22] DFT calculations for *selenopalladation* process do not contradict experimental findings. Since the axis of coordinated alkyne moiety is conformationally fixed to be parallel to the coordination plane of Pd center in the construction of four-memberd ring skeletons, subsequent alkyne insertion may occur smoothly. Five-membered palladacycles undergo reductive elimination to afford cyclized products and active Pd(0) species. Facile formation of five-membered palladacycle via thio- or selenopalladation of an alkyne moiety is a key to the effective construction of strained four-membered ring skeletons.

1-4 Experimental Section

Genaral Comments

THF was distilled from benzophenone ketyl just prior to use. 1-Octyne, toluene, and CH_2Cl_2 were distilled from CaH_2. $Pd(PPh_3)_4$ was prepared according to the literature procedure.[23] Carbamoyl chlorides except *N,N*-dimethylcarbamoyl chloride were synthesized from triphosgene and *N*-alkyl-*N*-alk-2-ynylamines. Melting points were determined on a Yanagimoto Micro Melting Point apparatus. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ALICE-400 (400 MHz and 100 MHz, respectively) spectrometer using Me_4Si (in $CDCl_3$) as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Preparative TLC was conducted by using Wakogel B-5F silica gel (325 mesh). Mass spectra (EI) were taken on a SHIMAZU GCMS-QP2000 operating in the electron impact

mode (70 eV) equipped with CBP1-M25-025 column. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus.

Preparation of Carbamoyl Chlorides

***N*-Butyl-*N*-prop-2-ynylcarbamoyl chloride: Typical Procedure.**[24] Into a 200-mL flask were placed triphosgene (8.3 mmol) and CH_2Cl_2 (8 mL) under N_2. After cooling to -78 °C, pyridine (2.5 mmol) was added. To the solution was then added slowly *N*-butyl-*N*-prop-2-ynylamine (25 mmol), prepared from prop-2-ynyl chloride and *n*-butylamine, in CH_2Cl_2 (4 mL) at the same temperature. After the mixture was warmed up to room temperature, the stirring was continued for 2 days until gas-emission ceased. The expected carbamoyl chloride was obtained in 66% yield by distillation (4 mmHg, 80 °C) as colorless oil contaminated with a small amount of pyridine hydrochloride and was used without further purification.

CAUSION: Triphosgene decomposes slightly to generate highly-poisonous phosgene in air. All operation should be carried out in a well-ventilated hood.

Procedures and Characterization of Reaction Materials

***Se*-Phenyl *N,N*-dimethylcarbamoselenoate (1, eq 1): Typical procedure.**

Into a 100-mL flask were placed elemental selenium (16 mmol) and THF (20 mL) under Ar and the suspension was cooled to 0 °C. PhLi (0.94 M in Et_2O-cyclohexane, 16 mL, 15 mmol) was added slowly to prepare PhSeLi and the stirring was continued for 5 min. To the pale yellow solution of PhSeLi was then added *N,N*-dimethylcarbamoyl chloride (16 mmol) in 10 mL of THF at the same temperature, and the mixture was warmed up to room temperature and stirred overnight. After the mixture was poured into brine (50 mL) and extracted with Et_2O (30 mL X 4), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) to afford *Se*-phenyl *N,N*-dimethylcarbamoselenoate (**1**) in 73% yield: white solid; mp 34 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 6 H), 7.33-7.58 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.7, 37.1, 126.4 ($^1J_{Se\text{-}C}$ = 91.7 Hz), 128.4, 128.6, 136.2 ($^2J_{Se\text{-}C}$ = 10.6 Hz), 163.9; IR(KBr) 2925, 1678 (C=O), 1477, 1361, 1255, 1094, 891, 746, 692, 624, 480 cm^{-1}; MS(EI), m/e (relative intensity, %) 229 (M^+, 5), 157(6), 77(5), 72(100). Anal. Calcd for $C_9H_{11}NOSe$: C, 47.38; H, 4.86; N, 6.14. Found: C, 47.27; H, 4.76; N, 6.20.

***Se*-Phenyl *N*-methyl-*N*-prop-2-ynyl carbamoselenoate (3a, runs 1 and 2, Table 1).**

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (brs, 1 H), 3.09 (brs, 3 H), 4.22 (brs, 2 H), 7.33-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.6 (major, minor), 37.7 (major), 40.0

(minor), 72.5 (major), 73.3 (minor), 77.0 (major), 77.5 (minor), 126.0, 128.8, 128.9, 136.2 ($^2J_{Se-C}$ = 9.7 Hz), 164.6(br); IR(NaCl) 3292, 3056, 1674 (C=O), 1438, 1373, 1256, 1192, 1067, 1022, 740, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 253 (M^+, 4), 157(10), 96(100), 77(9), 55(15). Anal. Calcd for $C_{11}H_{11}NOSe$: C, 52.39; H, 4.40; N, 5.55. Found: C, 52.10; H, 4.22; N, 5.61.

***Se*-Phenyl *N*-butyl-*N*-prop-2-ynylcarbamoselenoate (3b, run 3, Table 1).**
Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (br, 3 H), 1.40 (br, 2 H), 1.70 (br, 2 H), 2.25 (br, 1 H), 3.44 (br, 2 H), 4.21 (br, 2 H), 7.32-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5 (major, minor), 20.0 (major, minor), 29.6 (minor), 29.9 (major), 35.8 (major), 38.2 (minor), 48.0 (major, minor), 72.2 (major), 73.0 (minor), 77.0 (major), 78.0 (minor), 126.1, 128.8, 128.9, 136.3 ($^2J_{Se-C}$ = 10.0 Hz), 164; IR(NaCl) 3293, 2959, 1674 (C=O), 1439, 1393, 1303, 1199, 1105, 1022, 740, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 295 (M^+, 2), 157 (13), 138 (100), 82 (16), 77(8), 57(57). Anal. Calcd for $C_{14}H_{17}NOSe$: C, 57.10; H, 5.92; N, 4.92. Found: C, 57.15; H, 5.82; N, 4.76.

***Se*-Phenyl *N*-benzyl-*N*-prop-2-ynylcarbamoselenoate (3c, run 4, Table 1).**
Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.27-2.37 (m, 1 H), 4.02-4.15 (m, 2 H), 4.70 (brs, 2 H), 7.32-7.61 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.2 (major), 37.0 (minor), 49.9 (minor), 51.1 (major), 72.6 (major), 73.3 (minor), 77.1 (major), 77.5 (minor), 126.0, 127.4 (br), 127.7 (br), 128.5 (br), 128.7, 128.8, 134.6 (br), 136.3 ($^2J_{Se-C}$ = 10.1 Hz), 164.5; IR(NaCl) 3290, 3061, 1667 (C=O), 1496, 1455, 1393, 1184, 1076, 959, 740 cm^{-1}; MS(EI), m/e (relative intensity, %) 329 (M^+, 1), 172 (23), 157 (3), 91 (100), 77 (3). Anal. Calcd for $C_{17}H_{15}NOSe$: C, 62.20; H, 4.61; N, 4.27. Found: C, 62.43; H, 4.57; N, 4.26.

***Se*-Phenyl *N*-benzyl-*N*-pent-2-ynylcarbamoselenoate (3d, run 5, Table 1).**
Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.14-1.27 (m, 3 H), 2.21 (brs, 2 H), 4.01-4.14 (m, 2 H), 4.69 (s, 2 H) 7.34-7.65(m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5 (major, minor), 13.9 (major, minor), 35.9 (major), 37.8 (minor), 50.0 (minor), 51.1 (major), 72.7 (minor), 73.1 (major), 86.6 (major), 87.3 (minor), 126.4, 127.4 (br), 127.7 (br), 127.7 (br), 128.4, 128.7, 134.0 (br) 136.4 ($^2J_{Se-C}$ = 10.6 Hz), 164.4; IR(NaCl) 2976, 1673 (C=O), 1438, 1392, 1173, 982, 740, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 357 (M^+, 0.2), 200 (22), 157 (9), 143 (4), 91 (100), 77 (3). Anal. Calcd for $C_{19}H_{19}NOSe$: C, 64.04; H, 5.37; N, 3.93. Found: C, 63.76; H, 5.40; N, 3.97.

***Se*-Phenyl *N*-methyl-*N*-[3-(*p*-chlorophenyl)prop-2-ynyl]carbamoselenoate (3e, run 6, Table 1).**

Pale yellow solid; mp 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 3 H), 4.44 (brs, 2 H), 7.30-7.62(m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$ at 23 °C) δ 34.6 (major, minor), 38.5 (major), 41.2 (minor), 83.3 (major, minor), 84.1 (major, minor), 120.7 (br), 126.3, 128.5, 128.8, 128.9, 132.8, 134.4 (br), 136.4, 164.7 (br); ^{13}C NMR (100 MHz, $CDCl_3$ at -40 °C); 34.6 (major), 34.8 (minor), 38.2 (major), 40.7 (minor), 82.6 (major), 82.9 (minor), 83.5 (minor), 83.7 (major), 119.9 (minor), 120.2 (major), 125.6 (major, minor), 128.2 (major, minor), 128.8 (major, minor), 132.6 (major, minor), 133.9 (major), 134.1 (minor), 136.3 (major), 136.3 (minor), 164.3 (major), 165.0 (minor); IR(KBr) 3070, 2931, 1671 (C=O), 1488, 1376, 1263, 1089, 831, 752, 688cm^{-1}; MS(EI), m/e (relative intensity, %) 363 (M^+, 1), 157(3), 151 (31), 149 (100), 114 (5), 77(2). Anal. Calcd for $C_{17}H_{14}ClNOSe$: C, 56.29; H, 3.89; N, 3.86. Found: C, 56.02; H, 3.83; N, 3.82.

***Se*-Phenyl *N*-benzyl-*N*-but-3-ynylcarbamoselenoate (5a, run 1, Table 2).**
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98-2.07 (m, 1 H), 2.45-2.54 (m, 2 H), 3.39 (brs, 2 H), 4.19-4.67 (m, 2 H), 7.27-7.64 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 17.6 (major), 18.7 (minor), 46.5 (major, minor), 50.9 (minor), 53.3 (major), 69.9 (major), 70.9 (minor), 80.4 (major), 81.4 (minor), 126.4, 126.6, 127.3, 127.8, 128.0, 128.2, 128.6, 128.8, 128.9, 129.0, 129.1, 135.7, 136.7 ($^2J_{Se\text{-}C}$ = 11.0 Hz), 164.9 (br); IR(NaCl) 3293, 3062, 2944, 1661 (C=O), 1455, 1398, 1253, 1176, 1021, 964, 741 cm^{-1}; MS(EI), m/e (relative intensity, %) 343 (M^+, 0.1), 186 (20), 143 (3), 91 (100). Anal. Calcd for $C_{18}H_{17}NOSe$: C, 63.16; H, 5.01; N, 4.09. Found: C, 63.27; H, 5.15; N, 4.28.

***Se*-Phenyl *N*-butyl-*N*-dec-3-ynylcarbamoselenoate (5b, run 2, Table 2).**
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87-1.01 (m, 6 H), 1.26-1.72 (m, 12 H), 2.12-2.16 (m, 2 H), 2.43-2.55 (m, 2 H), 3.34-3.48 (m, 4 H), 7.25-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 14.1, 18.2, 18.7, 19.4, 20.1, 22.6, 28.6, 28.9, 29.9, 30.9, 31.4, 47.5, 48.4, 49.7, 76.1, 77.0, 82.0, 83.0, 126.8, 128.8, 129.0, 136.7 ($^2J_{Se\text{-}C}$ = 10.5 Hz), 163.7; IR(NaCl) 2931, 2859, 1682 (C=O), 1398, 1199, 1160, 1108, 1022, 739 cm^{-1}; MS(CI), m/e (relative intensity, %) 394 (M+1, 80), 236 (100). HRMS calcd for $C_{21}H_{32}NOSe$: 394.1649. Found 394.1655.

***Se*-Phenyl *N*-butyl-*N*-pent-4-ynylcarbamoselenoate (5c, run 3, Table 2).**
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90-1.00 (m, 3 H), 1.30-2.05 (m, 9 H), 3.29-3.45 (m, 4 H), 7.25-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (major, minor), 16.0 (major, minor), 20.0 (major, minor), 26.4 (major), 27.4 (minor), 29.8 (minor), 30.8 (major), 47.1 (major), 47.7 (minor), 48.0 (minor), 49.2 (major), 68.8 (major), 69.4 (minor), 82.4 (minor), 83.4 (major), 126.4, 128.4, 128.6, 136.2 ($^2J_{Se\text{-}C}$ = 9.7 Hz), 163.4; IR(NaCl) 3296, 2958, 1668

(C=O), 1438, 1402, 1200, 1155, 1108, 942, 740, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 323(M^+, 0.2), 166 (100), 157 (9), 82 (8), 77(6). Anal. Calcd for $C_{16}H_{21}NOSe$: C, 59.62; H, 6.57; N, 4.35. Found: C, 59.24; H, 6.28; N, 4.41.

***Se*-Phenyl *N*-butyl-*N*-dec-4-ynylcarbamoselenoate (5d, run 4, Table 2).**
Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90-1.00 (m, 6 H), 1.32-1.87 (m, 12 H), 2.15-2.25 (m, 4 H), 3.30-3.43 (m, 4 H), 7.32-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 14.0, 16.4, 18.7, 20.1, 22.2, 27.1, 28.1, 28.8, 29.7, 29.9, 30.9, 31.1, 47.4, 48.0, 48.1, 49.3, 78.2 (major), 78.8 (minor), 81.2 (minor), 81.8 (major), 126.9, 128.7, 129.0, 136.7 ($^2J_{Se\text{-}C}$ = 10.5 Hz), 163.7; IR(NaCl) 2931, 1674 (C=O), 1402, 1155, 739 cm^{-1}; MS(CI), m/e (relative intensity, %) 394 (M+1, 89), 236 (100). Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 63.98; H, 7.96; N, 3.57.

***Se*-Phenyl *N*-butyl-*N*-hex-5-ynylcarbamoselenoate (5e, run 5, Table 2).**
Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90-1.00 (m, 3 H), 1.28-1.99 (m, 9 H), 2.19-2.28 (m, 2 H), 3.28-3.37 (m, 4 H), 7.25-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (major, minor), 18.2 (major, minor), 20.2 (major, minor), 25.7 (major, minor), 26.9 (major), 27.9 (minor), 29.9 (minor), 31.0 (major), 47.6 (major), 47.9 (minor), 48.6 (minor), 48.9 (major), 68.6 (major), 68.9 (minor), 83.5 (minor), 83.9 (major), 126.6, 128.5, 128.8, 136.4 ($^2J_{Se\text{-}C}$ = 9.7 Hz), 163.4; IR(NaCl) 3296, 2956, 1673 (C=O), 1438, 1402, 1199, 1149, 1107, 740, 690, 631 cm^{-1}; MS(EI), m/e (relative intensity, %) 357(M^+, 0.6), 180 (100), 157 (10), 81 (71), 79 (22). Anal. Calcd for $C_{17}H_{23}NOSe$: C, 60.71; H, 6.89; N, 4.16. Found: C, 60.48; H, 6.81; N, 4.36.

***Se*-Phenyl *N*-butyl-*N*-hept-6-ynylcarbamoselenoate (5f, run 6, Table 2).**
Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90-0.99 (m, 3 H), 1.20-1.66 (m, 10 H), 1.92-1.96 (m, 1 H), 2.16-2.23 (m, 2 H), 3.25-3.34 (m, 4 H), 7.32-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$ at -40 °C); 14.1, 18.3, 18.4, 20.1, 25.8 (two peaks overlapped), 27.2, 27.9, 28.0, 28.2, 29.7, 30.7, 47.8, 48.8, 48.9, 68.4, 68.6, 84.2, 84.3, 126.0, 126.1, 128.6, 128.8, 136.5, 163.3, 163.4; IR(NaCl) 2934, 2862, 1682 (C=O), 1477, 1402, 1199, 1142, 1108, 740 cm^{-1}; MS(EI), m/e (relative intensity, %) 351 (M^+, 0.2), 194 (100), 157 (16), 138 (27), 95 (71). Anal. Calcd for $C_{18}H_{25}NOSe$: C, 61.71; H, 7.19; N, 4.00. Found: C, 61.57; H, 7.23; N, 4.10.

***S*-Phenyl *N*-methyl-*N*-prop-2-ynylcarbamothiolate (7, eq 3).**

Into a 50-mL flask equipped with a dropping funnel were placed *N*-methyl *N*-prop-2-ynylcarbamoyl chloride (4.3 mmol) and THF (15 mL) under Ar. A solution of benzenethiol (4.7 mmol) and pyridine (21.5 mmol) in 5 mL of THF was added dropwise at 0°C. The mixture was then warmed up to room temperature and stirred overnight. After white

precipitates were filtered off, Et_2O was added to the filtrate and washed with brine, and dried with $MgSO_4$. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et_2O = 3/1) afforded **7** in 66% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (brs, 1 H), 3.12 (brs, 3 H), 4.21 (brs, 2 H) 7.37-7.50 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.1, 37.8, 72.5, 77.5, 128.8, 128.5, 128.9, 135.3, 166.6(br); IR(NaCl) 3292, 3060, 2918, 1666 (C=O), 1476, 1441, 1375, 1262, 1199, 1077, 750, 689 cm^{-1}; MS(EI), m/e (relative intensity, %) 205 (M^+, 12), 109 (17), 96 (100). Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.07; H, 5.41; N, 6.72.

***Se*-Phenyl 2,2-dimethylpent-4-ynoylselenoate (9a, runs 1-3, Table 3).**

Selenol ester **9a** was prepared from 2,2-dimethylpent-4-ynoyl chloride[25] according to the typical procedure of carbamoselenoates and was purified by silica gel column chromatography (*n*-hexane/Et_2O = 10/1); 34% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 6 H), 2.06 (t, J = 2.7 Hz, 1 H), 2.50 (d, J = 2.7 Hz, 2 H), 7.34-7.49 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 29,3, 52.2, 71.0, 79.9, 125.5, 128.4, 128.8, 135.9 ($^2J_{Se\text{-}C}$ = 9.2 Hz), 205.8; IR(NaCl) 3295, 2971, 1714 (C=O), 1465, 1366, 911, 739, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 266 (M^+, 4), 157 (10), 109 (52), 81 (100). Anal. Calcd for $C_{13}H_{14}OSe$: C, 58.88; H, 5.32. Found: C, 58.87; H, 5.32.

***Se*-Phenyl 4-pentynecarboselenoate (9b, runs 4 and 5, Table 3)**

Into a 50-mL flask were placed Ph_2Se_2 (15 mmol), CH_2Cl_2 (23 mL) and 4-pentynoic acid (10 mmol) under N_2 and then $^nBu_3P$ (15 mmol) and CH_2Cl_2 (3 mL) were added cooling with ice-bath, and the stirring was continued for 4 h at room temperature. After the mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (30 mL x 3) and Et_2O (30 mL x 2), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 10/1) to afford *Se*-phenyl 4-pentynecarboselenoate (**9b**) in 69% yield as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.00 (t, J = 2.8 Hz, 1 H), 2.55 (td, J = 2.8 Hz, 7.2 Hz, 2 H), 2.94 (t, J = 7.2 Hz, 2 H), 7.35-7.40 (m, 3 H), 7.49-7.53 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 45.7, 69.4, 81.4, 125.6, 128.9, 129.0, 135.3, 197.9; IR (NaCl) 3294, 3058, 1720 (C=O), 1578, 1438, 1044, 961, 740 cm^{-1}; MS (EI) m/z (relative intensity, %) 238 (M^+, 5), 157 (8), 81 (100), 53 (45). Anal. Calcd for $C_{11}H_{10}OSe$: C, 55.71; H, 4.25. Found: C, 55.75; H, 4.22.

***Se*-Phenyl hex-5-ynoylselenoate (9c, run 6, Table 3).**

Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87-1.94 (m, 2 H), 2.00 (t, J = 2.7 Hz, 1 H), 2.29 (tt, J = 2.7 , 7.3 Hz, 2 H), 2.86 (t, J = 7.6 Hz, 2 H), 7.36-7.52 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$); 17.6, 23.9, 46.0, 69.5, 82.9, 126.3, 128.9, 129.4, 135.8, 199.8; IR(NaCl) 3296,

3059, 2940, 1715 (C=O), 1579, 1478, 1439, 1066, 960, 740 cm^{-1}; MS(CI), m/e (relative intensity, %) 253 (M+1, 100), 95 (80). Anal. Calcd for $C_{12}H_{12}OSe$: C, 57.38; H, 4.82. Found: C, 57.57; H, 4.86.

***Se*-Phenyl hept-6-ynoylselenoate (9d, runs 7 and 8, Table 3).**

Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.55-1.63 (m, 2 H), 1.78-1.85 (m, 2 H), 1.96 (t, J = 2.6 Hz, 1 H), 2.21 (tt, J = 2.6 , 7.1 Hz, 2 H), 2.73 (t, J = 7.1 Hz, 2 H), 7.35-7.52 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$); 18.1, 24.3, 27.4, 46.9, 68.8, 83.6, 126.4, 128.9, 129.3, 135.8, 200.0; IR(NaCl) 3296, 3059, 2945, 1715 (C=O), 1580, 1478, 1439, 1087, 952, 740 cm^{-1}; MS(CI), m/e (relative intensity, %) 267 (M+1, 100), 109 (61). Anal. Calcd for $C_{13}H_{14}OSe$: C, 58.87; H, 5.32. Found: C, 58.67; H, 5.33.

***Se*-Phenyl *N*-pent-4-ynyl-*N*-prop-2-ynylcarbamoselenoate (16, eq 5).**

Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.80-2.33 (m, 6 H), 3.58 (t, J = 7.4 Hz, 2 H), 4.23 (brs, 2 H), 7.33-7.61 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9 (major, minor), 26.4 (minor), 26.9 (major), 36.2 (major), 38.6 (minor), 47.3 (major, minor), 68.9 (minor), 69.5 (major), 72.5 (major), 73.2 (minor), 77.5 (minor), 77.8 (major), 82.4 (major), 82.9 (minor), 125.9 ($^1J_{Se\text{-}C}$ = 93.2 Hz), 128.7 (two peaks overlapped), 136.3 ($^2J_{Se\text{-}C}$ = 10.6 Hz), 164.2; IR(NaCl) 3295, 2937, 1668 (C=O), 1440, 1394, 1259, 1186, 1153, 1065, 741, 690 cm^{-1}; MS(EI), m/e (relative intensity, %) 305(M^+, 1), 157 (11), 148 (100), 120(14), 77(10), 68(18). Anal. Calcd for $C_{15}H_{15}NOSe$: C, 59.22; H, 4.97; N, 4.60. Found: C, 58.95; H, 4.88; N, 4.47.

Procedures and Characterization of Reaction Products

(*Z*)-*N,N*-Dimethy-3-(phenylseleno)non-2-enamide (2, eq 1).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **1** (0.5 mmol), toluene (0.3 mL), 1-octyne (1.5 mmol), and $Pd(PPh_3)_4$ (0.025 mmol) at room temperature under Ar and the solution turned immediately red. After the mixture was refluxed for 14 h, excess 1-octyne and toluene were removed *in vacuo*. The crude product was separated by preparative TLC (*n*-hexane/Et_2O = 5/1) to give (Z)-*N,N*-dimethy-3-(phenylseleno)non-2-enamide (**2**) in 40% yield: brown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, J = 7.3 Hz, 3 H), 1.02-1.37(m, 8 H), 2.19 (t, J = 7.3 Hz, 2 H), 3.02 (s, 3 H), 3.07 (s, 3 H), 6.48 (s, 1 H), 7.27-7.38 (m, 3 H), 7.66-7.68 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.3, 28.4, 29.9, 31.2, 35.4, 37.4, 37.9, 112.9, 128.2, 128.4, 128.9, 137.0 ($^2J_{Se\text{-}C}$ = 9.7 Hz), 158.5, 166.9; NOE experiment: irradiation of the vinyl singlet at δ 6.48 resulted in 13% and 6% enhancements of the signals at δ 3.02-3.07 (NMe_2) and δ 2.19 (C-3 methylene triplet), respectively; IR(NaCl) 2928, 2857, 1622 (C=O), 1574, 1395, 1316, 1262, 1161, 818, 743, 696. cm^{-1}; MS(EI), m/e (relative intensity, %) 339 (M^+, 10), 295 (10), 182 (100), 157 (4),

72(36). Anal. Calcd for $C_{17}H_{25}NOSe$: C, 60.35; H, 7.45; N, 4.14. Found: C, 60.27; H, 7.37; N, 4.10.

(*Z*)-1-Methyl-3-phenylselenomethyleneazetidin-2-one (4a, runs 1 and 2, Table 1).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3a** (0.4 mmol), toluene (0.5 mL), and $Pd(PPh_3)_4$ (0.020 mmol) at room temperature under Ar and the solution turned immediately red. After the mixture was refluxed for 1 h, toluene was removed *in vacuo*. The crude product was purified by preparative recycling HPLC (eluted with $CHCl_3$) to provide (*Z*)-1-methyl-3-phenylselenomethyleneazetidin-2-one (**4a**) in 74% yield: white solid; mp 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.97 (s, 3 H), 3.72 (s, 2 H), 6.70 (s, 1 H), 7.32-7.57 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 50.8, 119.6 ($^1J_{Se\text{-}C}$ = 121.7 Hz), 127.7, 129.2, 130.1, 132.6 ($^2J_{Se\text{-}C}$ = 10.6 Hz), 135.3, 163.0; NOE experiment: irradiation of the allylic proton singlet at δ 3.72 resulted in 2.9% enhancement of the signal at δ 6.70 (vinyl singlet); IR(KBr) 3045, 2901, 1728 (C=O), 1578, 1476, 1437, 1416, 1386, 1257, 1242, 1194, 1035, 902, 816, 741, 690, 464 cm^{-1}; MS(EI), m/e (relative intensity, %) 253 (M^+, 100), 251 (49), 250 (19), 249 (19), 195 (49), 157 (31), 115 (65), 77(25). Anal. Calcd for $C_{11}H_{11}NOSe$: C, 52.39; H, 4.40; N, 5.55. Found: C, 52.31; H, 4.28; N, 5.56.

1-Butyl-3-phenylselenomethyleneazetidin-2-one (4b, run 3, Table 1).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3b** (0.4 mmol), toluene (0.5 mL), and $Pd(PPh_3)_4$ (0.020 mmol) at room temperature under Ar and the solution turned immediately red. The mixture was refluxed for 1 h and toluene was removed *in vacuo*. After the NMR yield and the *E*/*Z* ratio were determined by ^{1}H NMR (85%, *E*/*Z* = 2/98), the crude product was purified by preparative recycling HPLC (eluted with $CHCl_3$) to provide 1-*n*-Butyl-3-phenylselenomethyleneazetidin-2-one (**4b**) in 60% yield. An attempt for isolation of isomers failed, so the following spectra and analytical data were obtained from the *E*/*Z* mixture: brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* =7.3 Hz, 3 H), 1.31-1.40 (tq, *J* = 7.3 , 7.1 Hz, 2 H), 1.50-1.58 (dt, *J* = 7.1, 7.3 Hz, 2 H), 3.27 (t, *J* =7.3 Hz, *E* (2H)), 3.32 (t, *J* =7.3 Hz, *Z* (2 H)), 3.49 (s, *E* (2 H)) 3.71 (s, *Z* (2 H)), 6.69 (s, *Z* (1 H)), 7.19 (s, *E* (1 H)), 7.29-7.31 (m, 3 H), 7.54-7.57 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (*E*), 13.8 (*Z*), 20.2 (*E*), 20.3 (*Z*), 29.8 (*Z*), 29.9 (*E*), 41.6 (*E*), 41.7 (*Z*), 48.3 (*Z*), 48.9 (*E*), 118.6, 119.6 ($^1J_{Se\text{-}C}$ = 121.2 Hz (*Z*)), 127.7, 128.2, 129.2, 129.3, 130.2, 132.6 Hz ($^2J_{Se\text{-}C}$ = 11.1 Hz (*Z*)), 133.4, 134.8, 162.7 (*Z*); NOE experiment: Irradiation of the allylic proton singlet at δ 3.71 resulted in 2.1% enhancement of the signal at δ 6.69 (vinyl singlet); IR(NaCl) 2956, 1739 (C=O), 1670, 1477, 1393, 1072, 740 cm^{-1}; MS(EI), m/e (relative intensity, %) 295 (M^+, 100), 293 (49), 252 (34), 223 (37), 195 (57), 157 (31), 115 (70), 77(30). Anal. Calcd for $C_{14}H_{17}NOSe$: C, 57.15; H, 5.82; N, 4.76. Found: C, 56.98; H, 5.76; N, 5.56.

(*Z*)-1-Benzyl-3-phenylselenomethyleneazetidin-2-one (4c, run 4, Table 1).

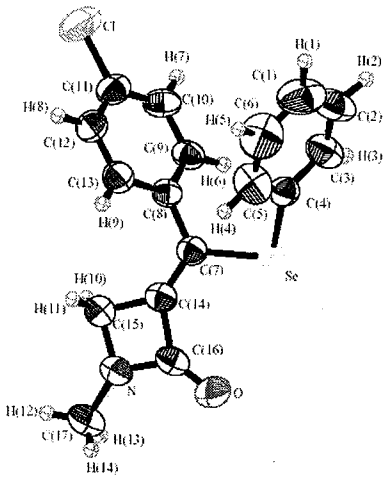
Pure (*Z*)-**4c** was obtained by recrystalization from *n*-hexane/$CHCl_3$ = 1/1: white solid; mp 88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 2 H), 4.51 (s, 2 H), 6.73 (s, 1 H), 7.25-7.37 (m, 8 H), 7.55-7.58 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.1, 48.4, 120.6 ($^1J_{Se\text{-}C}$ = 122.6 Hz), 127.4, 127.6, 127.8, 128.4, 129.0, 129.9, 132.6 ($^2J_{Se\text{-}C}$ = 11.1 Hz), 134.5, 135.1, 162.6; NOE experiment: Irradiation of the allyl-proton singlet at δ 3.62 resulted in 4.5% and 3.1% enhancements of the signals at δ 4.51 (benzyl singlet) and δ 6.73 (vinyl triplet), respectively; IR(KBr) 3060, 1720 (C=O), 1576, 1398, 1345, 1111, 1073, 822, 743, 700 cm^{-1}; MS(EI), m/e (relative intensity, %) 329 (M^+, 46), 195 (26), 157 (8), 115 (30), 91 (100). Anal. Calcd for $C_{17}H_{15}NOSe$: C, 62.20; H, 4.61; N, 4.27. Found: C, 61.88; H, 4.40; N, 4.28.

(*Z*)-1-Benzyl-3-(1-phenylseleno)propylideneazetidin-2-one (4d, run 5, Table 1).

Pure (*Z*)-**4d** was obtained by recrystalization from *n*-hexane/$CHCl_3$ = 1/1: white solid; mp 102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.3, 3 H), 2.07 (q, *J* = 7.3, 2 H), 3.66 (s, 2 H), 4.52 (s, 2 H), 7.27-7.37 (m, 8 H), 7.61-7.64 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 27.8, 46.0, 47.8, 126.9, 127.3, 127.9, 128.0, 128.4, 128.7, 133.0, 135.1, 135.4, 135.5 ($^2J_{Se\text{-}C}$ = 10.6 Hz), 162.6; NOE experiment: Irradiation of the allylic proton singlet at δ 3.66 resulted in 2.2% and 1.6% enhancements of the signals at δ 2.07 (methylene quartet) and δ 4.52 (benzyl singlet), respectively; IR(KBr) 3058, 2969, 1730 (C=O), 1678, 1456, 1393, 1275, 1118, 1072, 962, 855, 749, 704, 638 cm^{-1}; MS(EI), m/e (relative intensity, %) 357 (M^+, 17), 200 (26), 157 (4), 91 (100). Anal. Calcd for $C_{19}H_{19}NOSe$: C, 64.04; H, 5.37; N, 3.93. Found: C, 63.93; H, 5.34; N, 3.95.

(*Z*)-1-Methyl-3-[(*p*-chlorophenyl)phenylselenomethylene]azetidin-2-one (4e, run 6, Table 1).

Pure (Z)-**4e** was obtained by recrystalization from *n*-hexane/$CHCl_3$ = 1/1: pale yellow solid; mp 128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 (s, 3 H), 3.91 (s, 2 H), 7.06-7.32 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 51.1, 127.4, 128.2, 128.3, 128.6, 129.7, 129.9, 133.9 ($^2J_{Se\text{-}C}$ = 11.1 Hz), 134.1, 135.0, 137.7, 162.7; IR (KBr) 3084, 2948, 2874, 1746 (C=O), 1675, 1577, 1381, 1260, 1120, 1081, 750, 704 cm^{-1}; MS(EI), m/e (relative intensity, %) 363 (M^+, 16), 225 (11), 163 (12), 157 (2) 149 (100). Anal. Calcd for $C_{17}H_{14}ClNOSe$: C, 56.29; H, 3.89; N, 3.86. Found: C, 56.26; H, 3.75; N, 3.86. The structure of (*Z*)-**4e** was confirmed by X-ray analysis.



(*Z*)-1-Benzyl-3-phenylselenomethylenepyrrolidin-2-one (6a, run 1, Table 2)
White solid; mp 127.5-128.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (tt, J = 2.1 , 7.0 Hz, 2 H), 3.30 (t, J = 7.0 Hz, 2 H), 4.52 (s, 2 H), 7.03 (t, J = 2.1 Hz, 1 H), 7.26-7.35 (m, 3 H), 7.61-7.63 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 44.2, 47.1, 127.6, 127.7, 128.4, 128.7, 129.2, 130.5, 133.0, 133.3, 136.3 ($^2J_{Se-C}$ = 10.5 Hz), 168.9; NOE experiment: irradiation of the vinylic proton triplet at δ 7.03 resulted in 6.3% enhancement of the signal at δ 2.68 (allylic triplet-triplet); IR (KBr) 3033, 2924, 1667 (C=O), 1490, 1445, 1309, 1256, 1018, 757, 702 cm^{-1}; MS (EI) m/z (relative intensity, %) 343 (M$^+$, 46), 262 (22), 91 (100). Anal. Calcd for $C_{18}H_{17}NOSe$: C, 63.16; H, 5.01; N, 4.09. Found: C, 62.87; H, 5.04; N, 4.15.

(*Z*)-1-Butyl-3-(1-phenylselenoheptylidene)pyrrolidin-2-one (6b, run 2, Table 2).
Colorless oil;^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, J = 7.2 Hz, 3 H), 0.87-1.58 (m, 15 H), 2.10 (t, J = 8.3 Hz, 2 H), 2.70 (t, J = 7.0 Hz, 2 H), 3.33 (t, J = 7.3 Hz, 2 H), 3.41 (t, J = 7.0 Hz, 2 H), 7.28-7.39 (m, 3 H), 7.70-7.71 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 14.0, 20.1, 22.4, 25.0, 28.2, 28.8, 29.4, 31.2, 34.1, 42.8, 44.4, 123.5, 128.1, 128.7 (two peaks overlapped), 138.1, 143.5, 169.0; NOE experiment: irradiation of the allylic proton triplet at δ 2.70 resulted in 2.2% enhancement of the signal at δ 2.10 (allylic proton triplet of *n*-hexyl group); IR (NaCl) 2956, 2859, 1668 (C=O), 1620, 1427, 1294, 742 cm^{-1}; MS (EI) m/z (relative intensity, %) 393 (M$^+$, 7), 236 (100). Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 64.38; H, 8.04; N, 3.69.

(*Z*)-1-Butyl-3-phenylselenomethylenepiperidin-2-one (6c, run 3, Table 2).
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, J = 7.3 Hz, 3 H), 1.30-1.39 (tq, J = 7.3, 7.6 Hz, 2 H), 1.54-1.62 (dt, J = 7.8, 7.3 Hz, 2H), 1.85 (t, J = 5.7 Hz, 2H), 2.52-2.55 (m, 2 H), 3.34 (t, J = 5.7 Hz, 2 H), 3.42 (t, J = 7.6 Hz, 2 H), 7.05 (s, 1 H), 7.28-7.62 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 20.3, 22.9, 29.3, 31.2, 47.4, 48.2, 125.1, 127.2, 128.7, 132.9 ($^2J_{Se-C}$ = 9.2 Hz), 134.9, 137.3 ($^1J_{Se-C}$ = 131.4 Hz), 164.5; NOE experiment: Irradiation of the allylic proton multiplet at δ 2.53 resulted in 8.3% and 8.3% enhancements of the signals at δ 1.85 (C-2 methylene triplet) and δ 7.05 (vinyl singlet), respectively; IR(NaCl) 3330, 2930, 2512, 2102, 1634 (C=O), 1580, 1487, 1348, 1236, 1198, 828, 740, 695 cm^{-1}; MS(EI), m/e (relative intensity, %) 323 (M$^+$, 100), 294 (12), 280 (40), 246 (54), 190 (25), 157 (58), 143 (19), 123 (53), 95 (66), 77 (28). Anal. Calcd for $C_{16}H_{21}NOSe$: C, 59.62; H, 6.57; N, 4.35. Found: C, 59.52; H, 6.51; N, 4.31.

(*Z*)-1-Butyl-3-(1-phenylselenohexylidene)piperidin-2-one (6d, run 4, Table 2).
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (t, J = 7.3 Hz, 3 H), 0.80-1.43 (m, 11 H), 1.55-1.62 (m, 2 H), 1.84-1.88 (m, 2 H), 2.18-2.21 (m, 2 H), 2.54 (t, J = 6.3 Hz, 2 H), 3.33 (t, J

= 5.7 Hz, 2 H), 3.42 (t, J = 7.6 Hz, 2 H), 7.27-7.37 (m, 3 H), 7.69-7.71 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 20.5, 22.1, 23.0, 28.1, 28.5, 29.6, 31.5, 33.4, 47.8, 47.9, 120.3, 128.3, 128.4, 131.4, 137.5 ($^2J_{Se\text{-}C}$ = 9.6 Hz), 150.7, 165.5; NOE experiment: irradiation of the allylic proton triplet (*n*-pentyl group) at δ 2.54 resulted in 5.3% enhancement of the multiplet at δ 2.18-2.21 (allylic multiplet on the ring); IR (NaCl) 2930, 2859, 1622 (C=O), 1455, 1310, 1200, 743 cm^{-1}; MS (EI) m/z (relative intensity, %) 393 (M^+, 7), 236 (100). HRMS calcd for $C_{21}H_{31}NOSe$: 393.1571. Found 393.1569.

(*Z*)-1-Butyl-3-phenylselenomethyleneazepan-2-one (6e, run 5, Table 2).
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.6 Hz, 3 H), 1.33-1.76 (m, 8 H), 2.41-2.44 (m, 2 H), 3.35 (t, J = 6.1 Hz, 2 H), 3.44 (t, J = 7.6 Hz, 2 H), 6.86 (s, 1 H), 7.27-7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.3, 27.2, 27.3, 30.3, 33.0, 48.2, 48.3, 127.1, 128.9, 130.7, 132.5, 132.8, 136.1, 164.5; NOE experiment: Irradiation of the allylic proton multiplet at δ 2.42 resulted in 12.7% and 7.8% enhancements of the signals at δ 1.73 (C-2 methylene multiplet) and δ 6.86 (vinyl singlet), respectively; IR(NaCl) 2930, 1621 (C=O), 1477, 1423, 1236, 822, 741, 693 cm^{-1}; MS(EI), m/e (relative intensity, %) 337 (M^+, 100), 294 (28), 256 (31), 206 (12), 180 (38), 157 (15), 138 (35), 126 (34), 77 (19). Anal. Calcd for $C_{17}H_{23}NOSe$: C, 60.71; H, 6.89; N, 4.16. Found: C, 60.56; H, 6.93; N, 4.21.

(*Z*)-1-Butyl-3-phenylselenomethyleneazocan-2-one (6f, run 6, Table 2).
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, J = 7.4 Hz, 3 H), 1.36-1.67 (m, 10 H), 2.49 (t, J = 5.6 Hz, 2 H), 3.38 (t, J = 7.5 Hz, 2 H), 3.46 (t, J = 5.6 Hz, 2 H), 6.41 (s, 1 H), 7.24-7.51 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 20.5, 24.7, 27.3, 29.2, 29.9, 39.1, 44.2, 46.5, 117.2, 127.0, 129.0, 130.4, 132.0 ($^2J_{Se\text{-}C}$ = 11.5 Hz), 143.1, 170.6; NOE experiment: irradiation of the allylic proton triplet at δ 2.49 resulted in 6.0% enhancement of the signal at δ 6.41 (vinylic singlet); IR (NaCl) 2929, 1634 (C=O), 1477, 1428, 1192, 738 cm^{-1}; MS (EI) m/z (relative intensity, %) 351 (M^+, 100), 270 (25), 194 (86), 166 (90). Anal. Calcd for $C_{18}H_{25}NOSe$: C, 61.71; H, 7.19; N, 4.00. Found: C, 61.96; H, 7.36; N, 3.94.

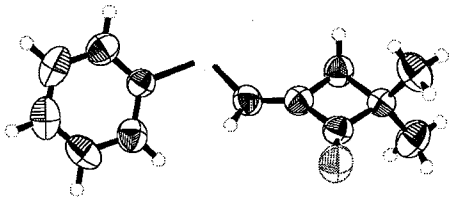
(*Z*)-1-Methyl-3-phenylthiomethyleneazetidin-2-one (8, eq 3).
Pale yellow solid; mp 128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 3 H), 3.73 (s, 2 H), 6.40 (s, 1 H), 7.27-7.43 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 49.6, 122.7, 127.2, 128.9, 129.7, 133.3, 134.5, 162.2; NOE experiment: Irradiation of the allylic proton singlet at δ 3.73 resulted in 1.6% enhancement of the signal at δ 6.40 (vinyl singlet); IR(KBr) 3037, 2948, 1726 (C=O), 1582, 1480, 1384, 1253, 1193, 1088, 1031, 901, 843, 792, 749, 692 cm^{-1}; MS(EI), m/e (relative intensity, %) 205 (M^+, 73), 147 (100), 134 (28), 109 (10), 96 (4), 77(5). Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.08; H, 5.31; N, 6.80.

2,2-Dimethyl-4-phenylselenomethylenecyclobutanone (10a, runs 1-3, Table 3).

For run 2: Into a 3-mL flask equipped with a reflux condenser were placed selenol ester **9a** (0.96 mmol), toluene (1.25 mL), and $Pd(PPh_3)_4$ (0.048 mmol) at room temperature under Ar and the solution turned immediately red. The mixture was refluxed for 1 h and toluene was removed *in vacuo*. After the NMR yield and the *E/Z* ratio were determined by ^{1}H NMR (73%, *E/Z* = 74/26), the crude product was purified by twice preparative TLC (*n*-hexane/Et_2O = 8/1 and *n*-hexane/Et_2O = 20/1, respectively) to provide pure (*E*)- and (*Z*)-**10a**.

(*Z*)-**10a**: yellow solid: mp 39 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 6 H), 2.42 (d, *J* = 2.0 Hz, 2 H), 7.00 (t, *J* = 2.0 Hz, 1 H), 7.33-7.36 (m, 3 H), 7.56-7.59 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 39.9, 56.6, 120.9, 128.0, 129.3, 130.5, 133.3 ($^2J_{Se\text{-}C}$ = 11.1 Hz), 139.2, 203.7; NOE experiment: Irradiation of the allylic proton doublet at δ 2.42 resulted in 2.3% enhancement of the signal at δ 7.00 (vinyl singlet); IR(KBr) 2924, 1729 (C=O), 1602, 1478, 1439, 1275, 1058, 999, 742, 692, 465 cm^{-1}; MS(EI), m/e (relative intensity, %) 266 (M^+, 37), 238 (29), 182 (83), 180 (41), 157 (23), 109 (59), 102 (42), 81 (100), 77 (44). HRMS calcd for $C_{13}H_{14}OSe$: 266.0210. Found 266.0204.

(*E*)-**10a**: pale yellow solid: mp 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 6 H), 2.24 (d, *J* = 2.9 Hz, 2 H), 7.33-7.36 (m, 3 H), 7.55-7.57 (m, 2 H), 7.72 (t, *J* = 2.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 38.6, 56.7, 128.0, 128.3, 129.3, 130.5, 133.3 ($^2J_{Se\text{-}C}$ = 10.6 Hz), 143.0, 200.8; IR(KBr) 2954, 1733 (C=O), 1609, 1466, 1438, 1269, 1183, 1089, 1020, 832, 743, 688, 466 cm^{-1}; MS(EI), m/e (relative intensity, %) 266 (M^+, 24), 238 (33), 182 (47), 180 (23), 157 (18), 109 (20), 102 (25), 81 (100), 77 (33). HRMS calcd for $C_{13}H_{14}OSe$: 266.0210. Found 266.0219. The structure of (*E*)-**10a** was confirmed by X-ray analysis.



2-Phenylselenomethylene cyclobutanone (10b, runs 4 and 5, Table 3).

Since isomerization proceeded under purification, each isomers could not be separated: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40-2.44 (m, *E* (2 H)), 2.60-2.64 (m, *Z* (2 H)), 2.95-2.99 (m, *E, Z* (2 H)), 6.96 (t, *J* = 2.1 Hz, *Z* (1 H)), 7.26-7.59 (m, 5 H), 7.63 (t, *J* = 2.8 Hz, *E* (1 H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 23.2, 43.9 (two peaks overlapped), 128.0, 128.3, 128.6 (two peaks overlapped), 129.2, 129.6, 130.5, 133.0, 133.5, 133.6, 143.1, 146.9, 194.5; NOE experiment for *Z*-isomer: irradiation of the allylic proton multiplet at δ 2.60-2.64 resulted in 2.3% enhancement of the signal at δ 6.96 (vinylic triplet); IR (NaCl) 3056, 2930, 1745 (C=O), 1614, 1478, 1393, 1218, 1089, 819, 738 cm^{-1}; MS (EI) m/z (relative intensity, %) 238 (M^+, 27), 210 (100), 182 (21), 129 (46). Anal. Calcd for $C_{11}H_{10}OSe$: C, 55.71; H, 4.25. Found: C, 55.75; H, 4.35.

2-Phenylselenomethylene pentenone (10c, run 6, Table 3).

White solid; mp 70.0-71.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (tt, J = 7.6 , 7.7 Hz, 2 H), 2.39 (t, J = 7.7 Hz, 2 H), 2.66 (dt, J = 2.0 , 7.6 Hz, 2 H), 7.31-7.38 (m, 3 H), 7.39 (t, J = 2.0 Hz, 1 H), 7.58-7.62 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 31.3, 38.8, 128.1, 129.3, 133.1 ($^2J_{Se\text{-}C}$ = 8.3 Hz), 133.2, 137.4, 207.2; NOE experiment: irradiation of the vinylic proton triplet at δ 7.40 resulted in 3.2% enhancement of the signal at δ 2.66 (allylic doublet-triplet); IR (KBr) 2956, 2896, 1684 (C=O), 1578, 1442, 1312, 1272, 1154, 1070, 746 cm^{-1}; MS (EI) m/z (relative intensity, %) 252 (M^+, 100), 171 (37), 157 (23), 115 (42). Anal. Calcd for $C_{12}H_{12}OSe$: C, 57.38; H, 4.82. Found: C, 57.46; H, 4.83.

2-Phenylselenomethylene cyclohexenone (10d, runs 7 and 8, Table 3).

Purification by HPLC ($CHCl_3$) to provide pure (*Z*)-**10d** and (*E*)-**10d**.

(*Z*)-**10d**: Slight yellow solid; mp 69.0-69.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72-1.78 (m, 2 H), 1.85-1.91 (m, 2 H), 2.49 (t, J = 6.7 Hz, 2 H), 2.60 (dt, J = 1.6 , 6.6 Hz, 2 H), 7.31-7.35 (m, 3 H), 7.40 (t, J = 1.6 Hz, 1 H), 7.58-7.62 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0, 23.5, 38.8, 128.0, 129.2, 131.8, 133.0 ($^2J_{Se\text{-}C}$ = 9.6 Hz), 134.8, 144.1, 199.7; NOE experiment: irradiation of the vinylic proton triplet at δ 7.40 resulted in 10.5% enhancement of the signal at δ 2.60 (allylic doublet-triplet); IR (KBr) 3056, 2934, 2868, 1646 (C=O), 1519, 1478, 1338, 1150, 938, 815, 740 cm^{-1}; MS (EI) m/z (relative intensity, %) 266 (M^+, 100), 189 (61), 157 (18), 129 (24). Anal. Calcd for $C_{13}H_{14}OSe$: C, 58.87; H, 5.32. Found: C, 58.76; H, 5.30.

(*E*)-**10d**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.79-1.92 (m, 4 H), 2.40-2.48 (m, 4 H), 7.31-7.35 (m, 3 H), 7.55-7.58 (m, 2 H), 8.05 (t, J = 1.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 23.4, 29.7, 39.5, 128.3, 129.2, 129.5, 133.2, 135.1, 140.8, 196.3; IR (NaCl) 3056, 2934, 2868, 1646 (C=O), 1519, 1478, 1338, 1150, 938, 815, 740 cm^{-1}; MS (EI) m/z (relative intensity, %) 266 (M^+, 100), 189 (46), 157 (28), 129 (22). HRMS calcd for $C_{13}H_{14}OSe$: 266.0210. Found 266.0213.

1-Pent-4-ynyl-3-phenylselenomethyleneazetidin-2-one (17a, eq 5) ***and***
1-Prop-2-ynyl-3-phenylselenomethylenepiperidin-2-one (17b, eq 5).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **16** (0.85 mmol), toluene (4 mL), and $Pd(PPh_3)_4$ (0.085 mmol) at room temperature under Ar and the solution turned immediately red. After the mixture was refluxed for 1 h, toluene was removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/Et_2O = 2/1) to provide colorless oil of **17a** (50%, *E*/*Z* = 5/95) and white solid of **17b** (10%, *E*/*Z* = 11/89). The following spectra and analytical data were obtained from *E*/*Z* mixtures.

17a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77-1.84 (tt, J = 7.1, 6.8 Hz, 3 H), 2.00 (t, J = 2.7 Hz, 1 H), 2.24-2.28 (dt, J = 2.7, 7.1 Hz, 2 H), 3.44 (t, J = 6.8 Hz, 2 H), 3.51 (s, *E* (2 H)), 3.75 (s, *Z* (2

H)), 6.73 (s, *Z* (1 H)), 7.22 (s, *E* (1 H)), 7.31-7.57 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (*E*, *Z*), 26.5 (*E*), 26.6 (*Z*), 40.9 (*E*), 41.0 (*Z*), 48.4 (*E*), 49.2 (*Z*), 69.1, 82.6, 118.5, 120.1 ($^1J_{Se\text{-}C}$ = 122.2 Hz, (*Z*)), 127.6, 128.1, 129.0, 129.1, 129.9, 132.5 ($^2J_{Se\text{-}C}$ = 11.1 Hz, (*Z*)), 133.3, 134.3, 138.0, 162.7 (*Z*); NOE experiment: Irradiation of the allylic proton singlet at δ 3.75 resulted in 3.9% enhancement of the signal at δ 6.73 (vinyl singlet); IR(NaCl) 3293, 3055, 2948, 1732 (C=O), 1674, 1478, 1439, 1393, 1247, 1118, 1022, 826, 742, 692 cm^{-1}; MS(EI), m/e (relative intensity, %) 305 (M^+, 16), 224 (76), 195 (27), 157 (23), 148 (100), 115 (41), 95 (14), 77 (29). Anal. Calcd for $C_{15}H_{15}NOSe$: C, 59.22; H, 4.97; N, 4.60. Found: C, 58.83; H, 4.84; N, 4.58.

17b: mp 78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.89-1.95 (tt, *J* = 6.1, 5.9 Hz, 3 H), 2.20 (t, *J* = 2.4 Hz, 1 H), 2.55-2.58 (t, *J* = 6.1 Hz, 2 H), 3.34 (t, *J* = 5.7 Hz, *E* (2 H)), 3.49 (t, *J* = 5.9 Hz, *Z* (2 H)), 4.12 (d, *J* = 6.3 Hz, *E* (2 H)), 4.33 (d, *J* = 2.4 Hz, *Z* (2 H)), 7.15 (s, *Z* (1 H)), 7.30-7.63 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2 (*E*), 22.5 (*Z*), 27.8 (*E*), 31.0 (*Z*), 35.7 (*Z*), 36.1 (*E*), 46.9 (*E*), 47.1 (*Z*), 71.5, 71.7, 77.0, 78.3, 124.5, 127.3, 127.6, 128.7, 129.0, 132.6, 132.9 ($^2J_{Se\text{-}C}$ = 9.2 Hz, (*Z*)), 134.4, 139.1 ($^1J_{Se\text{-}C}$ = 133.2 Hz, (*Z*)), 164.3 (*Z*); NOE experiment: Irradiation of the allylic proton triplet at δ 2.53 resulted in 7.3% and 6.5% enhancements of the signals at δ 1.92 (C-3 methylene quintet) and δ 7.15 (vinyl singlet), respectively.; IR(KBr) 3252, 2943, 1624 (C=O), 1578, 1486, 1351, 1234, 1198, 947, 831, 741, 696 cm^{-1}; MS(EI), m/e (relative intensity, %) 305 (M^+, 100), 303 (50), 225 (82), 157 (15), 148 (11), 129 (13), 115 (13), 77 (20). $C_{15}H_{15}NOSe$: C, 59.22; H, 4.97; N, 4.60. Found: C, 59.09; H, 4.96; N, 4.61.

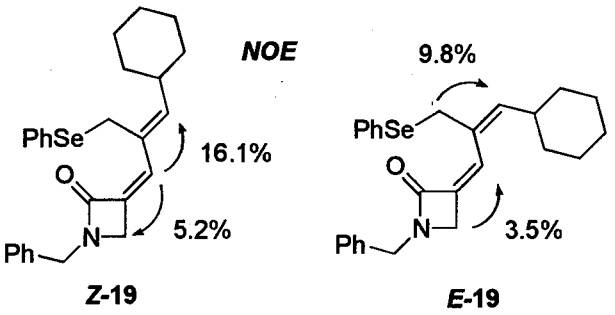
1-Benzyl-3-*sec*-butylidene azetidin-2-one (18, eq 6).

Into a 10-mL flask were placed copper iodide (0.52 mmol) and Et_2O (3 mL) under N_2 and the suspension was cooled to -15 °C (ethylene glycol/CO_2 bath). MeLi (1.00 M in Et_2O, 1.1 mL, 1.1 mmol) was added slowly to prepare Me_2CuLi and stirring was continued for 1 h. To the colorless solution of Me_2CuLi was then added (*Z*)-**4d** (0.4 mmol) at the same temperature, and the mixture was turned yellow immediately. After stirring for 1 h at the same temperature, the purple-red solution was obtained. The mixture was poured into Et_2O (50 mL) and filtered through celite-pad to remove yellow precipitates. The solvents were removed *in vacuo* and the residue was purified by preparative PTLC (*n*-hexane/Et_2O = 1/1) to afford 1-benzyl-3-*sec*-butylidene azetidin-2-one (**18**) in 94% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.6 Hz, 3 H), 1.99 (q, *J* = 7.6 Hz, 2 H) 2.06 (s, 3 H), 3.57 (s, 2 H), 4.47 (s, 2 H), 7.24-7.36 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 17.3, 28.3, 45.8, 46.7, 127.6, 128.1, 128.7, 130.5, 136.2, 140.1, 164.9; NOE experiment: irradiation of the allylic proton singlet at δ 3.57 resulted in 5.5% enhancement of the signal at δ 1.99 (allylic quartet); IR (NaCl) 2968, 2877, 1738 (C=O), 1455, 1386, 1272, 1076, 960, 735 cm^{-1}; MS (EI) m/z (relative intensity, %) 215 (M^+, 100), 91 (64). HRMS calcd for $C_{14}H_{17}ON$: 215.1310. Found

215.1303.

1-Benzyl-3-(3-cyclohexyl-2-phenylselenomethyl-allylidene)-azetidin-2-one (19, eq 7).

Into a 3-mL flask equipped with a reflux condenser were placed β-lactam (*Z*)-**4c** (0.40 mmol), toluene (0.3 mL), cyclohexylallene (0.48 mmol) and $Pd(PPh_3)_4$ (0.005 mmol) at room temperature under N_2 and the solution turned immediately brown. After the mixture was refluxed for 13 h, filtered through the celite pad, toluene was removed *in vacuo*. The crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O = 3/1) to afford 1-Benzyl-3-(3-cyclohexyl-2-phenylselenomethyl-allylidene)-azetidin-2-one **19** in 77% yield (E/Z = 23/77) as white solid; mp 73.0-74.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82-1.73 (m, 10 H), 1.78-1.87 (m, *Z* (1 H)), 2.18-2.28 (m, *E* (1 H)), 3.56 (s, *Z* (2 H)), 3.62 (s, *E* (2 H)), 4.13 (s, $^2J_{Se\text{-}C}$ = 12.9 Hz, *E* (2 H)), 4.26 (s, $^2J_{Se\text{-}C}$ = 11.0 Hz, *Z* (2 H)), 4.50 (s, *Z* (2 H)), 4.52 (s, *E* (2 H)), 5.03 (d, *J* = 9.5 Hz, *E* (2 H)), 5.52 (d, *J* = 10.0 Hz, *Z* (2 H)), 5.83 (s, *Z* (2 H)), 6.21 (s, *E* (2 H)), 7.22-7.75 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 25.6, 25.7, 25.8, 26.7, 32.5, 32.8, 34.7, 37.3, 37.6, 46.2, 46.3, 46.8, 47.0, 122.9, 127.0, 127.1, 127.4, 127.9, 128.2, 128.3, 128.4, 128.5 (two peaks overlapped), 130.2 (two peaks overlapped), 131.2, 132.2, 132.3, 132.4, 133.2, 134.8, 134.9 (two peaks overlapped), 135.0, 135.3, 135.4, 135.6, 143.5, 146.2, 162.1, 162.2; NOE experiment for *Z*-isomer: irradiation of the vinylic proton singlet at δ 5.83 resulted in 16.1% and 5.2% enhancements of the signal at δ 5.52 (vinylic doublet) and the signal δ 3.56 (allyic singlet proton on the ring); NOE experiment for *E*-isomer: irradiation of the allylic proton (on the ring) singlet at δ 3.62 resulted 3.5% enhancement of the signal at δ 6.21 (vinylic singlet) and irradiation of the allylic proton (-CH_2SePh) singlet at δ 4.13 resulted 9.8% enhancement of the signal at δ 5.03 (vinylic doublet). Summary of the results shown below; IR (KBr) 2920, 2845, 1719 (C=O), 1436, 1391, 1276, 984, 738, 701 cm^{-1}; MS (CI) m/z (relative intensity, %) 452 (M+1, 100), 294 (47). Anal. Calcd for $C_{26}H_{29}NOSe$: C, 69.32; H, 6.49; N, 3.11. Found: C, 69.34; H, 6.63; N, 2.91.



Computational Details

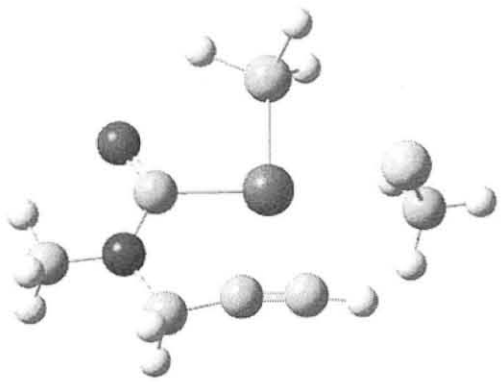
All calculations were performed with a Gaussian 03 package.[26] Density functional theory (DFT) method was employed using the B3LYP hybrid functional.[27] Structure were optimized with a basis set consisting of the LANL2DZ basis set for metallic atoms (Se, Pd)[28] and 6-31+G(d) for the rest. These method and basis sets used have been applied to the recent reports on Ni-catalyzed cross-coupling reaction using aryl fluorides[29] and Pd-catalyzed

allylstannylaion of alkynes.[30] Stationary points was confirmed by normal coordinate analysis (no imaginary frequency for an equilibrium structure and one imaginary frequency for a transition state). The intrinsic reaction coordinate (IRC) analysis[31] for each transition states were carried out to confirm that stationary points are smoothly connected to the corresponding equilibrium structures.

Energies and Ball-Stick Models of Stationary Points (Scheme 3 and 4)

(Cartesian coordinates were not shown here for simplification. For all data, see the published paper.[32])

A(1)

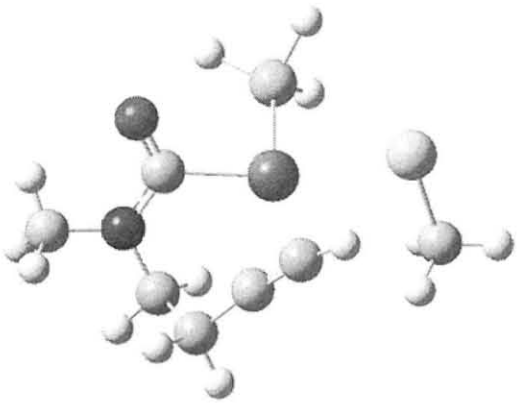


04_OxidativeAdduct_PH3_SeMe_N-Me_b3lyp

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-843.13513849	a.u.
RMS Gradient Norm	0.00000554	a.u.
Imaginary Freq	0	
Dipole Moment	3.1814	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 38 minutes 19.0 seconds.

A(2)

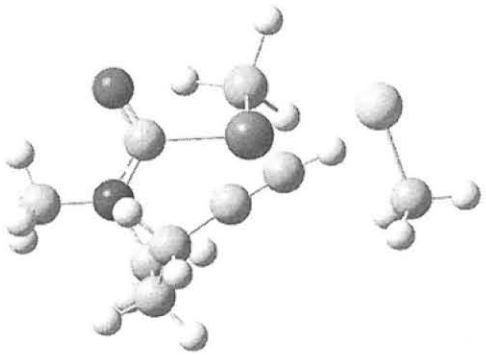


05_OxidativeAdduct_gammma_PH3_SeMe_N-Me_b3lyp

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-882.44924706	a.u.
RMS Gradient Norm	0.00001094	a.u.
Imaginary Freq	0	
Dipole Moment	6.0378	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 34 minutes 30.0 seconds.

A(3)

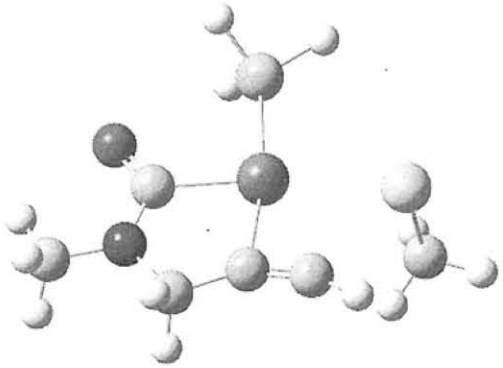


07_OxidativeAdduct_delta_PH3_SeMe_N-Me_b3lyp

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-921.76214833	a.u.
RMS Gradient Norm	0.00000987	a.u.
Imaginary Freq	0	
Dipole Moment	6.0199	Debye
Point Group	C1	

Job cpu time: 0 days 6 hours 20 minutes 1.0 seconds.

TS1(1)

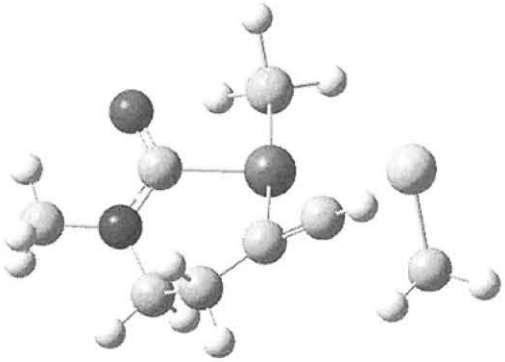


11_beta-lactam_TS-Search

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-843.12187789	a.u.
RMS Gradient Norm	0.00000313	a.u.
Imaginary Freq	1	
Dipole Moment	2.2507	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 37 minutes 13.0 seconds.

TS1(2)

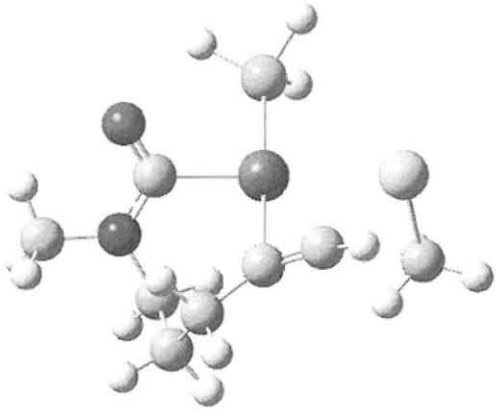


12_gamma-lactam_TS-Search_2

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-882.43252419	a.u.
RMS Gradient Norm	0.00009465	a.u.
Imaginary Freq	1	
Dipole Moment	3.3915	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 27 minutes 29.0 seconds.

TS1(3)

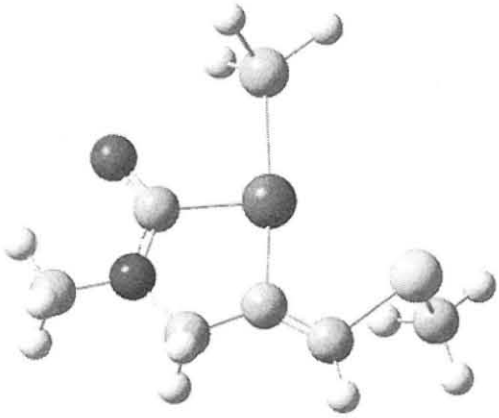


24_(true)_delta-lactam_TS_insertion_Pd-Se_freq

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-921.74552450	a.u.
RMS Gradient Norm	0.00000340	a.u.
Imaginary Freq	1	
Dipole Moment	3.6898	Debye
Point Group	C1	

Job cpu time: 0 days 7 hours 0 minutes 43.0 seconds.

B(1)

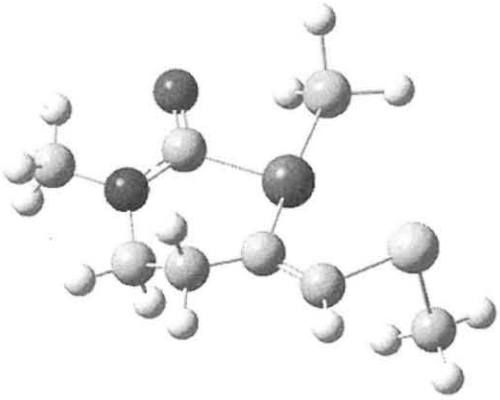


b

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-843.15898091	a.u.
RMS Gradient Norm	0.00001379	a.u.
Imaginary Freq	0	
Dipole Moment	2.1222	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 34 minutes 3.0 seconds.

B(2)

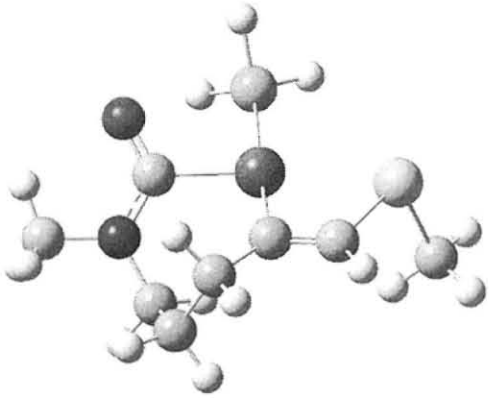


06_6-palladacycle_PH3_SeMe_N-Me_b3lyp.gjf

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-882.46943731	a.u.
RMS Gradient Norm	0.00001933	a.u.
Imaginary Freq	0	
Dipole Moment	2.7065	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 19 minutes 59.0 seconds.

B(3)

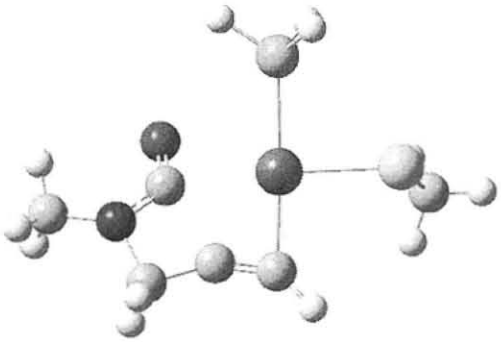


25_7-palladacycle_PH3_SeMe_N-Me

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-921.77973543	a.u.
RMS Gradient Norm	0.00001545	a.u.
Imaginary Freq	0	
Dipole Moment	3.6756	Debye
Point Group	C1	

Job cpu time: 0 days 6 hours 7 minutes 46.0 seconds.

TS2(1)

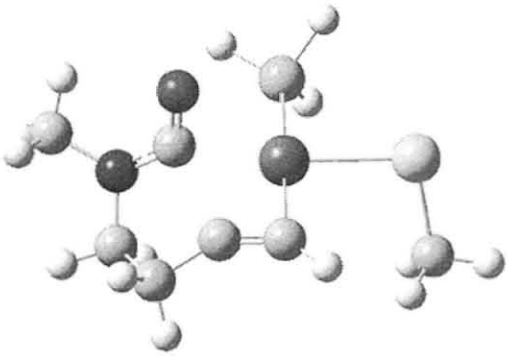


19_beta_insertion_to_Pd-C_5

File Type	.log	
Calculation Type	FTS	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-843.10017762	a.u.
RMS Gradient Norm	0.00000516	a.u.
Imaginary Freq	1	
Dipole Moment	5.1508	Debye
Point Group	C1	

Job cpu time: 1 days 10 hours 13 minutes 8.0 seconds.

TS2(2)

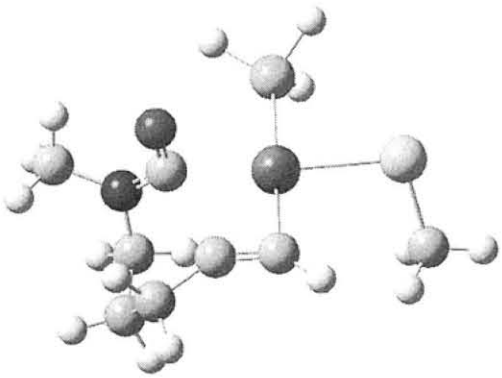


18_gamma_insertion_to_Pd-C_4

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-882.42380715	a.u.
RMS Gradient Norm	0.00000279	a.u.
Imaginary Freq	1	
Dipole Moment	7.4696	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 30 minutes 16.0 seconds.

TS2(3)

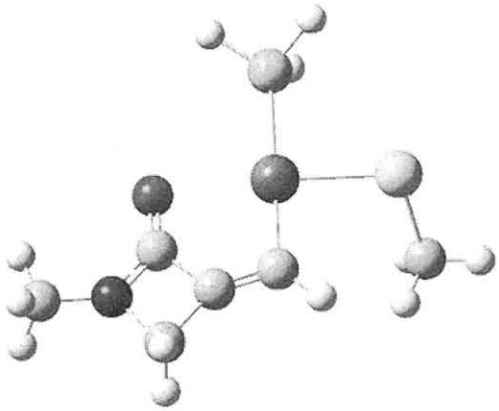


28_delta-lactam_TS_insertion_C-Pd_freq

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-921.73993071	a.u.
RMS Gradient Norm	0.00000279	a.u.
Imaginary Freq	1	
Dipole Moment	7.3242	Debye
Point Group	C1	

Job cpu time: 0 days 6 hours 59 minutes 2.0 seconds.

C(1)

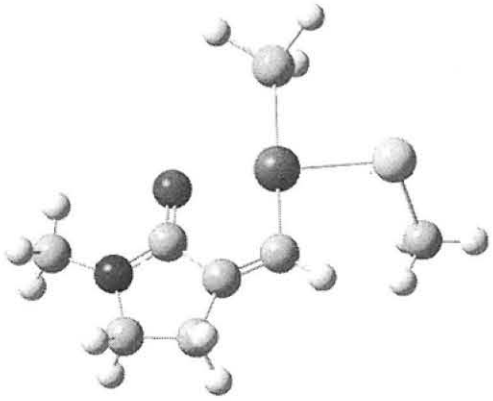


13_c

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-843.14909485	a.u.
RMS Gradient Norm	0.00000521	a.u.
Imaginary Freq	0	
Dipole Moment	3.9993	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 29 minutes 47.0 seconds.

C(2)

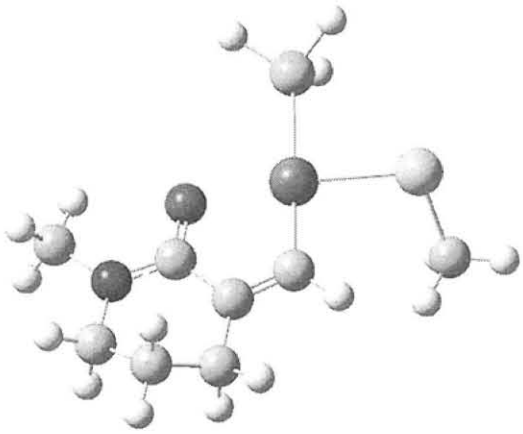


13_d

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-882.50945979	a.u.
RMS Gradient Norm	0.00000477	a.u.
Imaginary Freq	0	
Dipole Moment	5.5872	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 12 minutes 20.0 seconds.

C(3)

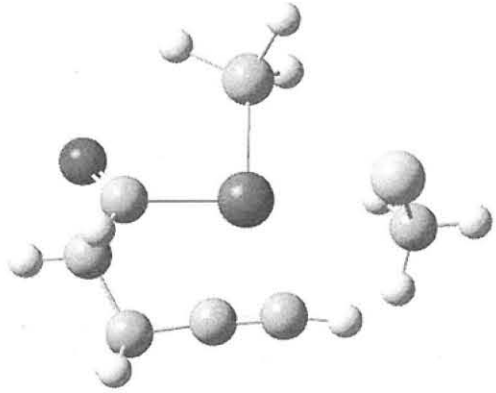


28_delta-lactam_insertion_C-Pd

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-921.82778247	a.u.
RMS Gradient Norm	0.00005385	a.u.
Imaginary Freq	0	
Dipole Moment	6.1831	Debye
Point Group	C1	

Job cpu time: 0 days 5 hours 50 minutes 17.0 seconds.

D(1)

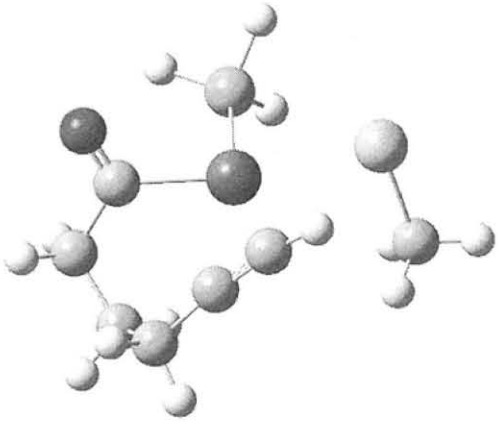


11_C4-Oxidative_adduct_no_Me

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-787.77332778	a.u.
RMS Gradient Norm	0.00000310	a.u.
Imaginary Freq	0	
Dipole Moment	2.6741	Debye
Point Group	C1	

Job cpu time: 0 days 1 hours 59 minutes 21.0 seconds.

D(2)

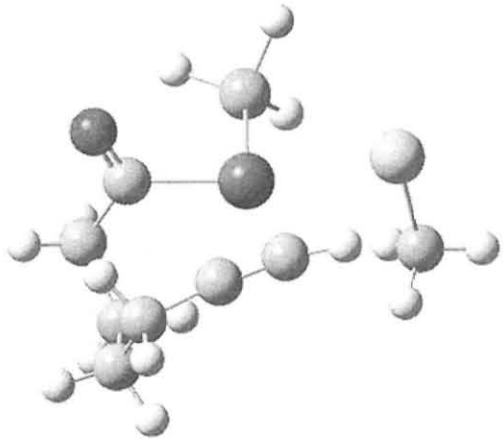


03_C5-Oxidative_adduct_acyl

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-827.08646941	a.u.
RMS Gradient Norm	0.00000468	a.u.
Imaginary Freq	0	
Dipole Moment	5.3489	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 59 minutes 7.0 seconds.

D(3)

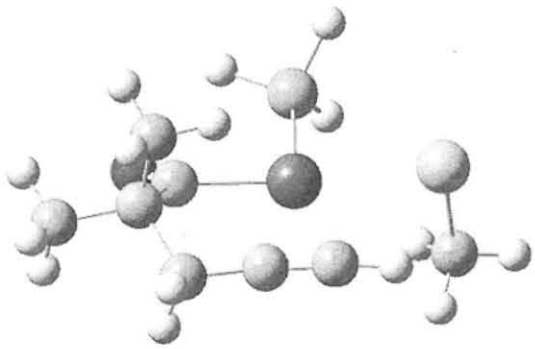


04_C6-Oxidative_adduct_acyl

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.39737352	a.u.
RMS Gradient Norm	0.00000813	a.u.
Imaginary Freq	0	
Dipole Moment	5.0461	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 52 minutes 26.0 seconds.

D'(1)

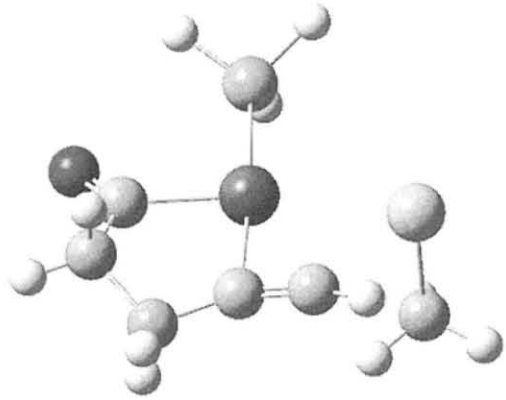


11_C4-Oxidative_adduct_Me

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.40360483	a.u.
RMS Gradient Norm	0.00003050	a.u.
Imaginary Freq	0	
Dipole Moment	3.0919	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 44 minutes 55.0 seconds.

TS3(1)

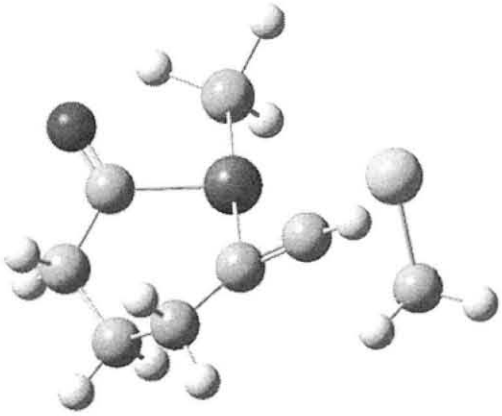


01_5-palladacycle_no_Me_insertionTS

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-787.75710531	a.u.
RMS Gradient Norm	0.00000318	a.u.
Imaginary Freq	1	
Dipole Moment	1.1466	Debye
Point Group	C1	

Job cpu time: 0 days 1 hours 59 minutes 8.0 seconds.

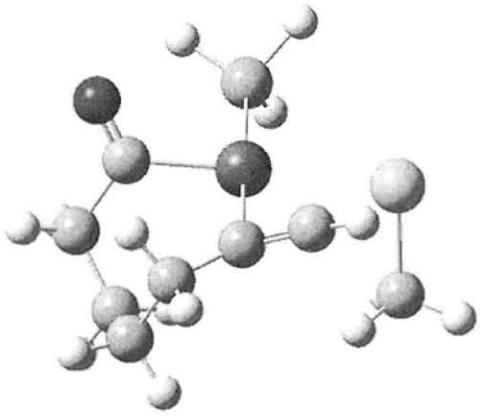
TS3(2)



06_7-palladacycle_TS		
File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.38004915	a.u.
RMS Gradient Norm	0.00000164	a.u.
Imaginary Freq	1	
Dipole Moment	2.8583	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 51 minutes 30.0 seconds.

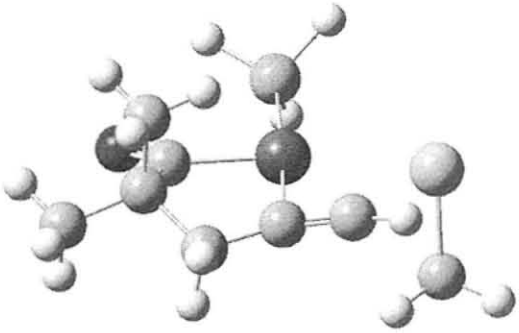
TS3(3)



06_7-palladacycle_TS		
File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.38004915	a.u.
RMS Gradient Norm	0.00000164	a.u.
Imaginary Freq	1	
Dipole Moment	2.8583	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 51 minutes 30.0 seconds.

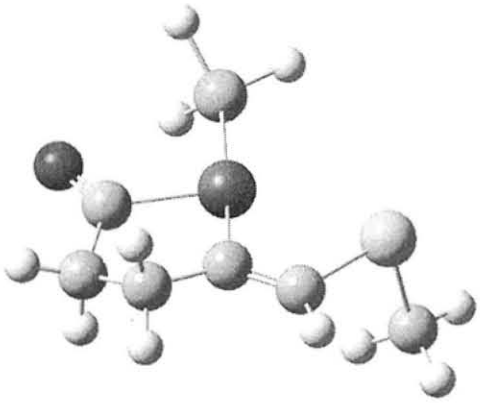
TS3'(1)



01_5-palladacycle_insertionTS		
File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.38702098	a.u.
RMS Gradient Norm	0.00000089	a.u.
Imaginary Freq	1	
Dipole Moment	1.1994	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 47 minutes 43.0 seconds.

E(1)

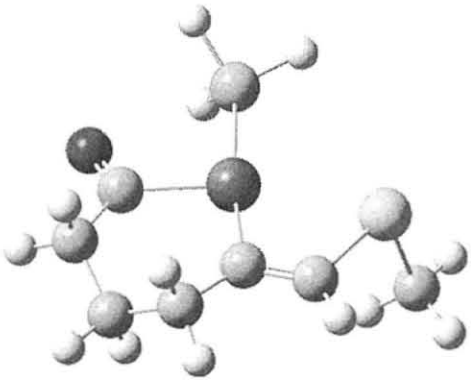


10_5-palladacycle_no_Me

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-787.79277104	a.u.
RMS Gradient Norm	0.00001015	a.u.
Imaginary Freq	0	
Dipole Moment	2.2767	Debye
Point Group	C1	

Job cpu time: 0 days 1 hours 56 minutes 32.0 seconds.

E(2)

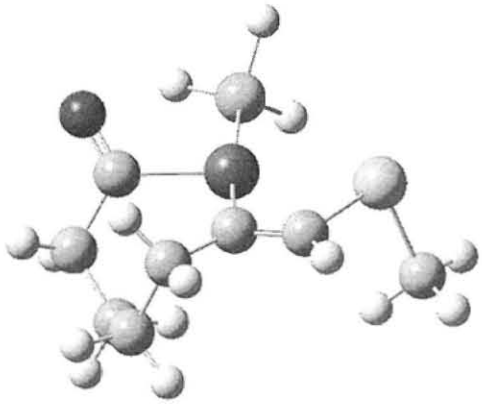


01_6-palladacycle_acyl

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-827.10676129	a.u.
RMS Gradient Norm	0.00000631	a.u.
Imaginary Freq	0	
Dipole Moment	1.8638	Debye
Point Group	C1	

Job cpu time: 0 days 2 hours 47 minutes 46.0 seconds.

E(3)

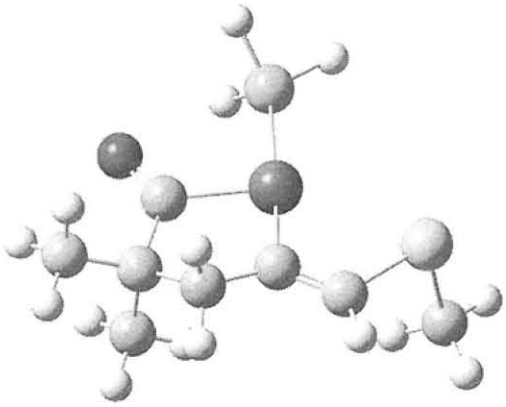


02_7-palladacycle_acyl

File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.41366882	a.u.
RMS Gradient Norm	0.00001102	a.u.
Imaginary Freq	0	
Dipole Moment	3.8252	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 44 minutes 46.0 seconds.

E'(1)



10_5-palladacycle_Me		
File Type	.log	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	Gen	
E(RB+HF-LYP)	-866.42230007	a.u.
RMS Gradient Norm	0.00000951	a.u.
Imaginary Freq	0	
Dipole Moment	2.1219	Debye
Point Group	C1	

Job cpu time: 0 days 4 hours 42 minutes 44.0 seconds.

1-5 References and Notes

[1] For recent reviews, see: (a) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, 106, 2320.

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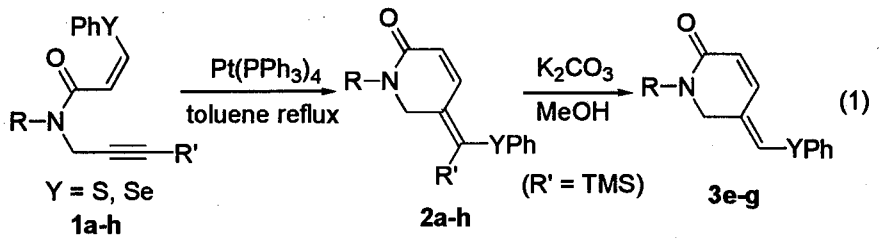
Chapter 2

Platinum(0)-Catalyzed Intramolecular Cyclization of Vinyl Sulfides and Selenides Having an Alkyne Moiety

2-1 Introduction

Simultaneous addition of carbon and heteroatom units (represented as "*C*" and "*E*", respectively) to alkynes with the cleavage of "*C-E*" bond by transition metal complexes has attracted great interest in recent organic and organometallic chemistry.[1-5] This reaction proceeds with *cis*-selective stereochemistry to give multi-functionalized alkenyl heteroatom compounds. Introduction of allyl,[1] alkynyl,[2] acyl[3] and cyano[4] groups as carbon units has been well studied. However the corresponding introduction of vinyl group (addition of the "vinyl-*E*" molecule across the triple bond) leading to 1,3-dienes remains as a challenging theme.[6-9] When the new "vinyl-*E*" unit exhibits the reactivity similar to that of starting vinyl heteroatom compounds, further reaction or oligomerization could be a serious problem.[5c] To the best of our knowledge, successful examples reported so far have been limited to the ring-expansion reaction via addition of three- or four-membered heterocyclic compounds such as silacyclopropenes,[5a] methylidenesiliranes,[5b] allene episulfides[5c] and silacyclobutenes[5d] to alkynes. In these systems, ring strain of starting compounds may promote the initial cleavage of the "vinyl-*E*" bond by the metal catalyst.

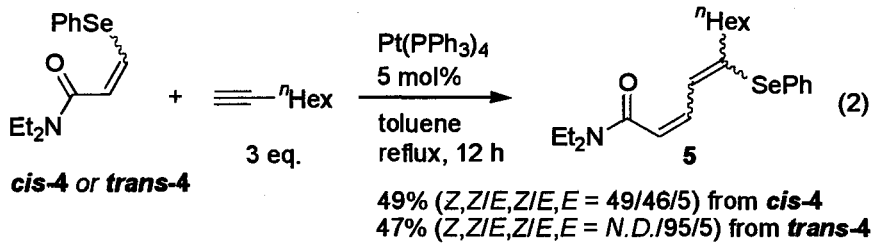
Recently, we found that an anion stabilizing group on the β-position of acyclic vinyl sulfides and selenides enhanced oxidative addition to Pt(0) complex.[10] This finding led us to develop a new type of catalytic reaction using vinyl sulfides and selenides.[11] Here we disclose Pt(0) catalyzes intramolecular *cis*-vinylthiolation and –selenation of alkynes leading to effective construction of six-membered lactam framework **2** or **3** having a high degree of unsaturation (eq 1).



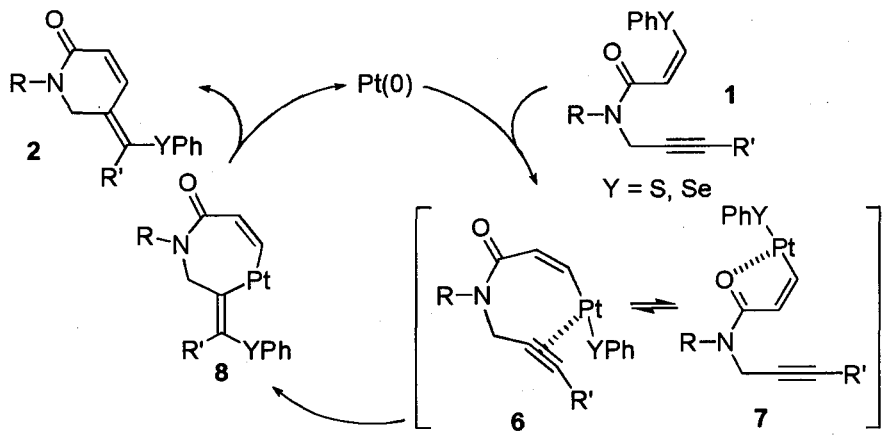
(1)

2-2 Results and Discussion

At first, the reaction of vinyl selenides **4** (*cis* and *trans*) having a carbamoyl group on β-position of vinyl moiety with 1-octyne was examined to check the possibility of vinylchalcogenation of alkynes, since this electron withdrawing group may accelerate oxidative addition of vinyl-SePh bond to Pt(0).[10b,12] When toluene (0.4 mL) containing ***cis*-4** or ***trans*-4** (0.3 mmol), 1-octyne (3 equiv), and $Pt(PPh_3)_4$ (5 mol%) was heated at reflux for 12 h, 1,3-dienes **5** were obtained in moderate yields (eq 2).



The stereochemistry of **4** did not affect the yield of **5**. Then, we undertook intramolecular vinylchalcogenation and the working hypothesis is shown in Scheme 1. The first step in this process is oxidative addition of vinyl-YPh (Y = S, Se) bond to Pt(0), giving rise to alkyne-coordinated complex **6** and/or carbonyl-coordinated complex **7**. Subsequent insertion of alkyne into the Pt-Y bond occurs on **6**, affording the platinacycle **8**. Reductive elimination leads to the cyclized products **2** and regenerates the Pt(0) species.



Scheme 1. A Possible Pathwa Leading to Six-membered Lactams

When toluene (0.5 mL) containing a vinyl sulfide **1a** (0.2 mmol) and $Pt(PPh_3)_4$ (5 mol%) was heated at reflux for 2.5 h, intramolecular vinylthiolation product **2a** was obtained in 90% yield

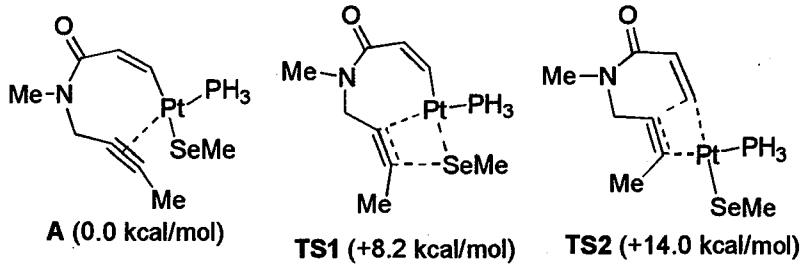
with excellent stereoselectivity (Table 1, run 1).[13] In contrast with intermolecular reaction (eq 2), stereochemistry of the substrates was essential in this cyclization. While intramolecular vinylselenation of **1b** took place efficiently to form lactam **2b** (run 2), the reaction of the *trans*-isomer of **1b** gave no detectable product under similar reaction conditions. In the oxidative addition adduct of *trans*-isomer, intramolecular alkyne coordination affording the intermediate like **6** might be conformationally impossible. Bulkier alkyl substituents on nitrogen, e.g. 1-phenylethyl, did not retard the reaction (run 3). The reaction of vinyl sulfide **1d** and selenide **1e** having a TMS group at the terminus gave the corresponding lactam **2d** and **2e** in high yields (runs 4 and 5). This catalytic system was not able to apply to terminal alkynes (R' = H, eq 1) probably due to further reaction or oligomerization.[14] However, **2e** easily underwent desilylation with K_2CO_3 in MeOH to afford **3e** in 90% total yield from **1e** (run 6). Longer alkyl substituents on nitrogen of **1f**, e.g. 2-phenylethyl, affected the reaction rate and stereoselectivity (run 7). Interestingly, a crude *E*/*Z* mixture of **2f** was treated with K_2CO_3 in MeOH to form desilylated lactam **3f** with high *E*-selectively in a high yield (run 8).[15] Similarly, **1g** having unprotected indole ring gave desilylated *E*-lactam **3g** in 86% yield (run 9). Vinyl sulfide **1h** having aryl group at the terminus also underwent intramolecular vinylthiolation to afford the desired lactam **2h** (run 10).[16]

Table 1. Pt(0)-Catalyzed Intramolecular Vinylchalcogenation of Alkynes to Form Six-membered Lactams (eq 1)[a]

run	1	Y	R	R'	Product, %[b]	*E*/*Z*[c]
1	**1a**	S	CH_2Ph	Et	**2a**, 90	>99/1[d]
2	**1b**	Se	CH_2Ph	Et	**2b**, 92 (99)	>99/1[d]
3	**1c**	S	CH(Me)Ph	Et	**2c**, 88	>99/1[d]
4	**1d**	S	CH_2Ph	TMS	**2d**, 92	96/4
5	**1e**	Se	CH_2Ph	TMS	**2e**, 95	96/4
6[f]	**1e**	Se	CH_2Ph	TMS	**3e**, 90	>99/1[d]
7[e]	**1f**	Se	$(CH_2)_2Ph$	TMS	**2f**, (94)	71/29
8[e,f]	**1f**	Se	$(CH_2)_2Ph$	TMS	**3f**, 78 (85)	95/5
9[e,f]	**1g**	Se	$(CH_2)_2$(3-Indolenyl)	TMS	**3g**, 86	>99/1[d]
10	**1h**	S	CH_2Ph	*p*-ClC_6H_4	**2h**, (82)	96/4

[a]Conditions: **1** (0.2 or 0.3 mmol), $Pt(PPh_3)_4$ (5 mol %), toluene (0.5 or 0.8 mL), reflux, 2.0-3.5 h. [b]Isolated yields. Numbers in parentheses are NMR yields. [c]Determined by ^{1}H NMR. [d]*Z*-isomer was not detected in crude ^{1}H-NMR analysis. [e]12 h. [f]Sequential treatment of crude **2** with K_2CO_3 (5 eq) in MeOH (2-3 mL) at rt for 12-14 h.

Next, DFT calculations were performed to get information on the mechanism. In Scheme 2, **A** is the model compound for alkyne-coordinated complex **6**. **TS1** and **TS2** are transition state models for reaction proceeding from **A** and calculated energies of optimized **TS1** and **TS2** relative to **A** are shown in parentheses.[17] **TS1** is 5.8 kcal/mol more stable than **TS2** and this result indicates that *selenoplatination* leading to platinacycle like **8** is kinetically more favored pathway than *carboplatination*.[18] In the case of Pd, the transition state for *selenopalladation* (+9.1 kcal) is less stable than **TS1** (+8.2 kcal). In fact, $Pd(PPh_3)_4$ worked as catalyst in this system but the efficiency was lower than $Pt(PPh_3)_4$.[19]



Scheme 2. Computational Models for Alkyne Insertion Processes

2-3 Conclusions

$Pt(PPh_3)_4$ catalyzes intramolecular vinylthiolation and -selenation of internal alkynes with vinyl chalcogenides having a carbamoyl group on the *cis*-β-position of the vinyl moiety, giving rise to the highly-conjugated δ-lactam frameworks.[20] DFT calculations for alkyne insertion processes suggest the formation of seven-membered platinacycle is kinetically favored. Introduction of electron withdrawing groups to β-position on vinyl moiety may be a key to develop a new type of catalytic reaction using vinyl heteroatom compounds.

2-4 Experimental Section

Genaral Comments

Toluene was distilled from CaH_2 under N_2. $Pt(PPh_3)_4$ [21] and $Pd(PPh_3)_4$ [22] were prepared according to the literature procedure. Commercially available dehydrated CH_2Cl_2, DMF, MeOH and EtOH (Wako Chemicals) were used without further distillation. THF was distilled from benzophenone ketyl just prior to use. Other reagents were purchased from commercial source and used without further purification. Melting points were determined on a Yanagimoto Micro Melting Point apparatus. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a JEOL JNM-ALICE-400 (400 MHz, 100 MHz, and 160 MHz, respectively) spectrometer. The chemical shifts of ^1H and ^{13}C NMR spectra were recorded using Me_4Si (in $CDCl_3$) as an internal standard. The chemical shifts of ^{31}P NMR spectra were recorded using H_3PO_4 (aq) (in

C_6D_6) as an external standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Preparative TLC was conducted by using Wakogel B-5F silica gel (325 mesh). Mass spectra (CI and EI) were taken on a SHIMAZU GCMS-QP2000 operating in the electron impact mode (70 eV) equipped with CBP1-M25-025 column. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus. For the copies of ^{1}H and ^{13}C NMR spectrum of samples without elemental analysis, see Supporting Information of the published paper.[23]

Preparation of (*Z*)-3-Phenylthio acrylic acid and (*Z*)-3-phenylseleno acrylic acid

(*Z*)-3-Phenylthio acrylic acid was synthesized according to the modified literature procedure[24]: Into a flame-dried 200-mL flask equipped with a reflux condenser and a dropping funnel was placed pieces of Na (ca. 5 mm x 5 mm, 83 mmol) under N_2. Anhydrous EtOH (60 mL) was added slowly cooling with ice-bath (vigorous gas emission was observed). After 40 min, the ice-bath was removed and the mixture was stirred until the colorless solution (slight cloudy) was obtained. A solution of benzenethiol (64 mmol) in 5 mL of EtOH was added dropwise cooling with ice-bath. Then the mixture was warmed up to room temperature and stirred for 10 min. To the solution was added propiolic acid (69 mmol) and stirred to generate white-precipitates. THF (25 mL) was added and the mixture was heated with oil bath (90 °C, bath temp.) for 10 min. Another THF (30 mL) and water (10 mL) were added to form the yellow-brown homogenous solution. Then the mixture was refluxed for 2 h and stirred overnight at room temperature. EtOH and THF were removed *in vacuo* and aqueous residue was obtained. Water (200 mL x 2) was poured into the flask and washed with *n*-hexane (200 mL x 4). The aqueous phase was acidified with 2M HCl *aq* to precipitate white solid and extracted with Et_2O (150 mL x 3). The combined organic phase was dried over anhydrous $MgSO_4$. The solvents of filtrate were removed *in vacuo* to form (*Z*)-3-phenylthio acrylic acid in 98% yield as milky-white crystalline solid. Further purification was not need.

(*Z*)-3-Phenylseleno acrylic acid was synthesized according to the modified literature procedure[25]: Into a 500-mL flask equipped with a reflux condenser were placed diphenyl diselenide (25.1 mmol) and EtOH (180 mL) under N_2. After vigorous stirring and warming with hot water bath (ca. 40 °C), homogeneous red-orange solution was obtained. After cooling to room temperature, small portions of $NaBH_4$ were added successively until the solution turned slight yellow. To the solution was added ethyl propiolate (49.8 mmol) after gas emission ceased. Then the mixture was refluxed for 3 h under stirring (oil bath, 94 °C). Subsequently NaOH *aq* (2.2 M, 39 mL) was added and white precipitate was generated. The mixture was refluxed for another 3 h. EtOH was removed *in vacuo* and aqueous residue was obtained. Water (400 mL) was poured into the flask and washed with *n*-hexane until yellow color was removed

from aqueous phase. The aqueous phase was acidified with 2M HCl *aq* to precipitate white solid and extracted with Et_2O (150 mL x 3). The combined organic phase was dried over anhydrous $MgSO_4$. The solvents of filtrate were removed *in vacuo* and the residue was purified by recrystalization from hot *n*-hexane/$CHCl_3$ to afford (*Z*)-3-phenylseleno acrylic acid in 65% yield as off-white crystal.

Procedures and Characterization of Reaction Materials

(*Z*)-*N*-Benzyl-*N*-pent-2-ynyl-3-phenylthioacrylamide (1a, run 1, Table 1) : Typical procedure.

Into a 20-mL flask were placed (*Z*)-3-phenylthio acrylic acid (4.0 mmol), anhydrous CH_2Cl_2 (5 mL) and catalytic amount of DMF (1 drop) under air. $(COCl)_2$ (4.4 mmol) was added slowly at room temperature to prepare the corresponding acid chloride and the stirring was continued at same temperature until gas (CO, HCl and CO_2) emission ceased (for 1.5 h). The volatiles were removed *in vacuo*. Into a flame-dried 30-mL flask equipped with a dropping funnel were placed benzyl(pent-2-ynyl)amine (4.0 mmol), anhydrous CH_2Cl_2 (9 mL) and Na_2CO_3 (5 mmol). A solution of the prepared acid chloride in 3 mL of CH_2Cl_2 was added dropwise cooling with ice-bath. The mixture was then warmed up to room temperature and stirred overnight. Et_2O was added and washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) afforded **1a** in 84% yield as a *s-cis/trans* mixture: slight-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.11 (br, 3 H), 2.12-2.18 (br, 2 H), 3.94 (brs, 2 H, minor), 4.32 (brs, 2 H, major), 4,72-4.74 (two brs peaks overlapped, 2 H), 6.18-6.38 (m, 1 H), 7.14-7.51 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3 (minor), 12.4 (major), 13.8 (major, minor), 35.0 (major), 36.9 (minor), 48.4 (minor), 50.0 (major), 73.9 (minor), 74.1 (major), 85.8 (major), 86.4 (minor), 111.9 (major), 112.1 (minor), 126.6, 127.4, 127.5, 127.8, 128.5, 128.8, 129.2, 130.9, 136.9, 137.2, 137.6, 148.0 (minor), 148.5 (major), 166.5 (two peaks overlapped); IR (NaCl) 3060, 2976, 1634 (C=O), 1557, 1440, 1221, 738 cm^{-1}; MS (CI), m/z (relative intensity, %) 336 (M^++1, 100). Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18. Found: C, 74.94; H, 6.16; N, 4.13.

(*Z*)-*N*-Benzyl-*N*-pent-2-ynyl-3-phenylselenoacrylamide (1b, run 2, Table 1)
and
(*E*)-*N*-Benzyl-*N*-pent-2-ynyl-3-phenylselenoacrylamide (*trans*-1b).

1b and ***trans*-1b** were prepared and separated through the reaction of *crude* 3-phenylseleno acrylic acid (before recrystalization) according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 4/1/4).

1b; 66% yield as a *s-cis/trans* mixture: slight-yellow solid; mp 38.0-39.0 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 1.08 (m, 3 H), 2.14 (m, 2 H), 3.94 (brs, 2 H, minor), 4.32 (brs, 2 H, major), 4.72-4.76 (two brs peaks overlapped, 2 H), 6.65-6.85 (m, 1 H), 7.22-7.77 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4 (major, minor), 13.7 (major, minor), 35.2 (major), 36.8 (minor), 48.7 (minor), 50.0 (major), 73.8 (minor), 74.0 (major), 85.9 (major), 86.5 (minor), 114.8 (major), 114.9 (minor), 126.6, 127.4, 127.6, 127.9, 128.5 (two peaks overlapped), 128.8, 129.2, 133.1, 134.2, 134.3, 136.7, 137.0, 148.6 (minor), 149.0 (major), 167.1 (major, minor) ; IR (KBr) 3057, 2976, 1621 (C=O), 1552, 1436, 1219, 943, 740 cm^{-1}; MS (CI), m/z (relative intensity, %) 384 (M^++1, 100). HRMS calcd for $C_{21}H_{22}NOSe$: 384.0866. Found 384.0863.

***trans*-1b**; 20% yield as a *s-cis/trans* mixture: slight-yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (m, 3 H), 2.11 (m, 2 H), 3.80 (brs, 2 H, minor), 4.22 (brs, 2 H, major), 4.53-4.66 (two brs peaks overlapped, 2 H), 6.24-6.53 (m, 1 H), 7.08-7.57 (m, 10 H), 8.16 (d, J = 14.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3 (major, minor), 13.7 (major, minor), 35.4 (major), 36.9 (minor), 48.8 (minor), 49.8 (major), 73.8 (minor), 74.0 (major), 85.7 (major), 86.4 (minor), 119.4 (major), 119.7 (minor), 126.5, 127.0, 127.4, 128.2, 128.4, 128.6, 129.1, 129.5, 133.1, 134.4, 136.7, 137.0, 142.1 (minor), 142.5 (major), 164.8 (major, minor) ; IR (NaCl) 3060, 2976, 1634 (C=O), 1568, 1417, 1225, 943, 739 cm^{-1}; MS (CI), m/z (relative intensity, %) 384 (M^++1, 100). HRMS calcd for $C_{21}H_{22}NOSe$: 384.0866. Found 384.0862. The copies of ^1H and ^{13}C NMR spectra of ***trans*-1b** in $CDCl_3$ were shown below.

(*Z*)-*N*-Pent-2-ynyl-*N*-(1-phenylethyl)-3-phenylthioacrylamide (1c, run 3, Table 1).

Purified by silica gel column chromatography (*n*-hexane/Et_2O = 2/1); 80% yield as a *s-cis/trans* mixture; slight-yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, J = 7.3 Hz, 3 H), 1.49-1.87 (br, 3 H), 2.09 (q, J = 7.3 Hz, 2 H), 3.60-3.83 (m, 2 H), 6.14 (brs, 1 H), 6.39 (br, 1 H), 7.24-7.52 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$, The major-minor peak sprits were not observed.) δ 12.3, 13.7, 16.5 (br), 33.1 (br), 51.0 (br), 75.9, 85.6 (br), 113.1 (br), 127.4, 127.7, 127.8, 128.4, 129.2, 130.9, 137.8, 140.6 (br), 147.7 (br), 166.5 (br); IR (NaCl) 3058, 2976, 1634 (C=O), 1557, 1417, 1308, 1203, 917, 760 cm^{-1}; MS (CI), m/z (relative intensity, %) 350 (M^++1, 100). Anal. Calcd for $C_{22}H_{23}NOS$: C, 75.61; H, 6.63; N, 4.01. Found: C, 75.32; H, 6.45; N, 4.03.

(*Z*)-*N*-Benzyl-*N*-(3-trimethylsilyl-prop-2-ynyl)-3-phenylthioacrylamide (1d, run 4, Table 1).

Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 3/1/1); 79% yield as a *s-cis/trans* mixture; white solid; mp 97.9-98.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.13 (two brs peaks overlapped, 9 H), 3.98 (brs, 2 H, minor), 4.40 (brs, 2 H, major), 4,74-4.76 (two brs peaks overlapped, 2 H), 6.19-6.38 (m, 1 H), 7.17-7.49 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.21 (major, minor), 35.5 (major), 37.5 (minor), 48.6 (minor), 50.1 (major), 89.2 (major),

89.7 (minor), 100.0 (minor), 100.6 (major), 111.7 (major), 111.9 (minor), 126.6, 127.5, 127.6, 127.9, 128.6, 128.8, 129.2, 130.9, 136.7, 136.9, 137.5, 148.3, 136.4, 148.8, 166.5 (major, minor); IR (KBr) 3058, 2956, 2177, 1625 (C=O), 1563, 1434, 1200, 1006, 843, 734 cm^{-1}; MS (CI), m/z (relative intensity, %) 380 (M^{+}+1, 100). Anal. Calcd for $C_{22}H_{25}NOSeSi$: C, 69.61; H, 6.64; N, 3.69. Found: C, 69.58; H, 6.68; N, 3.84.

(*Z*)-*N*-Benzyl-*N*-(3-trimethylsilyl-prop2-ynyl)-3-phenylselenoacrylamide (1e, runs 5 and 6, Table 1).

1e was prepared from (*Z*)-3-phenylseleno acrylic acid according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 4/1/4); 89% yield as a *s-cis/trans* mixture; white solid; mp 97.8-98.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.13 (two brs peaks overlapped, 9 H), 3.99 (brs, 2 H, minor), 4.40 (brs, 2 H, major), 4,74-4.76 (two brs peaks overlapped, 2 H), 6.66-6.84 (m, 1 H), 7.25-7.79 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$ at -40 °C) δ -0.29 (minor), -0.28 (major), 35.5 (major), 37.1 (minor), 48.6 (minor), 49.7 (major), 88.8 (major), 89.4 (minor), 99.5 (minor), 100.0 (major), 114.2 (major), 114.4 (minor), 126.3, 127.5, 127.6, 128.0, 128.4, 128.5, 128.7, 129.2 (two peaks overlapped), 133.2 (two peaks overlapped), 133.7 (major), 133.8 (minor), 136.1 (major), 136.4 (minor), 149.6 (minor), 150.0 (major), 167.0 (major), 167.1 (minor); IR (KBr) 3056, 2957, 2178, 1620 (C=O), 1522, 1464, 1225, 1005, 846, 740 cm^{-1}; MS (CI), m/z (relative intensity, %) 428 (M^{+}+1, 100). Anal. Calcd for $C_{22}H_{25}NOSeSi$: C, 61.96; H, 5.91; N, 3.28. Found: C, 61.99; H, 6.00; N, 3.41.

(*Z*)-*N*-(2-phenylethyl)-*N*-(3-trimethylsilyl-prop-2-ynyl)-3-phenylselenoacrylamide (1f, runs 7 and 8, Table 1).

1f was prepared from (*Z*)-3-phenylseleno acrylic acid according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 2/1); 74% yield as a *s-cis/trans* mixture; slight-yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.16 (two brs peaks overlapped, 9 H), 2.97 (m, 2 H), 3.72 (m, 2 H), 3.98 (brs, 2 H, minor), 4.36 (brs, 2 H, major), 6.56-6.77 (m, 1 H), 7.19-7.74 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.25 (minor), -0.15 (major), 34.3 (minor), 35.6 (major), 35.9 (major), 39.2 (minor), 48.8 (major), 49.1 (minor), 89.2 (major), 89.8 (minor), 100.2 (minor), 100.8 (major), 114.4 (major), 114.9 (minor), 126.4, 126.7, 127.9, 128.5, 128.7, 128.8, 128.9, 129.2, 129.5, 133.1, 134.2, 138.2, 139.1, 148.3 (minor), 148.5 (major), 166.5 (major), 166.8 (minor); IR (NaCl) 3060, 2959, 2177, 1622 (C=O), 1556, 1436, 1250, 1022, 845, 740 cm^{-1}; MS (CI), m/z (relative intensity, %) 442 (M^{+}+1, 100). HRMS calcd for $C_{23}H_{28}NOSiSe$: 442.1105. Found 442.1101.

(*Z*)-*N*-[2-(1*H*-Indol-3-yl)-ethyl)]-*N*-(3-trimethylsilyl-prop-2-ynyl)-3-phenylselenoacrylamide (1g, run 9, Table 1).

1g was prepared from (*Z*)-3-phenylseleno acrylic acid according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 5/1); 70% yield as a *s-cis/trans* mixture; white solid; mp 136.5-137.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.14-0.17 (two brs peaks overlapped, 9 H), 3.14 (m, 2 H), 3.81 (m, 2 H), 4.02 (brs, 2 H, minor), 4.42 (brs, 2 H, major), 6.49-6.80 (m, 1 H), 7.01-7.75 (m, 11 H), 8.13 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.25 (minor), -0.14 (major), 23.8 (minor), 25.0 (major), 35.9 (major), 39.2 (minor), 47.8 (major), 48.1 (minor), 89.0 (major), 89.7 (minor), 100.3 (minor), 101.0 (major), 111.2, 111.4, 112.0, 113.0, 114.7, 115.1, 118.3, 118.8, 119.3, 119.5, 121.9, 122.2, 122.4, 127.1, 127.4, 127.8, 127.9, 129.2 (two peaks overlapped), 130.8, 133.1 (two peaks overlapped), 133.2, 134.1, 136.3, 147.8(minor), 148.1(major), 166.7 (major), 166.9 (minor); IR (NaCl) 3359 (N-H), 2958, 2178, 1622 (C=O), 1465, 1221, 1010, 848, 744 cm^{-1}; MS (CI), m/z (relative intensity, %) 481 (M^++1, 100). Anal. Calcd for $C_{25}H_{28}N_2OSeSi$: C, 62.61; H, 5.89; N, 5.84. Found: C, 62.86; H, 5.97; N, 5.91.

(*Z*)-*N*-Benzyl-*N*-[3-(4-chlorophenyl)-prop-2-ynyl]-3-phenylthioacrylamide (1h, run 10, Table 1).

Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 4/1/4); 85% yield as a *s-cis/trans* mixture; yellow solid; mp 107.9-108.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (brs, 2 H, minor), 4.57 (brs, 2 H, major), 4,78-4.81 (two brs peaks overlapped, 2 H), 6.22-6.43 (m, 1 H), 7.20-7.50 (m, 15 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.4 (major), 37.4 (minor), 48.8 (minor), 50.5 (major), 82.8 (major), 83.3 (minor), 84.9 (minor), 85.5 (major), 111.6 (major), 111.7 (minor), 120.8 (major), 121.3 (minor), 126.6, 127.6, 127.7, 127.9, 128.6, 128.9, 129.2, 130.9, 133.0, 134.3, 134.6, 136.6, 137.0, 137.4, 148.7 (minor), 149.2 (major), 166.5 (minor), 166.6 (major); IR (KBr) 3060, 2926, 1626 (C=O), 1567, 1461, 1345, 1213, 1089, 821, 734 cm^{-1}; MS (CI), m/z (relative intensity, %) 418 (M^++1, 100). Anal. Calcd for $C_{25}H_{20}ClNOS$: C, 71.84; H, 4.82; N, 3.35. Found: C, 71.62; H, 4.82; N, 3.15.

(*Z*)-*N*-Benzyl-*N*-prop-2-ynyl-3-phenylthioacrylamide (1i).

1i was prepared from (*Z*)-3-phenylseleno acrylic acid according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 3/1/1); 66% yield as a *s-cis/trans* mixture; white solid; mp 62.7-63.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21-2.26 (two brs peaks overlapped, 1 H), 3.97 (brs, 2 H, minor), 4.32 (brs, 2 H, major), 4,73-4.76 (two brs peaks overlapped, 2 H), 6.68-6.83 (m, 1 H), 7.21-7.60 (m, 10 H), 7.70-7.80 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.7 (major), 36.3 (minor), 48.7 (minor), 50.1 (major), 72.2 (major), 72.8 (minor), 78.3 (minor), 78.7 (major), 114.4 (major), 114.5 (minor), 126.6, 127.6, 127.8, 127.9, 128.5, 128.6, 128.9, 129.2, 133.1, 133.2 (two peaks overlapped), 134.0, 136.2, 136.6, 149.4 (minor), 149.7 (major), 167.0 (minor), 167.1 (major); IR (KBr) 3280, 3056, 2920,

1621 (C=O), 1557, 1464, 1435, 1226, 1167, 789, 743 cm^{-1}; MS (CI), m/z (relative intensity, %) 356 (M^++1, 100). Anal. Calcd for $C_{19}H_{17}NOSe$: C, 64.41; H, 4.84; N, 3.95. Found: C, 64.12; H, 4.78; N, 4.22.

(*Z*)-*N,N*-Diethyl-3-phenylselenoacrylamide (*cis*-4, eq 2)
and
(*E*)-*N,N*-Diethyl-3-phenylselenoacrylamide (*trans*-4, eq 2).

***cis*-4** and ***trans*-4** were prepared and separated through the reaction of *crude* 3-phenylseleno acrylic acid (before recrystalization) according to the typical procedure. Purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 4/1/4).

***cis*-4**; 56% yield: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (m, 6 H), 3.38 (q, J = 7.3 Hz, 2 H), 3.48 (q, J = 7.3 Hz, 2 H), 6.68 (d, J = 9.3 Hz, $^2J_{Se\text{-}H}$ = 9.0 Hz, 1 H), 7.31 (m, 3 H), 7.61-7.64 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 14.7, 40.8, 42.2, 115.0, 127.7, 129.1, 133.2, 146.9, 166.3; IR (NaCl) 3053, 2975, 1622 (C=O), 1579, 1434, 1261, 1144, 843, 788, 741 cm^{-1}; MS (EI), m/z (relative intensity, %) 283 (M^+, 71), 211 (76), 157 (40), 126 (100). Anal. Calcd for $C_{13}H_{17}NOSe$: C, 55.32; H, 6.07; N, 4.96. Found: C, 55.17; H, 6.10; N, 5.03.

***trans*-4**; 18% yield: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (m, 6 H), 3.22 (q, J = 6.8 Hz, 2 H), 3.39 (q, J = 6.8 Hz, 2 H), 6.33 (d, J = 14.9 Hz, $^2J_{Se\text{-}H}$ = 7.8 Hz, 1 H), 7.34 (m, 3 H), 7.56-7.59 (m, 2 H), 8.06 (d, J = 14.9 Hz, $^1J_{Se\text{-}H}$ = 24.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 14.8, 40.9, 42.0, 120.1, 127.5, 128.5, 129.5, 134.3, 140.4, 163.9; IR (NaCl) 3056, 2974, 1633 (C=O), 1574, 1428, 1261, 1135, 946, 741 cm^{-1}; MS (EI), m/z (relative intensity, %) 283 (M^+, 14), 211 (43), 157 (22), 126 (100). Anal. Calcd for $C_{13}H_{17}NOSe$: C, 55.32; H, 6.07; N, 4.96. Found: C, 55.04; H, 6.12; N, 5.05.

(*Z*)-3-Phenylseleno acrylic acid 2-butynyl ester (9).

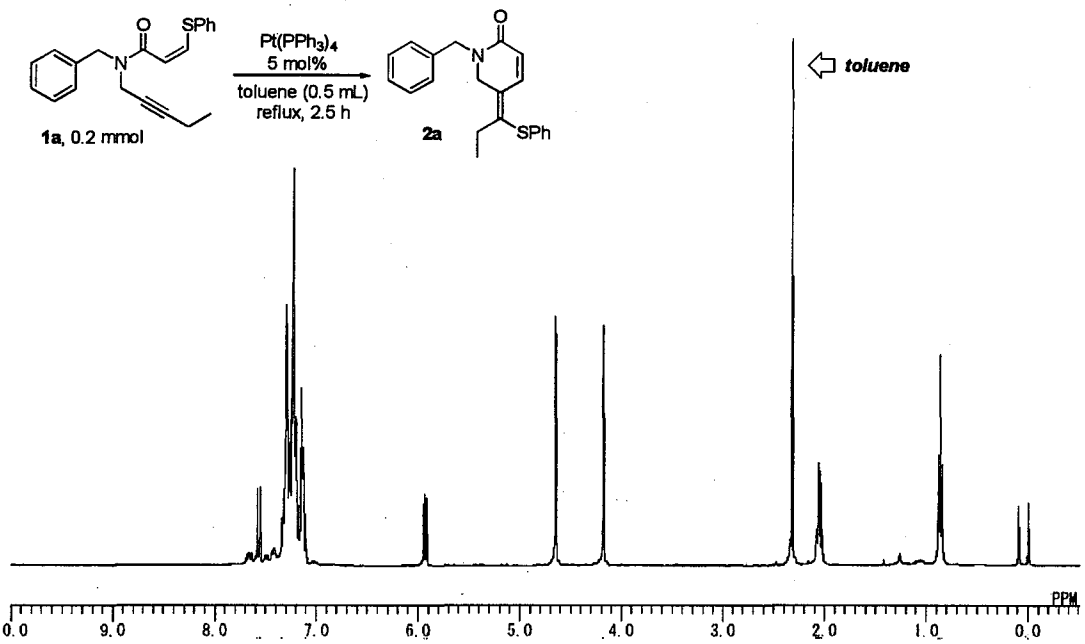
Into a 20-mL flask were placed (*Z*)-3-phenylseleno acrylic acid (4.0 mmol), anhydrous CH_2Cl_2 (5 mL) and catalytic amount of DMF (1 drop) under air. $(COCl)_2$ (4.4 mmol) was added slowly at room temperature to prepare the corresponding acid chloride and the stirring was continued at same temperature until gas (CO, HCl and CO_2) emission ceased (for 1.5 h). The volatiles were removed *in vacuo*. Into a flame-dried 30-mL flask equipped with a dropping funnel were placed 2-butyn-1-ol (6.0 mmol), anhydrous THF (6 mL) and pyridine (8.0 mmol). A solution of the prepared acid chloride in 2 mL of THF was added dropwise cooling with ice-bath. The mixture was then warmed up to room temperature and stirred overnight. Et_2O was added and washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et_2O = 10/1) afforded **9** in 57% yield: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (t, J = 2.4 Hz, 3 H), 4.78 (q, J = 2.4 Hz, 2 H), 6.40 (d, J = 9.5 Hz, 1 H), 7.33-7.38 (m, 3 H), 7.59-7.62 (m, 2 H), 7.82 (d, J =

9.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.63, 52.8, 73.0, 83.3, 115.8, 128.3, 129.3, 132.2, 133.3, 151.5, 166.5; IR (NaCl) 3054, 2919, 1694 (C=O), 1568, 1438, 1192, 1151, 977, 739 cm^{-1}; MS (EI), m/z (relative intensity, %) 280 (M^+, 39), 211 (37), 157 (100), 131 (44). Anal. Calcd for $C_{13}H_{12}O_2Se$: C, 55.93; H, 4.33. Found: C, 56.15; H, 4.46.

Procedures and Characterization of Reaction Products

(*Z*)-1-Benzyl-5-(1-phenylthiopropylidene)-5,6-dihydro-1*H*-pyridin-2-one (2a, run 1, Table 1): Typical procedure.

Into a 3-mL flask equipped with a reflux condenser were placed vinyl sulfide **1a** (0.2 mmol), toluene (0.5 mL), and $Pt(PPh_3)_4$ (0.01 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 2.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The copy of ^1H NMR spectra of crude **2a** in $CDCl_3$ was shown below. No stereoisomer was detected.



The crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) to afford (*Z*)-1-benzyl-5-(1-phenylthiopropylidene)-5,6-dihydro-1*H*-pyridin-2-one **2a** in 90% yield: white needle crystal; mp 74.1-75.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.3 Hz, 3 H), 2.07 (q, J = 7.3 Hz, 2 H), 4.21 (s, 2 H), 4.67 (s, 2 H), 5.94 (d, J = 10.2 Hz, 1 H), 7.20-7.36 (m, 10 H), 7.58 (d, J = 10.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 26.1, 48.2, 49.7, 122.7, 127.1, 127.5, 128.0, 128.7, 129.1, 130.4, 130.8, 134.1, 136.1, 136.7, 139.3, 163.5; NOE experiment: irradiation of the allyl singlet at δ 4.21 resulted in 3.4% enhancements of the quartet at δ 2.07 ($-CH_2CH_3$); IR (KBr) 2967, 2867, 1656 (C=O), 1570, 1476, 1238, 1139, 823, 731, 697 cm^{-1}; MS (CI), m/z (relative intensity, %) 336 (M^++1, 100). Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18; S, 9.65. Found: C, 75.22; H, 6.30; N, 4.14; S, 9.51.

(*Z*)-1-Benzyl-5-(1-phenylselenopropylidene)-5,6-dihydro-1*H*-pyridin-2-one (2b, run 2, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1b** (0.3 mmol), toluene (0.8 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 3.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) to afford (*Z*)-1-benzyl-5-(1-phenylselenopropylidene)-5,6-dihydro-1*H*-pyridin-2-one **2b** in 92% yield (99% NMR yield): white needle crystal; mp 108.0-109.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.6 Hz, 3 H), 2.15 (q, J = 7.6 Hz, 2 H), 4.19 (s, 2 H), 4.66 (s, 2 H), 5.92 (d, J = 10.0 Hz, 1 H), 7.25-7.40 (m, 10 H), 7.47 (d, J = 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.6, 28.1, 47.9, 49.6, 122.7, 127.5, 127.6, 128.0, 128.7, 129.3, 129.5, 130.0, 133.2, 136.7, 138.1, 140.0, 163.6; NOE experiment: irradiation of the allyl singlet at δ 4.19 resulted in 3.9% enhancements of the quartet at δ 2.15 (-C*H*$_2$CH$_3$); IR (KBr) 3023, 2964, 1657 (C=O), 1574, 1436, 1240, 1140, 820, 754, 696 cm^{-1}; MS (CI), m/z (relative intensity, %) 384 (M^++1, 100). Anal. Calcd for $C_{21}H_{21}NOSe$: C, 65.97; H, 5.54; N, 3.66. Found: C, 65.96; H, 5.58; N, 3.73.

(*Z*)-1-(1-Phenylethyl)-5-(1-phenylthiopropylidene)-5,6-dihydro-1*H*-pyridin-2-one (2c, run 3, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl sulfide **1c** (0.2 mmol), toluene (0.5 mL), and $Pt(PPh_3)_4$ (0.01 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 2.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. No stereoisomer was detected in ^{1}H-NMR analysis. The crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) to afford **2c** in 88% yield: white needle crystal; mp 101.7-102.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75 (t, J = 7.6 Hz, 3 H), 1.57 (d, J = 7.1 Hz, 3 H), 1.91-2.07 (m, 2 H), 3.79-3.82 (d, J = 15.6 Hz, 1 H), 4.07-4.11 (d, J = 15.6 Hz, 1 H), 5.94 (d, J = 10.0 Hz, 1 H), 6.10-6.15 (q, J = 7.1 Hz, 1 H), 7.20-7.35 (m, 10 H), 7.50 (d, J = 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 15.2, 26.2, 42.5, 49.7, 123.3, 127.1, 127.4, 127.5, 128.6, 129.1, 130.7, 130.8, 134.2, 135.8, 139.3, 140.1, 163.6; NOE experiment failed to confirm the stereochemistry of exomethylene moiety in **2c**. However, it would not be doubtful that *Z*-isomer was obtained selectively since the ^{1}H and ^{13}C NMR chemical shifts of Et group was similar to one of **2a**.; IR (KBr) 2969, 2934, 1657 (C=O), 1476, 1458, 1269, 1141, 822, 750, 696 cm^{-1}; MS (CI), m/z (relative intensity, %) 350 (M^++1, 100). HRMS calcd for $C_{22}H_{24}NOS$: 350.1579. Found 350.1573.

1-Benzyl-5-[(phenylthio)trimethylsilylmethylene]-5,6-dihydro-1*H*-pyridin-2-one (2d, run 4, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl sulfide **1d** (0.2 mmol), toluene (0.5 mL), and $Pt(PPh_3)_4$ (0.01 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 2.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The crude product was purified by preparative recycling HPLC (eluted with $CHCl_3$) to provide **2d** in 92% yield (*E*/*Z* = 4/96): yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ –0.06 (s, *Z* (9 H)), 0.19 (s, *E* (9 H)), 4.27 (s, 2 H), 4.68 (s, 2 H), 6.04 (d, *J* = 10.0 Hz, 1 H), 7.04-7.38 (m, 10H), 7.64 (d, *J* = 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.04, 49.6, 50.6, 125.6 (two peaks overlapped), 127.3, 127.9, 128.5, 128.8, 128.9, 136.0, 136.2, 136.6, 138.1, 148.4, 163.2; NOE experiment: irradiation of the allyl singlet at δ 4.27 resulted in 14.7% enhancements of the singlet at δ -0.06 (-Si*Me*$_3$); IR (NaCl) 3062, 2954, 1652 (C=O), 1592, 1479, 1252, 902, 841 cm^{-1}; MS (CI), m/z (relative intensity, %) 380 (M^++1, 100). HRMS calcd for $C_{22}H_{26}NOSSi$: 380.1504. Found 380.1508.

1-Benzyl-5-[(phenylseleno)trimethylsilylmethylene]-5,6-dihydro-1*H*-pyridin-2-one (2e, run 5, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1e** (0.2 mmol), toluene (0.5 mL), and $Pt(PPh_3)_4$ (0.01 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 3.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. After the *E*/*Z* ratio were determined by ^{1}H NMR (*E*/*Z* = 4/96), the crude product was purified by preparative recycling HPLC (eluted with $CHCl_3$) to provide **2e** in 95% yield (*E*/*Z* = 12/88). Isomerization of *Z*-isomer to *E*-isomer proceeded rapidly under purification by silica gel column chromatography to give the 1:1 mixture of *E*/*Z* isomers (80%, isolated yield). Since similar isomerization also occurred after the leaving isolated sample by HPLC even under N_2 and dark-condition for 1 day, the following spectra and analytical data were obtained from the *E*/*Z* mixture (= 12/88): yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ –0.02 (s, *Z* (9 H)), 0.25 (s, *E* (9 H)), 4.19 (s, *E* (2 H)), 4.25 (s, *Z* (2 H)), 4.52 (s, *E* (2 H)), 4.67 (s, *Z* (2 H)), 5.99 (d, *Z* (*J* = 10.2 Hz, 1 H)), 6.00 (overlapped, *E* (1 H)), 7.12-7.37 (m, 10 H), 7.58 (d, *J* = 10.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.4 (*Z*), 1.3 (*E*), 49.5 (*Z*), 51.0 (*Z*), 125.8 (*Z*), 126.2 (*Z*), 127.9 (*Z*), 128.3, 128.5 (*Z*), 128.6, 128.8 (two peaks overlapped), 129.2 (*Z*), 129.4, 129.7 (*Z*), 130.6, 133.6 (*Z*), 136.3, 136.4, 136.7 (*Z*), 139.0 (*Z*), 163.2 (*Z*); The stereochemistry was confirmed indirectly by the NOE experiment on desilylated product **3e**.; IR (NaCl) 3062, 2954, 1651 (C=O), 1593, 1476, 1251, 880, 735 cm^{-1}; MS (CI), m/z (relative intensity, %) 428 (M^++1, 100). HRMS calcd for $C_{22}H_{26}NOSiSe$: 428.0949. Found 428.0954.

(*Z*)-1-Benzyl-5-(1-phenylselenomethylene)-5,6-dihydro-1*H*-pyridin-2-one (3e, run 6, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1e** (0.3 mmol), toluene (0.8 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 2.5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. Into a 3-mL flask were placed a solution of crude **2e** in anhydrous MeOH (3 mL) and K_2CO_3 (1.5 mmol). After stirring under room temperature for 12 h, Et_2O was added and washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 2/2/1) afforded **3e** in 90% yield: light-yellow solid; mp 72.7-74.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 2 H), 4.95 (s, 2 H), 6.56 (d, J = 9.3 Hz, 1 H), 6.75 (d, J = 2.0 Hz, 1 H), 7.12-7.37 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 51.8, 116.7, 121.3, 127.9, 128.0 (two peaks overlapped), 128.7, 128.8, 129.1, 134.8 ($^2J_{Se\text{-}C}$ = 9.9 Hz), 135.1, 136.2, 141.0, 161.8; NOE experiment: irradiation of the allyl singlet at δ 3.72 resulted in 4.9% enhancements of the doublet at δ 6.75 (vinyl proton); IR (KBr) 3032, 2924, 1662 (C=O), 1604, 1539, 1272, 1151, 943, 836, 740, 722, 694 cm^{-1}; MS (CI), m/z (relative intensity, %) 356 (M^++1, 100). Anal. Calcd for $C_{19}H_{17}NOSe$: C, 64.41; H, 4.84; N, 3.95. Found: C, 64.17; H, 4.88; N, 4.23. When the 1:1 *E*/*Z* mixture of **2e** was treated with K_2CO_3 in MeOH, *Z*-**3e** was obtained quite selectively.

1-(1-Phenylethyl)-5-(1-phenylselenomethylene)-5,6-dihydro-1*H*-pyridin-2-one (3f, run 8, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1f** (0.3 mmol), toluene (0.8 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 12 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The NMR yield and the *E*/*Z* ratio of **2f** were determined by ^{1}H NMR (94%, *E*/*Z* = 29/71).[26] Into a 3-mL flask were placed a solution of crude **2f** in anhydrous MeOH (3 mL) and K_2CO_3 (1.5 mmol). After stirring under room temperature for 14 h, Et_2O was added and washed with brine, and dried over anhydrous $MgSO_4$. After the NMR yield and the *E*/*Z* ratio were determined by ^{1}H NMR (85%, *E*/*Z* = 5/95), the crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O/CH_2Cl_2 = 2/2/1) afforded **3f** in 78% yield (*E*/*Z* = 5/95). The following spectra and analytical data were obtained from the *E*/*Z* mixture: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (t, J = 7.3 Hz, *Z* (2 H)), 3.07 (t, J = 6.8 Hz, *E* (2 H)), 3.67 (s, *E* and *Z* (2 H)), 3.94 (t, J = 7.3 Hz, *Z* (2 H)), 4.22 (t, J = 6.8 Hz, *E* (2 H)), 6.50 (d, J = 5.4 Hz, *Z* (1 H)), 6.52 (s, *Z* (1 H)), 7.10-7.40 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.6, 35.2, 51.5, 116.0, 120.9, 126.7, 127.9, 128.6, 128.8, 129.0, 129.1, 134.8, 135.7, 137.8, 141.0, 161.6; NOE experiment: irradiation of the allyl singlet at δ 3.67 resulted in 6.5%

enhancements of the singlet at δ 6.52 (vinyl proton); IR (NaCl) 3026, 2938, 1667 (C=O), 1600, 1438, 1265, 1145, 831, 740, cm^{-1}; MS (CI), m/z (relative intensity, %) 370 (M^++1, 72), 212 (100). HRMS calcd for $C_{20}H_{20}NOSe$: 370.0710. Found 370.0707.

1-[2-(1*H*-Indol-3-yl)-ethyl)]-5-(1-phenylselenomethylene)-5,6-dihydro-1*H*-pyridin-2-one (3g, run 9, Table 1)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1g** (0.3 mmol), toluene (0.8 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 12 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The NMR yield and the *E/Z* ratio were determined by ^1H NMR (99%, *E/Z* = 60/40). Into a 3-mL flask were placed a solution of the crude in anhydrous MeOH (3 mL) and K_2CO_3 (1.5 mmol). After stirring under room temperature for 12 h, Et_2O was added and washed with brine, and dried over anhydrous $MgSO_4$. The crude product was purified by silica gel column chromatography (Et_2O/CH_2Cl_2 = 1/2 to 1/1) afforded **3g** in 86% yield: pale yellow solid; mp 114.0-114.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.04 (t, *J* = 7.3 Hz, 2 H), 3.62 (s, 2 H), 4.03 (t, *J* = 7.3 Hz, 2 H), 6.49 (s, 1 H), 6.55 (d, *J* = 8.8 Hz, 1 H), 6.87 (s, 1 H), 7.11-7.70 (m, 10 H), 8.32 (brs, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 28.6, 50.5, 111.4, 111.7, 116.0, 118.5, 119.5, 120.8, 122.1, 122.5, 127.1, 128.0, 129.1, 132.0, 134.5, 136.0, 136.3, 141.0, 161.8; NOE experiment: irradiation of the allyl singlet at δ 3.62 resulted in 5.0% enhancements of the singlet at δ 6.49 (vinyl proton); IR (NaCl) 3214 (N-H), 3058, 2923, 1655 (C=O), 1589, 1535, 1438, 1346, 1149, 1011, 830, 744, cm^{-1}; MS (CI), m/z (relative intensity, %) 409 (M^++1, 100), 251 (69). HRMS calcd for $C_{22}H_{21}N_2OSe$: 409.0819. Found 409.0816.

1-Benzyl-5-[(4-chlorophenyl)phenylthiomethylene)-5,6-dihydro-1*H*-pyridin-2-one (2h, run 10, Table 1) and its hydrolysate; 1-benzyl-5-(4-chlorobenzoyl)-2-pyridone (10)

Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide **1h** (0.2 mmol), toluene (0.5 mL), and $Pt(PPh_3)_4$ (0.01 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 2 h, filtered through the silica gel pad with Et_2O, volatiles were removed *in vacuo*. The NMR yield and the *E/Z* ratio of **2h** were determined by ^1H NMR (82%, *E/Z* = 4/96). Attempts to get pure product were failed since **2h** was easily isomerized, and hydrolyzed eventually under purification by preparative TLC, silica gel column chromatography or HPLC. The following spectra and analytical data were obtained from the crude product; ^1H NMR (400 MHz, $CDCl_3$) δ 4.03 (s, *Z* (1 H)), 4.45 (s, *E* (1 H)), 4.51 (s, *Z* (1 H)), 4.72 (s, *E* (1 H)), 6.07 (d, *J* = 10.0 Hz, *Z* (1 H)), 6.98-7.36 (m), 7.68 (d, *J* = 10.0 Hz, *Z* (1 H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.7, 49.8, 124.3, 127.5 (two peaks overlapped), 128.0, 128.4, 128.6, 128.9, 130.5, 131.1, 131.6, 132.9, 134.2, 135.6, 135.8, 136.6, 137.0,

163.6; MS (CI), m/z (relative intensity, %) 418 (M^++1, 100). HRMS calcd for $C_{25}H_{21}ClNOS$: 418.1032. Found 418.1034. The hydrolyzed product of **2h** was isolated under further purification by preparative TLC (*n*-hexane/Et_2O = 1/1). The following spectra and analytical data did not conflict with the structure **10** and a known analogue shown in **Figure 1**[27]; ^1H NMR (400 MHz, $CDCl_3$) δ 5.16 (s, 2 H), 6.64 (d, J = 9.3 Hz, 1 H), 7.26-7.55 (m, 9 H), 7.82 (dd, J = 9.3, 2.4 Hz, 1 H), 7.93 (d, J = 2.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.7, 117.1, 120.3, 128.4, 128.6, 128.9, 129.2, 130.5, 135.3, 135.4, 138.8 (two peaks overlapped), 144.1, 162.1, 190.3; IR (NaCl) 3064, 2930, 1673 (C=O), 1634 (C=O), 1588, 1435, 1312, 1132, 1091, 910, 844, 732, cm^{-1}; MS (CI), m/z (relative intensity, %) 324 (M^++1, 100). HRMS calcd for $C_{12}H_{15}ClNO_2$: 324.0791. Found 324.0797. The copies of ^1H and ^{13}C NMR spectra were shown below. A plausible mechanism for hydrolysis of **2h** to **10** was shown in **Scheme 1**. PhSSPh (generated by oxidation of PhSH) was also isolated under preparative TLC.

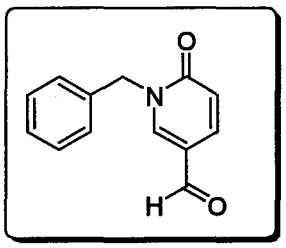
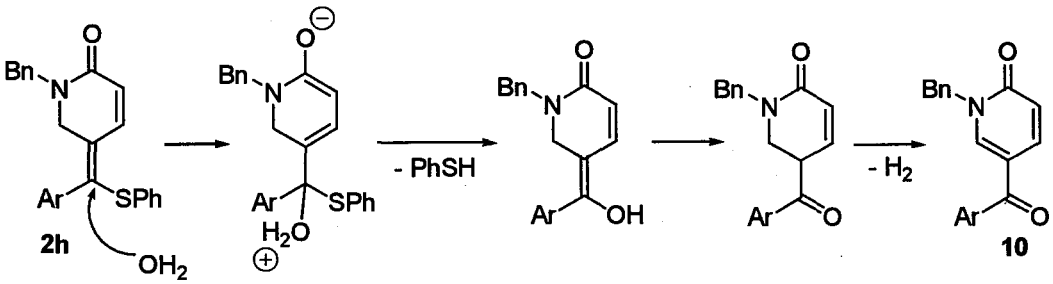


Figure 1. A known analogue of **10** [27]



Scheme 3. A plausible mechanism for hydrolysis of **2f** to **10**

5-Phenylseleno 2,4-undecadienoic acid diethylamide (5, eq 2)

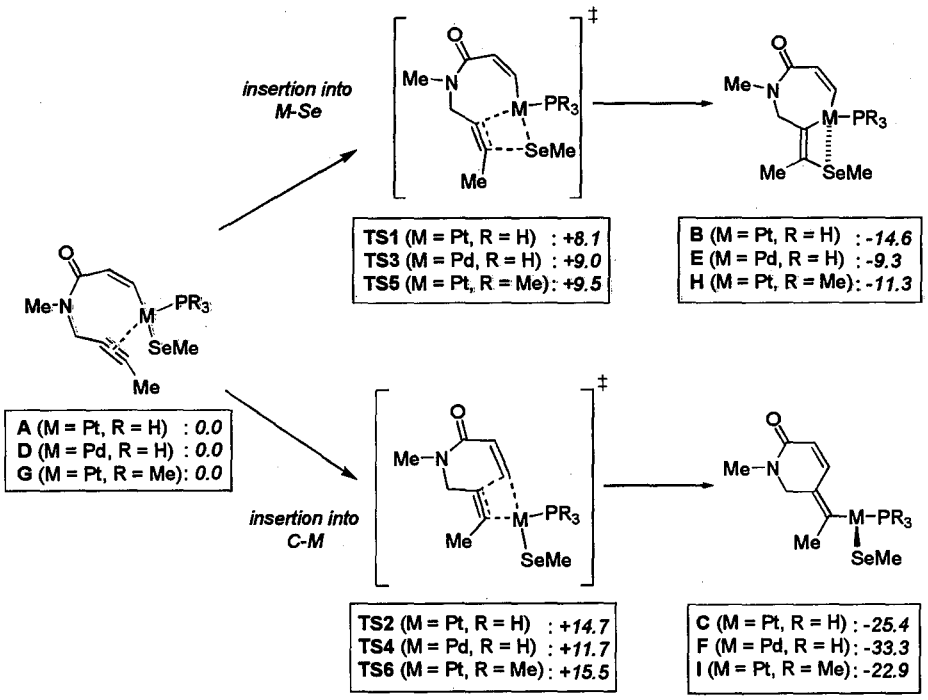
The reaction of ***cis*-4** with 1-octyne: Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide ***cis*-4** (0.3 mmol), 1-octyne (0.9 mmol), toluene (0.4 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 12 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/Et_2O = 1/1) to afford the mixture of stereoisomers of **5** (*Z,Z/E,Z/E,E* = 49/46/5) in 49% yield. Since

isomerization proceeded under purification, each isomers could not be separated: slight yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (m, 3 H), 1.12-1.53 (m, 14 H), 2.25 (t, J = 7.6 Hz, *E,Z* (2 H)), 2.30 (t, J = 7.6 Hz, *Z,Z* (2 H)), 2.51 (t, J = 8.1 Hz, *E,E* (2 H)), 3.34-3.48 (m, 4 H), 6.00 (d, J = 11.7 Hz, *Z,Z* (1 H)), 6.06 (d, J = 14.4 Hz, *E,E* (1 H)), 6.23 (d, J = 12.0 Hz, *E,E* (1 H)), 6.34 (d, J = 14.8 Hz, *E,Z* (1 H)), 6.52 (d, J = 11.0 Hz, *E,Z* (1 H)), 6.99 (m, *Z,Z* (1 H)), 7.24-7.57 (m, 6 H, a doublet peak was overlapped (J = 10.6 Hz, a vinyl proton of *Z,Z*)), 7.85 (dd, J = 11.0, 14.8 Hz, *E,Z* (1 H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2 (*E,Z*), 14.0 (*E,Z*), 14.5 (*Z,Z*), 15.0 (*E,Z*), 22.5 (two peaks overlapped), 28.5 (*E,Z*), 28.7 (*Z,Z*), 28.9 (*Z,Z*), 29.0 (*E,Z*), 29.2 (*E,Z*), 31.5 (*E,Z*), 31.6 (*Z,Z*), 39.3 (*E,Z*), 39.8 (*Z,Z*), 40.0 (*Z,Z*), 40.9 (*E,Z*), 42.1 (*Z,Z*), 42.2 (*E,Z*), 42.6 (*Z,Z*), 120.3 (*Z,Z*), 121.4 (*E,Z*), 127.2 (*Z,Z*), 127.6 (*E,Z*), 129.1 (two peaks overlapped), 129.4 (two peaks overlapped), 130.4 (*E,Z*), 133.2 (*Z,Z*), 134.1 (*E,Z*), 135.4 (*E,Z*), 136.7 (*Z,Z*), 140.1 (*E,Z*), 144.8 (*Z,Z*), 146.0 (*E,Z*), 166.0 (*E,Z*), 166.6 (*Z,Z*); NOE experiment to confirm the *Z,Z*-isomer (For *E,Z*- and *E,E*-isomers, see next paragraph): irradiation of the vinyl doublet at δ 6.00 (H_a in **5-*Z,Z***) resulted in 10.7% enhancements of the multiplet at δ 6.99 (H_b in **5-*Z,Z***); IR (NaCl) 2930, 2856, 1644 (C=O), 1456, 1269, 1133, 1022, 832, 739 cm^{-1}; MS (CI), m/z (relative intensity, %) 394 (M^++1, 100). Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 63.99; H, 7.92; N, 3.63.

The reaction of ***trans*-4** with 1-octyne: Into a 3-mL flask equipped with a reflux condenser were placed vinyl selenide ***trans*-4** (0.3 mmol), 1-octyne (0.9 mmol), toluene (0.4 mL), and $Pt(PPh_3)_4$ (0.015 mmol) at room temperature under N_2 and the solution turned yellow. After the mixture was refluxed for 12 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/Et_2O = 1/1) to afford the mixture of stereoisomers of **5** (*Z,Z/E,Z/E,E* = *N.D.*/95/5) in 47% yield. Isomerization proceeded to form the mixture of *Z,Z/E,Z/E,E* = 1/66/33 after 1 d: slight yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (m, 3 H), 1.12-1.48 (m, 14 H), 2.25 (t, J = 7.6 Hz, *E,Z* (2 H)), 2.51 (t, J = 8.1 Hz, *E,E* (2 H)), 3.34-3.48 (m, 4 H), 6.06 (d, J = 14.4 Hz, *E,E* (1 H)), 6.23 (d, J = 12.0 Hz, *E,E* (1 H)), 6.34 (d, J = 14.8 Hz, *E,Z* (1 H)), 6.52 (d, J = 11.0 Hz, *E,Z* (1 H)), 7.25-7.49 (m, 6 H), 7.85 (dd, J = 11.0, 14.8 Hz, *E,Z* (1 H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 14.0, 14.5, 15.0, 22.5, 28.5, 29.0, 29.2, 31.5, 39.3, 40.9, 42.2, 121.4, 127.6, 129.1, 129.4, 130.4, 134.1, 135.4, 140.1, 146.0, 166.0; NOE experiment to confirm the *E,Z*-isomer: irradiation of the allyl triplet at δ 2.25 and the vinyl doublet at δ 6.34 (H_a in **5-*E,Z***) resulted in 5.7% and 9.8% enhancements of the doublet at δ 6.52 (H_c in **5-*E,Z***) respectively; NOE experiment to confirm the *E,E*-isomer: irradiation of the vinyl doublet at δ 6.06 (H_a in **5-*E,E***) resulted in 15.6% enhancements of the doublet at δ 6.23 (H_c in **5-*E,E***); IR (NaCl) 2929, 1644 (C=O), 1602, 1428, 1272, 1131, 982, 740 cm^{-1}; MS (CI), m/z (relative intensity, %) 394 (M^++1, 100). Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 64.22; H, 8.01; N, 3.51.

Computational Details

All calculations were performed with a Gaussian 03 package.[28] Density functional theory (DFT) method was employed using the B3LYP hybrid functional.[29] Structure were optimized with a basis set consisting of the LANL2DZ basis set for metallic atoms (Se, Pt, Pd)[30] and 6-31G(d) for the rest. These method and basis sets used have been applied to the recent reports on Ni-catalyzed cross-coupling reaction using aryl fluorides[31] and Pd-catalyzed allylstannylaion of alkynes.[32] Stationary points was confirmed by normal coordinate analysis (no imaginary frequency for an equilibrium structure and one imaginary frequency for a transition state). The intrinsic reaction coordinate (IRC) analysis[33] for each transition states were carried out to confirm that stationary points are smoothly connected to the corresponding equilibrium structures. Models and optimized energies (numbers in italics: kcal/mol, relative to alkyne-coordinated complex) for alkyne insertion processes are shown in **Scheme 4**.



Scheme 4. Models for Alkyne Insertion Processes

Energies, Cartesian coordinates and the ball-stick models of stationary points were not shown here for simplification. For all data, see the published paper.[23]

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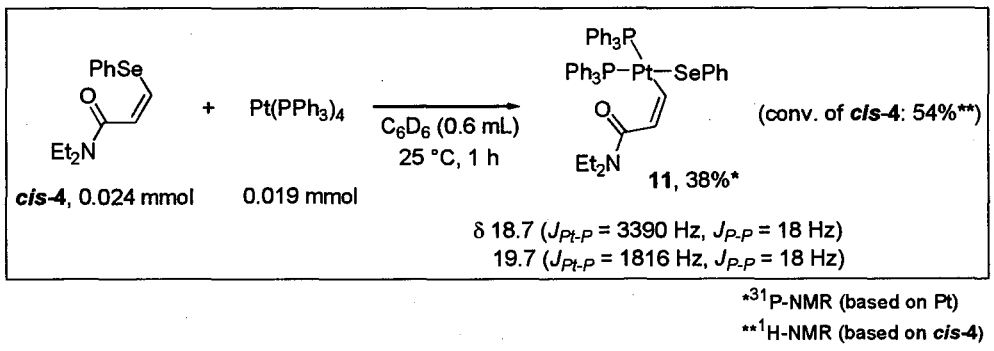
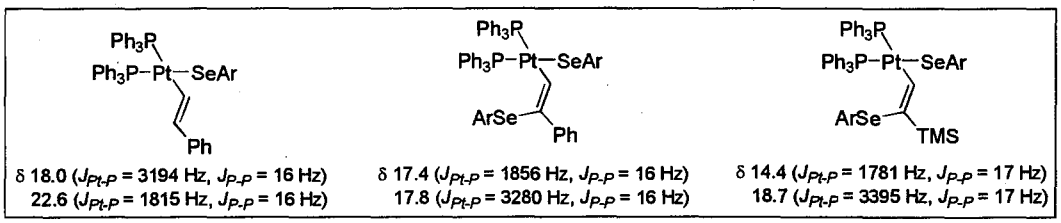
[12] In a stoichiometric reaction of ***cis*-4** with $Pt(PPh_3)_4$ in C_6D_6, formation of the oxidative adduct was confirmed by ^{31}P NMR analysis. Into a dry Pyrex NMR tube were added $S{=}P(C_6H_4Me\text{-}p)_3$ (internal standard to determine the yields, 2.0 mg, 0.006 mmol), $Pt(PPh_3)_4$ (23.8 mg, 0.019 mmol), ***cis*-4** (6.7 mg, 0.024 mmol) and C_6D_6 (0.6 mL) under a N_2 atmosphere (GB). Then the reaction was monitored by ^{31}P and ^{1}H NMR spectra at 25 °C. After 1 h, the ^{31}P NMR spectrum showed the formation of the oxidative adduct **11** in 38% yield: ^{31}P NMR (160 Hz, C_6D_6) δ 18.7 (d, $J_{Pt\text{-}P}$ = 3390 Hz, $J_{P\text{-}P}$ = 18 Hz), 19.7 (d, $J_{Pt\text{-}P}$ = 1816, $J_{P\text{-}P}$ = 18 Hz).



Although isolation of the adduct has not been tried, spectra did not conflict with the structure **11** and the known analogues shown in below: Kuniyasu, H.; Kato, T.; Inoue, M.; Terao, J.; Kambe, N. *J. Organomet. Chem.* **2006**, *691*, 1873.



Ar = p-ClC_6H_4

[13] Radical mechanism can be denied since radical scavengers such as TEMPO and galvinoxyl did not retard the reaction of **1a**.

[14] The reaction of vinyl selenide **1i** (Y=Se, R=CH_2Ph, R'=H, eq 1) gave a complex mixture and neither *Z*-**3e** nor *E*-**3e** was detected.

[15] Similar thermodynamic resolution of *E*/*Z* mixture was also observed in **2e**. See the Experimental Section for the details.

[16] **2h** was easily hydrolyzed during purification by PTLC or HPLC. Formation of **2h** was confirmed by crude ^{1}H NMR, ^{13}C NMR and HRMS analysis. In addition, the hydrolyzed product was isolated and characterized. the Experimental Section for the details.

[17] For the details about calculations, see the publised paper ref xx.

[18] For insertion of alkynes into Pt-SAr bond: Kuniyasu, H.; Yamashita, F.; Terao, J.; Kambe, N. *Angew. Chem. Int. Ed.* **2007**, *46*, 5929.

[19] Although $Pd(PPh_3)_4$ worked as catalyst for cyclization of **1a**, the reaction was slower and **2a** was obtained in 37% NMR yield after 2.5 h.

[20] Attempts to lactone synthesis using a vinyl selenide **9** (*Z*)-PhSe-CH=CH-C(O)OCH_2C≡CMe failed. This result as well as substituent effect on nitrogen described in the text may indicate that accessibility of alkyne unit to Pt is important for the present vinylchalcogenation to take place.

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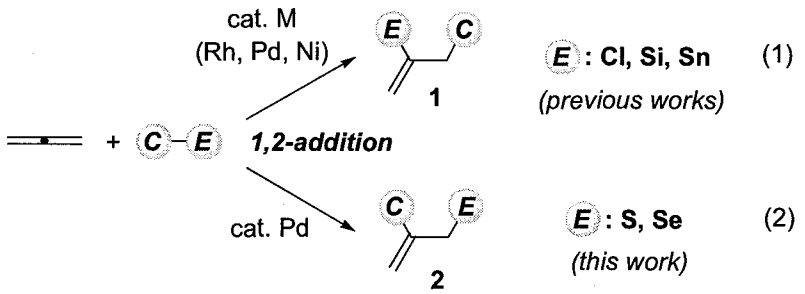
Chapter 3

Palladium(0)-Catalyzed Addition of Selenol Esters to Allenes Leading to Regioselective Formation of Allyl Selenides

3-1 Introduction

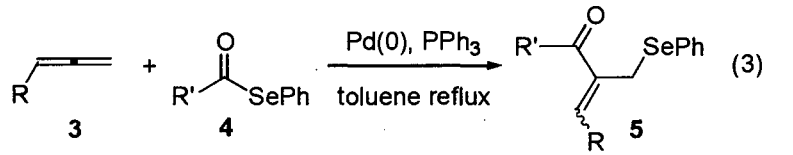
During the past two decades, allenes have been shown to be versatile building blocks in organic synthesis.[1] It is known that a variety of heteroatom compounds such as organotin, -borane, -selenium species add to allenes in the presence of transition metal catalysts such that an allene double bond inserts into R_3Sn-H, R_3Si-BR'_2, RSe-SeR' bonds.[2] There are fewer known examples, however, of allene insertion into carbon-heteroatom bonds:[3,4] Chatani and co-workers reported Ni or Pd catalyzed cyanosilylation of allenes with trimethylsilyl cyanide (NC-$SiMe_3$).[3a] Hua and Tanaka reported Rh catalyzed chloroesterification of allenes with chloro carbonates (ROC(O)-Cl).[3b] Shirakawa, Hiyama and co-workers described Ni catalyzed acylstannylation and alkynylstannylation of allenes with acyl stannanes and alkynyl stannanes (RC(O)-SnR'_3 and RC≡C-SnR'_3), respectively.[3c-e] In these cases, vinylic heteroatom products like **1** were obtained as the major products rather than allylic compounds **2** (eq 1). Here we disclose the first example of carbothiolation and carboselenation of allenes that proceeds with reverse regioselectivity leading to **2** (eq 2).

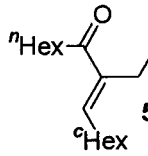
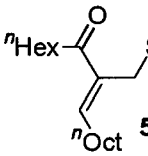
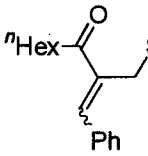
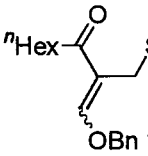
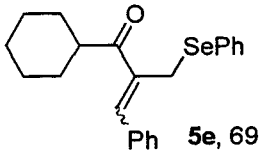
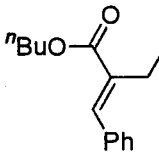
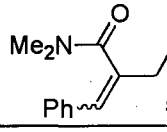


3-2 Results and Discussion

When a toluene solution (0.3 mL) containing selenol ester **4a** (R' = ^{n}Hex, 0.4 mmol), cyclohexylallene **3a** (R = ^{c}Hex, 1.2 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) and PPh_3 (10 mol%) was heated at reflux for 12 h, selenoacylation product, allyl selenide **5a**[5] (corresponds to **2** in eq 2), was obtained in 70% yield (Table 1, run 1) with exellent regio- and stereoselectivity.[6] In this reaction, the selenol ester adds to the terminal C-C double bond of the allene exclusively with the acyl moiety at the inner carbon and the SePh group at the terminal carbon to form an allyl selenide. Regioisomers such as vinyl selenide **1** or its stereoisomers were not detected by ^{1}H NMR analysis of the crude product.

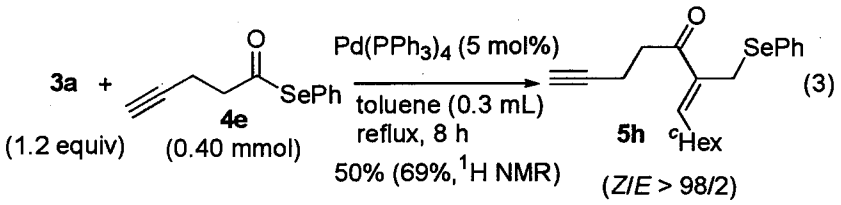
Table 1. Pd(0)-Catalyzed Selenoacylation of Allenes[a]

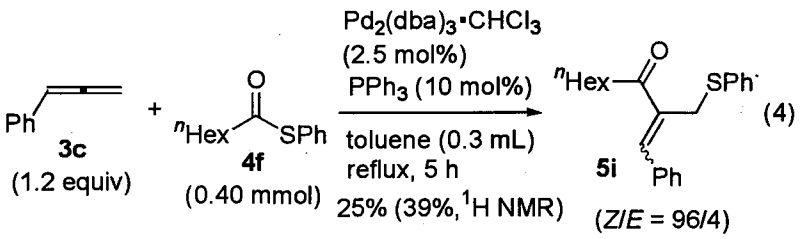


run	Allene **3**	Selenide **4**	Time, h	Allyl Selenide **5**, %[b]	*Z/E*[c]
1	**3a** (R = ^{c}Hex)	**4a** (R' = ^{n}Hex)	12	 **5a**, 70 (71)	>98/2
2[d]	**3b** (R = ^{n}Oct)	**4a**	22	 **5b**, 55 (71)	>98/2
3	**3c** (R = Ph)	**4a**	5	 **5c**, 90 (91)	98/2
4	**3d** (R = OBn)	**4a**	12	 **5d**, 87	98/2
5	**3c**	**4b** (R' = ^{c}Hex)	5	 **5e**, 69	91/9
6	**3c**	**4c** (R' = O^{n}Bu)	5	 **5f**, 70 (80)	>98/2
7[d]	**3c**	**4d** (R' = NMe_2)	3	 **5g**, 83	21/79

[a]Conditions: **4** (0.4 mmol), **3** (0.48 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%), PPh_3 (10 mol%), toluene (0.3 mL), reflux. [b]Isolated yields. Numbers in parentheses are NMR yields. [c]Determined by ^{1}H NMR. ">98/2" means no minor isomer was detected by NMR. [d]5 mol% of $Pd(PPh_3)_4$ was used as catalyst.

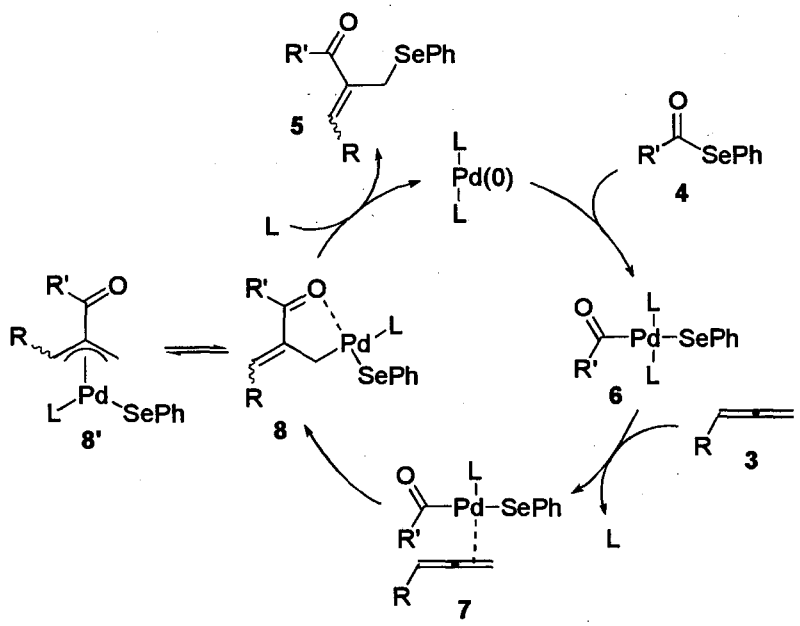
Table 1 summarizes the results obtained using several selenol esters and allenes. When *n*-octylallene **3b** was employed, allyl selenide **5b** was formed when $Pd(PPh_3)_4$ was used instead of $Pd_2(dba)_3{\cdot}CHCl_3$ and PPh_3 as a catalyst (run 2).[6] Although the reaction of phenylallene **3c** with **4a** gave allyl selenide **5c** in 90% yield (run 3) in 5 h, a small amount of *E* isomer was also detected.[7] Next, selenoacylation of allenes having an electron-donating or -withdrawing group was examined. For example, allene **3d** having a benzyloxy group can be subjected to selenoacylation using **4a** giving rise to allyl selenide **5d** in 87% yield (run 4); however, when ethyl 2,3-butadienoate (R = CO_2Et) was employed under similar reaction conditions, almost all of **4a** was recovered and the expected allyl selenide was not obtained probably due to oligomerization of the allene.[8,9] Selenol ester **4b** bearing a cyclohexyl group also underwent selenoacylation with **3c** to give **5e**; however, the stereoselectivity diminished in this case (run 5). In all case, no decarbonylative product was formed.[10] Next, selenoesterification and selenocarbamoylation of allene precursors were examined. When the reaction of selenocarbonate **4c** with phenylallene **3c** was carried out under similar conditions, the expected allyl selenide **5f** was obtained in a high yield with perfect regio- and stereoselectivity (run 6).[11] In contrast, although selenocarbamoylation of **3c** with carbamoselenoate **4d** proceeded to give **5g** in a high yield, the *E* isomer was formed predominantly (run 7).[12] Existence of an alkyne unit did not affect the reaction. For example, the reaction of cyclohexylallene **3a** with selenol ester **4e** bearing a terminal alkynyl group proceeded to give selenoacylation product **5h** selectively (eq 3). The reaction of a thiol ester **4f** with **3c** gave the thioacylation product **5i** with good regio- and stereoselectivity albeit in a low yield under similar conditions (eq 4).[13]





A plausible reaction pathway for allyl selenide formation involving a π-allylpalladium[14] intermediate is shown in Scheme 1, which explains the regioselectivity of the products. This

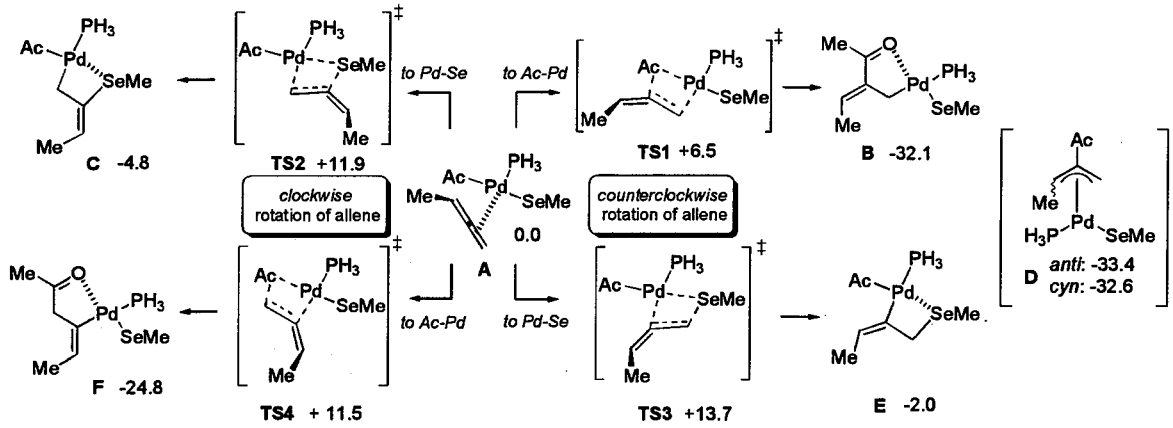
catalytic process is initiated by oxidative addition of the *acyl-Se* bond of selenol ester **4** to Pd(0), affording the *acyl-Pd-Se* complex **6**. Insertion of the coordinated allene into the *acyl-Pd* bond generates σ-allylpalladium **8** (in equilibrium with π-allylpalladium **8'**) having an acyl group at the central carbon of the allene unit prior to reductive elimination which produces allyl selenide **5**.



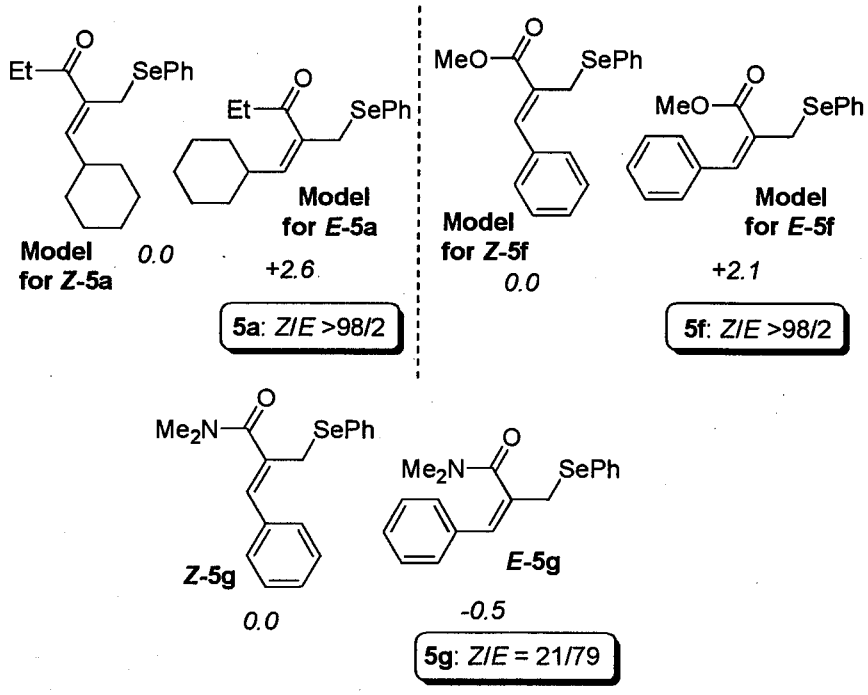
Scheme 1. A Proposed Pathway Leading to Allyl Selenide **5**

To shed light on the mechanism of the reaction and on the regio- and stereoselectivity of the process, DFT calculations were performed with methylallene and MeC(O)SeMe as substrates and PH_3 as the ligand for the Pd. Complex **A** shown in Scheme 2 is the optimized model for the allene coordinated intermediate (corresponds to **7** in Scheme 1). It is noteworthy that the axis of the Pd-coordinated allene leans to the side of the acyl group in **A**.[15] Subsequent allene insertion may occur in the *acyl-Pd* bond via counterclockwise rotation of the allene to give a σ-allylpalladium species **B**, which is the precursor of the π-allylpalladium intermediates **D**. Other possible pathways, i.e. formation of **C**, **E** and **F** are unlikely since **TS2**, **TS3** and **TS4** are less stable than **TS1** and **C**, **E** and **F** are also less stable than **B**. Accordingly, formation of **B** via **TS1** will be both kinetically and thermodynamically the most favored pathway. In the formation of **B** and **F**, 5-membered chelation by the intramolecular coordination of carbonyl oxygen to Pd could be important for structural stabilities (>20 kcal/mol more stable than **C** and **E**). In addition, the carbonyl group and the C=C unit are conjugated in **B** while not conjugated in **F**. These factors may be crucial for the predominant formation of the intermediate **B** in this system. Reductive elimination from **B** affords the allyl selenide products. In this step, the PPh_3

ligand may be essential based on Kurosawa's study of $[Pd(\pi\text{-allyl})(SPh)]_2$ reactions with PPh_3.[16] In fact, addition of **4a** to **3c** was sluggish (<5%) without the PPh_3 ligand (compare with run 3 in Table 1).[6]

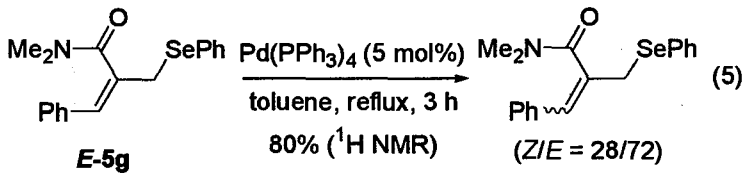


Scheme 2. Computational Calculations for Allene Inserion Step

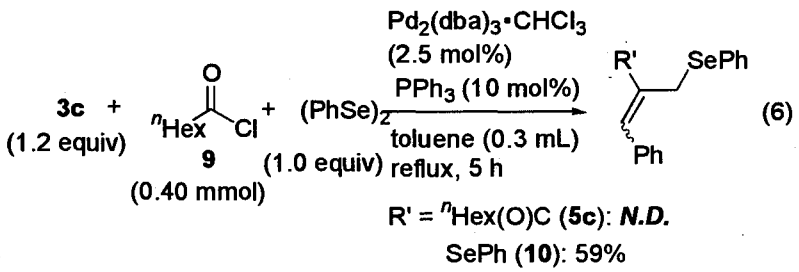


Scheme 3. Computational Calculations for Stablity of Products

As for the stereoselectivity of the products, the (*Z*)-adduct of EtC(O)SePh to **3a** (model of (*Z*)-**5a**) is calculated to be 2.6 kcal/mol more stable than the corresponding (*E*)-adduct. Similarly, the (*Z*)-adduct of MeOC(O)SePh to **3a** (model of (*Z*)-**5f**) is calculated to be 2.1 kcal/mol more stable than the corresponding (*E*)-adduct. However, (*Z*)-**5g** is 0.5 kcal/mol less stable than (*E*)-**5g**.[17] These results do not conflict with the observed stereoselectivities in runs 1, 6 and 7 (Scheme 3). In addition, when the isolated product (*E*)-**5g** was subjected to the same reaction conditions as in run 6, isomerization ensued to give the *Z/E* (28/72) mixture of **5g** while isomerization did not proceed in the presence of catalytic amount of PPh_3 without Pd (eq 5).



These results suggest that the stereoselectivities observed reflect the relative thermodynamic stabilities of the products. Furthermore, the evidence that Pd(0) inserts into the C-Se bond of allyl selenides[16] indicates that the last step of Scheme 1 (**8** to **5**) is reversible and *Z/E* isomerization proceeds via the π-allylpalladium intermediates **8'**. Cheng and co-workers revealed that Pd-catalyzed three-component assembly of allenes, acyl chlorides and bismetal reagents such as $(BPin)_2$ afforded allyl-metal species like **5**.[18] The authors proposed transmetalation between bismetal reagents and π-allylpalladium intermediate like **8'** prior to reductive elimination of the allyl-metal product. Thus, we examined to check the possibility of selenoacylation of allenes using diselenides as bismetal reagents. When the mixture of acyl chloride **9** (0.40 mmol), phenylallene **3c** (0.48 mmol), and $(PhSe)_2$ (0.40 mmol) was heated at reflux for 5 h with Pd(0)-PPh_3 catalyst, only bisselenation product **10** was obtained[2a] and no selenoacylation product such as **5c** was detected probably due to faster oxidative addition of $(PhSe)_2$ to Pd(0) over that of acyl chloride **9** (eq 6).



3-3 Conclusions

1,2-Addition of selenol esters onto allenes proceeds with excellent regioselectivity and high stereoselectivity in the presence of Pd(0)-PPh_3 catalyst, producing functionalized allyl selenides. A reaction pathway accounting for the observed regio- and stereoselectivity is proposed based on the results of DFT calculations.

3-4 Experimental Section

Genaral Comments

THF was distilled from benzophenone ketyl just prior to use. Toluene and CH_2Cl_2 were distilled from CaH_2. Cyclohexylallene (**3a**),[19] *n*-octylallene (**3b**),[19] phenylallene (**3c**),[20] Propa-1,2-dienyloxymethylbenzene (**3d**),[21] $Me_2NC(O)SePh$ (**4d**),[12] *n*-HexC(O)SPh (**4f**),[22] $Pd(PPh_3)_4$ [23] and $Pd_2(dba)_3 \cdot CHCl_3$ [24] were prepared according to the literature procedure. Other reagents and phosphine ligands were purchased from commercial source and used without further purification. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ALICE-400 (400 MHz and 100 MHz, respectively) spectrometer using Me_4Si (in $CDCl_3$) as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Preparative TLC was conducted by using Wakogel B-5F silica gel (325 mesh). Mass spectra (EI, CI) were taken on a SHIMAZU GCMS-QP2000 operating in the electron impact mode (70 eV) equipped with CBP1-M25-025 column. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus. For the copies of ^1H and ^{13}C NMR spectrum of all samples, see Supporting Information of the published paper.[25]

Procedures and Characterization of Reaction Materials

***Se*-Pheny hexanecarboselenoate (4a, runs 1-4, Table 1)[26] : Typical procedure.**

Into a 100-mL flask were placed elemental selenium (20 mmol) and THF (10 mL) under N_2 and the suspension was cooled to 0 °C. PhLi (0.94 M in Et_2O-cyclohexane, 23 mL, 22 mmol) was added slowly to prepare PhSeLi and the stirring was continued for 5 min. To the pale yellow solution of PhSeLi was then added heptanoyl chloride (20 mmol) in 20 mL of THF at the same temperature, and the mixture was warmed up to room temperature and stirred overnight. After the mixture was poured into brine (50 mL) and extracted with Et_2O (30 mL x 3), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 40/1) to afford *Se*-phenyl hexanecarboselenoate (**4a**) in 80% yield as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.21-1.39 (m, 6 H), 1.56-1.72 (m, 2 H), 2.69 (t, J =

7.6 Hz, 2 H), 7.34-7.52 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.4, 25.3, 28.5, 31.4, 47.5, 126.5, 128.8, 129.3, 135.8 (J_{Se-C} = 8.7 Hz), 200.4; IR (NaCl) 3059, 2928, 1724 (C=O), 1580, 1478, 1120, 1021, 738, 689 cm^{-1}; MS (EI) m/z (relative intensity, %) 270 (M^+, 4), 157 (15), 113 (100), 85 (26). Anal. Calcd for $C_{13}H_{18}OSe$: C, 57.99; H, 6.74. Found C, 58.23; H, 6.74.

***Se*-Phenyl cyclohexanecarboselenoate (4b, run 5, Table 1).**

Purified by silica gel column chromatography (*n*-hexane/Et_2O = 10/1); 55% yield as a colorless oil; Spectra data of **4b** were identical with those reported.[27]

***O*-Butyl *Se*-phenyl selenocarbonate (4c, run 6, Table 1).**

Into a 100-mL flask were placed Ph_2Se_2 (5 mmol), THF (35 mL) and $NaBH_4$ (15 mmol) under N_2 and then methanol (0.5 mL) was added slowly, and the stirring was continued for 30 min. To the yellow solution was added dropwise THF (10 mL) solution of *n*-butyl chloroformate (10 mmol), and the mixture was stirred overnight. After the mixture was poured into sat.NH_4Cl aq (50 mL) and extracted with Et_2O (30 mL x 3), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 7/1) to afford *O*-butyl *Se*-phenyl selenocarbonate (**4c**) in 59% yield as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3 H), 1.32-1.42 (m, 2 H), 1.61-1.68 (m, 2 H), 4.26 (t, J = 6.8 Hz, 2 H), 7.32-7.40 (m, 3 H), 7.60-7.63 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 18.9, 30.6, 68.1, 126.1, 129.0, 129.2, 135.7 ($^2J_{Se-C}$ = 10.5 Hz), 166.8; IR (NaCl) 3059, 2960, 1727 (C=O), 1478, 1380, 1120, 1074, 1022, 927, 823, 739 cm^{-1}; MS (EI) m/z (relative intensity, %) 270 (M^+, 10), 158 (100), 77 (22), 57 (48). Anal. Calcd for $C_{11}H_{14}O_2Se$: C, 51.37; H, 5.49. Found C, 51.39; H, 5.44.

***Se*-Phenyl 4-pentynecarboselenoate (4e, eq 3).** [27]

Into a 50-mL flask were placed Ph_2Se_2 (15 mmol), CH_2Cl_2 (23 mL) and 4-pentynoic acid (10 mmol) under N_2 and then $^nBu_3P$ (15 mmol) and CH_2Cl_2 (3 mL) were added cooling with ice-bath, and the stirring was continued for 4 h at room temperature. After the mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (30 mL x 3) and Et_2O (30 mL x 2), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 10/1) to afford *Se*-phenyl 4-pentynecarboselenoate (**4e**) in 69% yield as a pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.00 (t, J = 2.8 Hz, 1 H), 2.55 (td, J = 2.8 Hz, 7.2 Hz, 2 H), 2.94 (t, J = 7.2 Hz, 2 H), 7.35-7.40 (m, 3 H), 7.49-7.53 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 45.7, 69.4, 81.4, 125.6, 128.9, 129.0, 135.3, 197.9; IR (NaCl) 3294, 3058, 1720 (C=O), 1578, 1438, 1044, 961, 740 cm^{-1}; MS (EI) m/z (relative intensity, %) 238 (M^+, 5), 157 (8), 81 (100), 53 (45). Anal.

Calcd for $C_{11}H_{10}OSe$: C, 55.71; H, 4.25. Found C, 55.75; H, 4.22.

Procedures and Characterization of Reaction Products

(*Z*)-1-Cyclohexyl-2-(phenylselenomethyl)non-1-en-3-one (5a, run 1, Table 1); Typical procedure.

Into a 3-mL flask equipped with a reflux condenser were placed selenol ester **4a** (0.40 mmol), toluene (0.3 mL), cyclohexylallene **3a** (0.48 mmol), PPh_3 (0.020 mmol), and $Pd_2(dba)_3 \cdot CHCl_3$ (0.005 mmol) at room temperature under N_2 and the solution turned immediately brown. After the mixture was refluxed for 12 h, filtered through the celite pad, toluene was removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/Et_2O = 20/1) to afford (*Z*)-1-cyclohexyl-2-(phenylselenomethyl)non-1-en-3-one **5a** in 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86-1.64 (m, 21 H), 2.05-2.13 (m, 1 H), 2.61 (t, J = 7.6 Hz, 2 H), 3.80 (s, $^2J_{Se\text{-}H}$ = 10.8 Hz, 2 H), 6.36 (d, J = 13.2 Hz, 1 H), 7.25-7.27 (m, 3 H), 7.56-7.58 (m, 2 H); NOE experiment: irradiation at allyl triplet at δ 2.61 resulted in 8.6% enhancement of the signal at δ 6.36. ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 22.7, 24.8, 25.4, 25.7, 29.0, 31.6, 32.1, 37.4, 38.4, 127.4, 128.9, 130.6, 134.4, 136.6, 148.3, 201.0 ; IR (NaCl) 3056, 2924, 1673(C=O), 1579, 1476, 1448, 1132, 692, 670 cm^{-1}; MS (EI) m/z (relative intensity, %) 392 (M^+, 100), 381 (75), 367 (15), 355 (27), 343 (74). Anal. Calcd for $C_{22}H_{32}OSe$: C, 67.50; H, 8.24. Found: C, 67.63; H, 8.40.

(*Z*)-8-(Phenylselenomethyl)heptadec-8-en-7-one (5b, run 2, Table 1).

Purified by preparative TLC (*n*-hexane/Et_2O = 20/1); 55% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83-0.92 (m, 6 H), 1.26-1.59 (m, 20 H), 2.00 (q, J = 7.2 Hz, 2 H), 2.62 (t, J = 7.2 Hz, 2 H), 3.80 (s, $^2J_{Se\text{-}H}$ = 10.4 Hz, 2 H), 6.58 (t, J = 7.2 Hz, 1 H), 7.24-7.26 (m, 3 H), 7.54-7.57 (m, 2 H); NOE experiment: irradiation at vinyl triplet at δ 6.58 resulted in a 10.6% enhancement of the signal at δ 2.62. ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 22.4, 22.5, 22.6, 24.8, 28.7, 29.0, 29.1, 29.2, 29.3, 29.4, 31.7, 31.8, 37.4, 127.5, 128.8, 130.4, 134.5, 138.3, 144.0, 200.6; IR(NaCl) 3057, 2925, 2855, 1673 (C=O), 1579, 1466, 1378, 1299, 1187, 738, 692 cm^{-1}; MS(EI) m/z (relative intensity, %) 422 (M^+, 83), 405 (52), 393 (65), 381 (100), 367 (15). Anal Calcd for $C_{24}H_{38}OSe$: C, 68.39; H, 9.09. Found: C, 68.66; H, 9.31.

(*Z*)-1-Phenyl-2-(phenylselenomethyl)non-1-en-3-one (5c, run 3, Table 1).

Purified by preparative TLC (*n*-hexane/Et_2O = 10/1); 90% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, J = 6.8 Hz, 3 H), 1.24 (brs, 6 H), 1.59 (t, J = 6.8 Hz, 2 H), 2.69 (t, J = 6.8 Hz, 2 H), 3.96 (s, 2 H), 7.10-7.43 (m, 11 H); Determination of the stereochemistry by NOE experiment was unsuccessful because a signal of vinyl proton was overlapped with those of phenyl protons; however, the stereochemistry is expected to be *Z* from computational

calculations of the related products (vide infra);^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.7, 24.0, 24.8, 29.1, 31.8, 37.9, 127.1, 128.4, 128.6, 128.7, 129.2, 130.3, 133.6, 134.8, 138.2, 138.7, 200.8; IR(NaCl) 3051, 2947, 2912, 1666 (C=O), 1620, 1579, 1475, 1441, 1377, 1016, 739, 693 cm^{-1}; MS(CI) m/z (relative intensity, %) 387 (M^++1, 100), 229 (54), 113 (5). Anal. Calcd for $C_{22}H_{26}OSe$: C, 68.56; H, 6.80. Found: C, 68.56; H, 6.93.

(*Z*)-1-Benzyloxy-2-(phenylselenomethyl)non-1-en-3-one (5d, run 4, Table 1).
Purified by silica gel column chromatography (*n*-hexane/Et_2O = 2/1); 87% yield as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.1 Hz, 3 H), 1.20-1.32 (m, 6 H), 1.51-1.58 (m, 2 H), 2.44 (t, J = 7.3 Hz, 2 H), 3.86 (s, $^2J_{Se\text{-}H}$ = 11.2 Hz, 2 H), 4.92 (s, 2 H), 7.16-7.56 (m, 11 H); Determination of the stereochemistry by NOE experiment was unsuccessful because a signal of vinyl proton was overlapped with those of phenyl protons; however, the stereochemistry is expected to be *Z* from computational calculations of the related products (vide infra);^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.0, 22.5, 24.9, 29.0, 31.6, 37.5, 75.9, 119.9, 126.9, 127.5, 128.6, 128.7, 131.0, 133.7, 135.6, 158.2, 198.3; IR(NaCl) 3059, 2930, 1634 (C=O), 1456, 1378, 1289, 1171, 1022, 736, 693 cm^{-1}; MS(CI) m/z (relative intensity, %) 417 (M^++1, 100), 169 (57), 91 (35). HRMS (CI) calcd for $C_{23}H_{29}O_2Se$: 417.1333. Found 417.1328.

(*Z*)-1-Cyclohexyl-3-phenyl-2-(phenylselenomethyl)propenone (5e, run 5, Table 1).
Only (*Z*)-**5e** was isolated by preparative TLC (*n*-hexane/Et_2O = 5/1) in 69% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87-1.85 (m, 10 H), 3.11 (t, J = 10.4 Hz, 1 H), 4.04 (s, 2 H), 7.19-7.56 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.20 25.8, 25.9, 29.6, 44.8, 127.2, 128.6, 128.7, 128.9, 129.3, 130.6, 133.5, 135.1, 137.7, 138.2, 204.6; IR(NaCl) 3059, 2929, 2857, 2390, 1960, 1674 (C=O), 1481, 1212, 739, 699 cm^{-1}; MS(EI) m/z (relative intensity, %) 384 (M^+, 100), 306 (15). 226 (56). Anal. Calcd for $C_{22}H_{24}OSe$: C, 68.92; H, 6.31. Found: C, 69.08; H, 6.53. Isolation of (*E*)-**5e** was failed, however, the formation of (*E*)-**5e** was confirmed by NOE experiment of the crude product.

(*Z*)-Butyl 3-phenyl-2-(phenylselenomethyl)acryrate (5f, run 6, Table 1).
Purified by preparative TLC (*n*-hexane/Et_2O = 40/1); 70% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 t, J = 7.2 Hz, 3 H), 1.40-1.49 (m, 2 H), 1.65-1.72 (m, 2 H), 4.04 (s, $^2J_{Se\text{-}H}$ = 9.6 Hz, 2 H), 4.21 (t, J = 6.8 Hz, 2H), 7.18-7.67 (m, 11 H); Determination of the stereochemistry by NOE experiment was unsuccessful because a signal of vinyl proton was overlapped with those of phenyl protons; however, we reasoned the product as *Z*-configuration from the results of computational calculations of model compounds (vide infra);^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 19.4, 25.2, 30.8, 65.1, 127.3, 128.3, 128.4, 128.8, 129.1, 129.7, 129.9,

133.8, 134.7, 139.4, 167.1; IR(NaCl) 3054, 2962, 2869, 1708 (C=O), 1627, 1575, 1477, 1264, 1200, 1154, 1073, 1015, 744, 698 cm^{-1}; MS(CI) m/z (relative intensity, %) 375 (M^{+}+1, 93), 301 (100), 217 (89), 145 (10). Anal. Calcd for $C_{20}H_{22}O_2Se$: C, 64.34; H, 5.94. Found: C, 64.45; H, 5.86.

***N,N*-Dimethyl 3-phenyl-2-(phenylselenomethyl)acrylamide (5g, run 7, Table 1).**
Purified by preparative TLC (*n*-hexane/Et_2O = 1/1); the mixture of stereoisomers of **5g** (*E*/*Z* = 79/21); 83% yield as a pale yellow oil. Another purification by preparative TLC (*n*-hexane/Et_2O = 5/4) to provide pure (*E*)-**5g** and (*Z*)-**5g**.
(*E*)-**5g**: Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H, NCH_3), 2.85 (s, 3H, NCH_3), 3.92-4.05 (br, 2H, PhSeCH_2), 6.35 (s, 1H, vinyl), 7.11-7.55 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.3, 34.4, 37.6, 127.3, 127.6, 128.0, 128.4, 129.0, 129.1, 130.0, 132.9, 135.5, 170.0; IR(NaCl) 3056, 2926, 1622 (C=O), 1495, 1410, 1263, 1187, 1070, 738 cm^{-1}; MS(CI) m/z (relative intensity, %) 346 (M^{+}+1, 100), 344 (51), 188 (33). HRMS (CI) calcd for $C_{18}H_{20}NOSe$: 346.0710. Found 346.0712.
(*Z*)-**5g**: Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.92-3.10 (br, 6H, N$(CH_3)_2$), 4.11 (s, 2H, PhSeCH_2), 6.51 (s, 1H, vinyl), 7.20-7.44 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 35.1 (br), 39.3 (br), 127.1, 127.9, 128.5, 128.8, 129.0, 129.8, 130.7, 132.7, 133.9, 135.2, 171.9; NOE experiment: irradiation at vinyl singlet at δ 6.51 resulted in a 4.9% enhancement of the signal at δ 2.92-3.10.; IR(NaCl) 3055, 2928, 1634, 1494, 1394, 1140, 1056, 738 cm^{-1}; MS(CI) m/z (relative intensity, %) 346 (M^{+}+1, 100), 344 (51), 188 (31). Anal. Calcd for $C_{18}H_{19}NOSe$: C, 62.79; H, 5.56; N, 4.07. Found: C, 62.99; H, 5.62; N, 3.92.

(*Z*)-1-Cyclohexyl-2-(phenylselenomethyl)hept-1-en-6-yne-3-one (5h, eq 3).
Purified by silica gel column chromatography (*n*-hexane/Et_2O = 10/1); 50% yield as a pale yellow solid; mp 60.0-61.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98-1.67 (m, 10 H), 1.96 (t, J = 2.7 Hz, 1 H), 2.10 (m, 1 H), 2.48 (m, 2 H), 2.89 (t, J = 6.8 Hz, 2 H), 3.79 (s, $^2J_{Se\text{-}H}$ = 10.8 Hz, 2 H), 6.38 (d, J = 9.8 Hz, 1 H), 7.25-7.26 (m, 3 H), 7.55-7.57 (m, 2 H); NOE experiment: irradiation at allyl singlet at δ 3.79 resulted in a 4.8% enhancement of the allyl signal at δ 2.10.; ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 22.5, 25.4, 25.7, 32.0, 36.4, 38.5, 68.7, 83.6, 127.6, 129.0, 130.3, 134.7, 136.4, 149.2, 198.1; IR(NaCl) 3266, 2929, 2852.9, 1668 (C=O), 1436, 1300, 1125, 905, 749 cm^{-1}; MS(CI) m/z (relative intensity, %) 361 (M^{+}+1, 53), 203 (100). HRMS (CI) calcd for $C_{20}H_{25}OSe$: 361.1071. Found 361.1073.

(*Z*)-1-Phenyl-2-(phenylthiomethyl)non-1-en-3-one (5i, eq 4).
Purified by preparative TLC (*n*-hexane/Et_2O = 10/1); the mixture of stereoisomers of **5i** (*E*/*Z* = 4/96); 26% yield as a colorless oil; The following spectra and analytical data were obtained

from the *E*/*Z* mixture; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.3 Hz, *E*(3 H)), 0.90 (t, *J* = 7.1 Hz, *Z*(3 H)), 1.26-1.39 (m, 6 H), 1.68 (tt, *J* = 7.6 Hz, 6.8 Hz, *Z*(2 H)), 2.24 (t, *J* = 7.4 Hz, *E*(2 H)), 2.79 (t, *J* = 7.6 Hz, *Z*(2 H)), 3.83 (s, *E*(2 H)), 4.05 (s, *Z*(2 H)), 6.58 (s, *E*(1 H)), 7.16-7.26 (m, 3 H), 7.34-7.48 (m, 7 H), 7.57 (s, *Z*(1 H)); NOE experiment: irradiation at allyl triplet at δ 2.79 resulted in a 8.3% enhancement of the vinyl signal at δ 7.57.; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.5, 24.7, 29.0, 31.0, 31.7, 37.9, 126.5, 128.7, 128.8, 129.0, 129.5, 130.4, 134.9, 136.3, 136.9, 140.4, 201.0 IR(NaCl) 3059, 2928, 1668 (C=O), 1622, 1481, 1447, 1212, 1141, 739, 699 cm^{-1}; MS(CI) m/z (relative intensity, %) 339 (M^++1, 100), 229 (60), 113 (6). Anal. Calcd for $C_{22}H_{26}OS$: C, 78.06; H, 7.74. Found: C, 78.32; H, 7.89.

2,3-(bisphenylseleno)propenylbenzene (10, eq 5).

Into a 3-mL flask equipped with a reflux condenser were placed heptanoyl chloride **9** (0.40 mmol), toluene (0.3 mL), phenylallene **3c** (0.48 mmol), Ph_2Se_2 (0.40 mmol), PPh_3 (0.020 mmol), and $Pd_2(dba)_3 \cdot CHCl_3$ (0.005 mmol) at room temperature under N_2 and the solution turned immediately brown. After the mixture was refluxed for 5 h and filtered through celite by using Et_2O, the solvents were removed *in vacuo*. The crude product was purified by silica gel column chromatography (*n*-hexane/Et2O = 10/1), giving 2,3-(bisphenylseleno)propenylbenzene (**10**). Although the *E*/*Z* ratio was determined by ^{1}H NMR (*E*/*Z* = 58/42), an attempt for isolation of isomers by PTLC failed. Although there is the paper for the synthesis of **10**[2a], spectra and analytical data have never been reported. The following data were obtained from the *E*/*Z* mixture. (*E*)-**10**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 (s, $J^2_{Se\text{-}H}$ = 28 Hz, 2 H), 6.68 (s, 1 H), 7.16-7.60 (m, 15 H). (*Z*)-**10:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.01 (t, $J^2_{Se\text{-}H}$ = 28 Hz, 2 H), 6.85 (s, 1 H), 7.16-7.60 (m, 15 H). MS(EI) m/z (relative intensity, %) 428 (M^+, 10), 314 (12), 273 (20), 157 (16), 115 (100). HRMS calcd for $C_{21}H_{18}Se_2$: 428.2876. Found 428.3472.

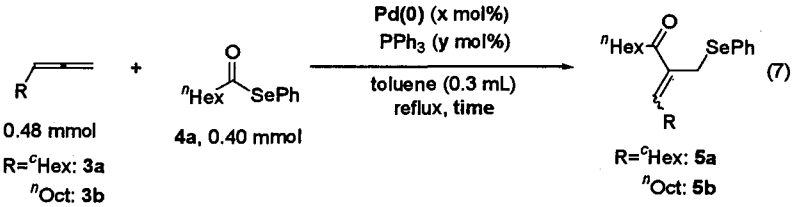
2-(Hydroxylphenylmethyl)-non-1-en-3-one (11, eq 9).

Into a flame-dried 30-mL flask equipped with a dropping funnel were placed allyl selenide **5c** (0.38 mmol) and anhydrous CH_2Cl_2 (3 mL) under N_2. A solution of *m*-CPBA (0.42 mmol) in 2 mL of CH_2Cl_2 was added dropwise at -78 °C (acetone/CO_2) and the mixture was stirred at same temperature. After 1 h, saturated $NaHCO_3$aq and Et_2O were added and washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by preparative recycling HPLC (eluted with $CHCl_3$) afforded **11** in 80% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.1 Hz, 3 H), 1.19-1.28 (m, 6 H), 1.49-1.56 (m, 2 H), 2.62-2.66 (m, 2 H), 3.35 (brs, 1 H), 5.58 (s, 1 H), 5.93 (s, 1 H), 6.14 (s, 1 H), 7.22-7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 22.1, 23.8, 28.4, 31.2, 38.0, 72.7, 127.8, 126.1, 127.2, 127.9, 141.3, 149.3, 202.6; IR(NaCl) 3470 (O-H), 2929, 1678 (C=O), 1455, 1026, 763, 699 cm^{-1}; MS(CI)

m/z (relative intensity, %) 229 (M^++1-H_2O, 100). HRMS (EI) calcd for $C_{16}H_{21}O_2$: 246.1620. Found 246.1602.

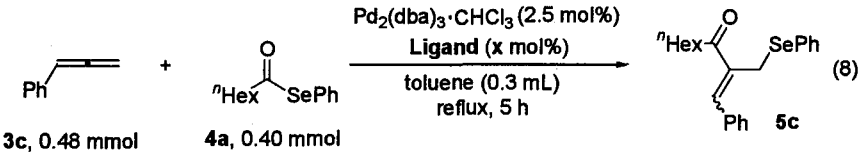
Effect of Ligands and Pd(0)-Source

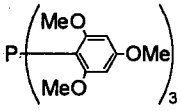
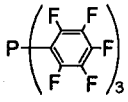
On the Reaction of Selenol Ester **4a** with Allenes **3a** and **3b** Giving **5a** and **5b** (eq 7)



run	3	Pd(0)	x	y	time, h	NMR Yield of 5, %	Z/E
1	3a	$Pd_2(dba)_3 \cdot CHCl_3$	2.5	10	12	71	>98/2
2	3a	$Pd(PPh_3)_4$	5	0	12	71	>98/2
3	3b	$Pd_2(dba)_3 \cdot CHCl_3$	2.5	10	12	23	>98/2
4	3b	$Pd_2(dba)_3 \cdot CHCl_3$	2.5	10	5	14	>98/2
5	3b	$Pd(PPh_3)_4$	5	0	5	40	>98/2
6	3b	$Pd(PPh_3)_4$	5	0	22	71	>98/2

On the Reaction of Selenol Ester **4a** with Allene **3c** Giving **5c** (eq 8)



run	Ligand	x	NMR Yield of 5c, %	Z/E
1	none	-	<5	-
2	PPh_3	5	58	98/2
3		**10**	**91**	**98/2**
4		15	74	92/8
5		20	66	90/10
6		50	38	94/6
7	PMe_2Ph	5	57	88/12
8		10	70	92/8
9		15	81	89/11
10		20	71	91/9
11		50	18	61/39
12	$PMePh_2$	20	32	75/25
13	$P(^cHex)_3$	20	16	-
14	$P(^nBu)_3$	20	15	-
15	$P(OEt)_3$	20	28	87/13
16	P(2-furyl)$_3$	20	16	-
17	$P(C_6H_4OMe\text{-}p)_3$	20	31	89/11
18	$P(C_6H_4F\text{-}p)_3$	20	27	92/8
19		20	15	-
20		20	28	-
21	dppe	20	14	-

Computational Details

All calculations were performed with a Gaussian 03 package.[28] Density functional theory (DFT) method was employed using the B3LYP hybrid functional.[29] Structure were optimized with a basis set consisting of the LANL2DZ basis set for metallic atoms (Se, Pd)[30] and 6-31G(d) for the rest. These method and basis sets used have been applied to the recent reports on Ni-catalyzed cross-coupling reaction using aryl fluorides[31] and Pd-catalyzed allylstannylaion of alkynes.[32] Stationary points was confirmed by normal coordinate analysis (no imaginary frequency for an equilibrium structure and one imaginary frequency for a transition state). The intrinsic reaction coordinate (IRC) analysis[33] for each transition states were carried out to confirm that stationary points are smoothly connected to the corresponding equilibrium structures. Cartesian coordinates and the ball-stick models of stationary points in **Scheme 2** and **3** were not shown here for simplification. For all data, see the published paper.[25]

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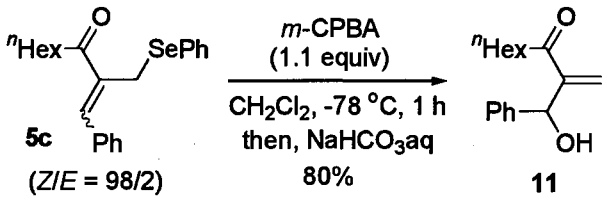
[6] For screening of phosphine ligands, see the Experimental Section.

[7] Oxidation of isolated **5c** with *m*-CPBA followed by hydrolysis resulted in the formation of allyl alcohol **11** in 80% yield (eq 9).



(9)

[8] Ethyl 2,3-butadienoate was reported to oligomerize in the presence of PPh_3, see: Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 2906.

[9] Selenoacylation of α,α-disubstituted allenes such as vinylidenecyclohexane with **4a** did not proceed at all.

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[13] Although starting material **4f** remained, yield of **5i** was not improved when the reaction time was prolonged to 10 h.

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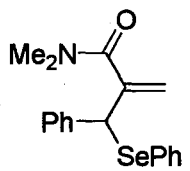
[17] Since the regioisomer of **5g** shown below is calculated to be ca. 5 kcal/mol less stable than (*Z*)-**5g**, formation of this isomer will be thermodynamically unfavored. In addition, reverce oxidative addition and reductive elimination leading to **5g** will proceed from the result of eq 5.



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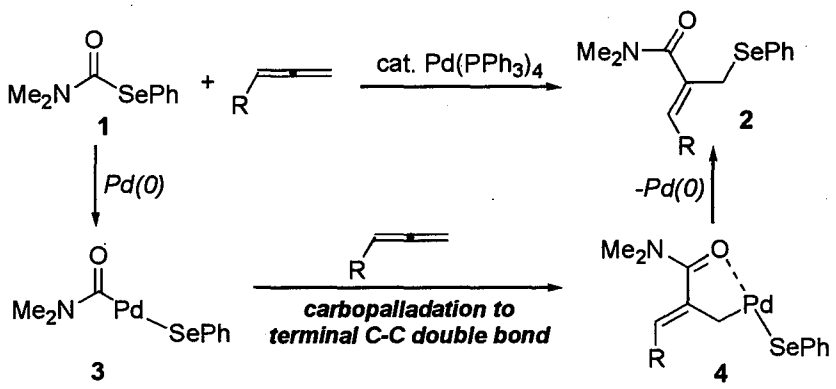
Chapter 4

Palladium(0)-Catalyzed Intramolecular Cyclization of Carbamothioates and –selenoates Having an Allene Moiety

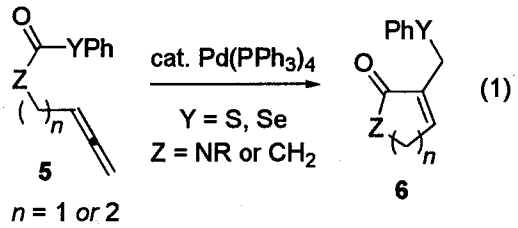
4-1 Introduction

We recently reported that selenol esters and a carbamoselenoate **1** added to the distal double bond of terminal allenes regioselectively in the presence of Pd(0) catalyst, giving rise to functionalized allyl selenides **2** (Scheme 1).[1] From density functional theory (DFT) calculations for allene insertion step, it was revealed that the carbonyl-coordinated σ-allylpalladium **4**, formed by carbopalladation of the distal double bond of the allene with oxidative adduct **3**, was the most kinetically and thermodynamically favored intermediate and would be a key species for the excellent regioselectivitiy of this transformation.



Scheme 1. A Proposed Pathway Leading to Allyl Selenide **5**

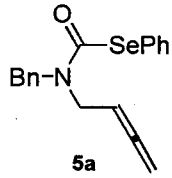
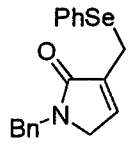
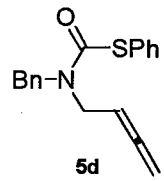
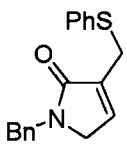
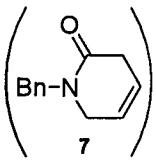
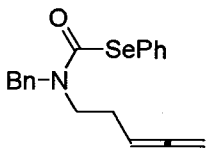
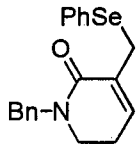
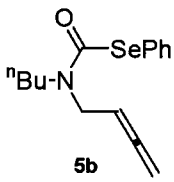
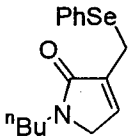
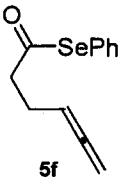
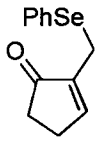
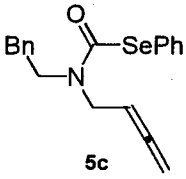
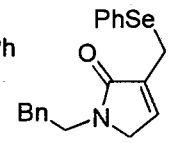
Although intramolecular addition of a carbon-hydrogen bond to the allene unit is a well known typical C-C bond-forming cyclization of allenes,[2] intramolecular insertion of allenes to carbon-heteroatom bonds has not been studied extensively.[3] We thus examined the intramolecular variation of selenocarbamoylation[4] of allenes, aiming for an efficient regioselective construction of α,β-unsaturated lactam frameworks as core structures for synthesis of several pharmacological active compounds and as useful synthetic intermediates.[5] In this chapter we report that Pd(0)-catalyzed intramolecular selenocarbamoylation of allenes with carbamoselenoates **5** resulted in the regioselective formation of five- and six-membered α,β-unsaturated lactams **6** having an allyl selenide unit (eq 1).



4-2 Results and Discussion

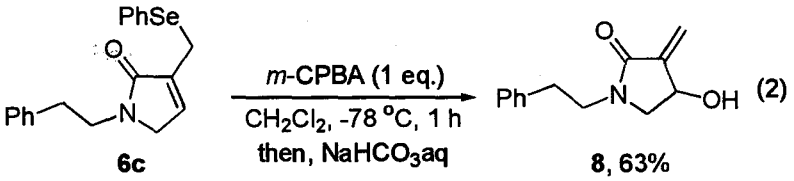
At first, we carried out the reaction of carbamoselenoate **5a** that has a terminal allene unit on the nitrogen atom under typical reaction conditions for the corresponding intermolecular system.[1] When toluene (0.5 mL) containing carbamoselenoate **5a** (0.4 mmol) and $Pd(PPh_3)_4$ (5 mol%) was heated at 110 °C for 5 h, α,β-unsaturated five-membered lactam **6a** was obtained in 50% yield along with 24% of an unexpected six-membered lactam **7** (without a SePh group) as a by-product.

Table 1. Intramolecular Cyclization of **5** to Form Products **6** (eq 1)[a]

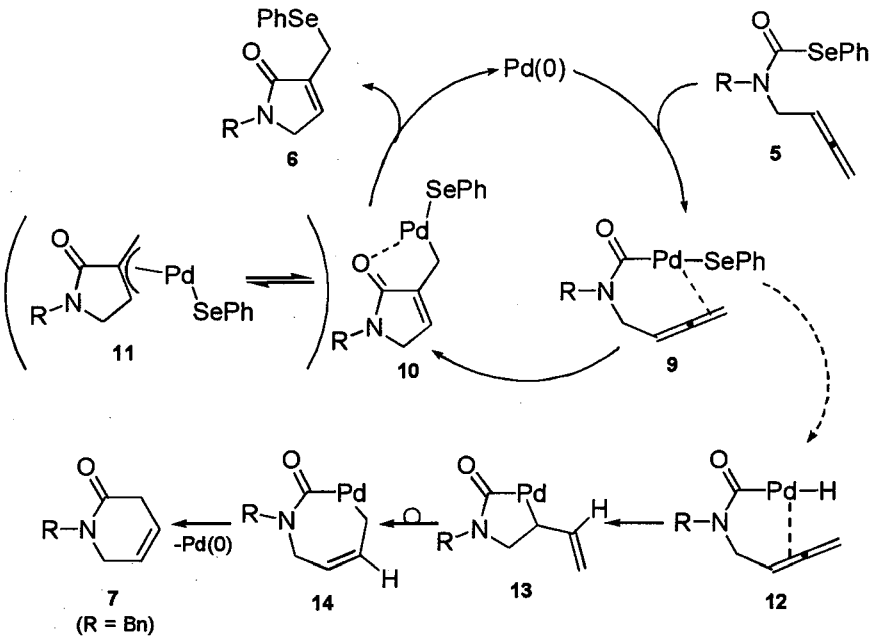
entry	5	6, Isolated Yield (%)	entry	5	6, Isolated Yield (%)
1[b]	 5a	 6a, 90	4	 5d	 6d, 76
		 7	5	 5e	 6e, 82(75)[c]
2	 5b	 6b, 76	6	 5f	 6f, (88)[c]
3	 5c	 6c, 85			

[a]Conditions: **5** (0.40 mmol), $Pd(PPh_3)_4$ (5 mol%), DMF (0.5 mL), 80 °C, 5 h. [b]Reaction run for 1 h. [c]Yield in parentheses was obtained by the reaction run in toluene 110 °C for 5 h (run 5) or 0.5 h (run 6).

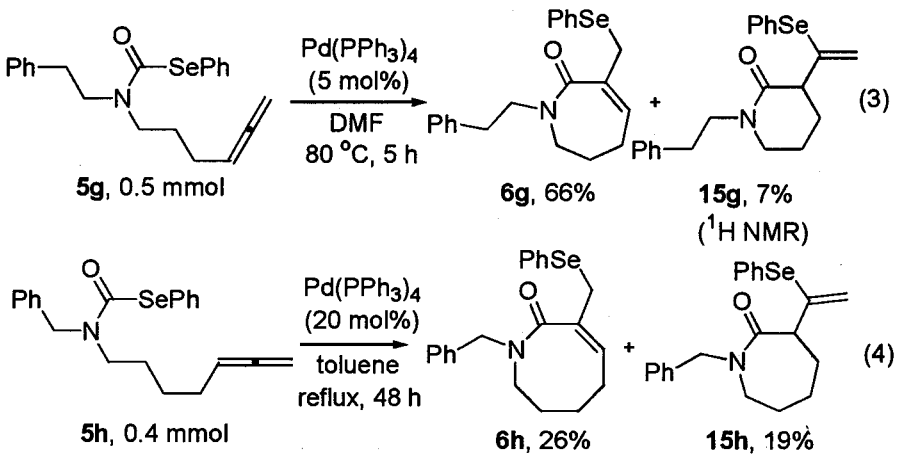
After optimizing the reaction conditions, we succeeded in the selective and efficient construction of five-membered lactam. For example, the reaction of carbamoselenoate **5a** in DMF at 80 °C for 1 h afforded lactam **6a** in 90% yield without formation of unexpected lactam **7** (Table 1, entry 1). Results obtained using several substrates are also summarized in Table 1.[6] As with **6a**, γ-lactams **6b** and **6c** formed readily in high yields with perfect regioselectivity, indicating that the substituent on the N-atom does not affect the reaction (entries 1-3). This cyclization system could be applied to intramolecular thiocarbamoylation resulting in the corresponding allyl sulfide **6d** in 76% yield (entry 4). The six-membered lactam **6e** was notably obtained in 82% yield with perfect regioselectivity when carbamoselenoate **5e** was subjected to similar reaction conditions. In contrast to the reaction of **5a**, the reaction of **5e** under toluene reflux conditions afforded **6e** in 75% yield and the by-product like **7** was not detected (entry 5). Similarly, the cyclopentenone **6f** could be constructed selectively in refluxing toluene (entry 6).[7] For all runs listed in Table 1, no regioisomer of **6** from inner double bond reactions of the allene unit were detected. The formed reaction products having the allyl selenide moiety can thus be subjected to further synthetic transformations.[8-10] For example, the isolated **6c** could be converted into allyl alcohol **8** by oxidation with *m*-CPBA followed by hydrolysis (eq 2).



Plausible reaction pathways for lactam construction are shown in Scheme 1 which explains how α,β-unsaturated lactams **6** and the by-product **7** are formed. The first step in these reactions is an oxidative addition of the carbamoyl-Se bond of carbamoselenoates **5** to Pd(0), giving rise to the allene-coordinated complexes **9**. Subsequent insertion of a distal C=C double bond from the coordinated allene into the carbamoyl-Pd bond generates σ-allylpalladium **10** which is in equilibrium with π-allylpalladium **11**. Five-membered chelation by coordination of the carbonyl oxygen to Pd as shown for σ-allylpalladium **10** may be a key to the regioselective carbopalladation pathway (**9** to **10**).[1] Reductive elimination leads to the five-membered lactams **6** and regenerates Pd(0).[11] Although the mechanism leading to by-product **7** is not clear, Se-H exchange of **9** to form **12** may account for the pathway. Hydropalladation of the proximal C=C double bond forms five-membered palladacycle **13** as an intermediate.[2c,d] Isomerization of **13** to seven-membered **14** via a π-allyl complex occurrs because of ring strain, and a subsequent reductive elimination affords **7**. Other possible pathways such as hydro- or carbopalladation of the allene leading to **7** might be sterically unfavorable.

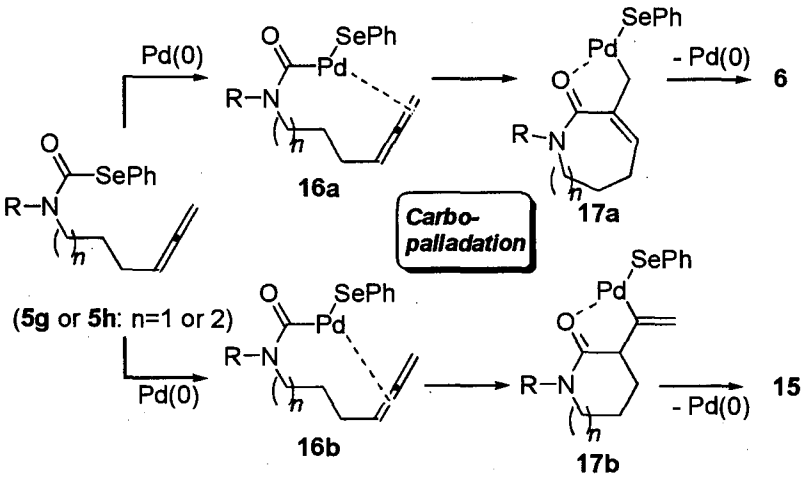


Scheme 1. Plausible Reaction Pathways Leading to **6** and **7**



The synthesis of medium-sized lactams was also examined. The reaction of carbamoselenoate **5g** that has a 4,5-hexadienyl group on the nitrogen atom gave the seven-membered lactam **6g** in 66% yield (eq 3). The six-membered lactam **15g** was, however, also obtained in 7% yield. When the isolated **6g** was subjected to the same reaction conditions as in eq 3, no isomerization to **15g** occurred. For carbamoselenoate **5h** that has a 5,6-heptadienyl group both an eight-membered lactam **6h** and a seven-membered lactam **15h** were formed in low yields with poor selectivity even when 20 mol% catalyst was used (eq 4). A reaction pathway accounting for the formation of regioisomers **15** as well as the formation of medium-sized lactams **6** is shown in Scheme 2. As described above desired medium-sized

lactams **6** are formed by carbopalladation of the distal double bond of allenes. Carbopalladation of the proximal double bond, giving rise to carbonyl-chelated vinyl palladium complexes like **17b**, is a possible pathway that leads to minor products **15**. A key to the selectivity would be relative stabilities of **17a** and **17b**. In the reactions of **5a-f**, intermediates like **10** (Scheme 2) have 5,5- or 5,6-membered bicyclic structures. On the contrary, in the reactions of **5g** and **5h**, **17a** have more skewed 5,7- and 5,8-membered bicyclic structures, respectively. These structures are less stable than **10** and thus the other route to form regioisomers **15** through **17b** becomes energetically reasonable.



Scheme 2. Plausible Reaction Pathways Leading to **6** and **15**

4-3 Conclusions

We report that intramolecular selenocarbamoylation of allenes proceeds in the presence of Pd(0) catalyst, producing α,β-unsaturated γ- and δ-lactams with perfect regioselectivity. This cyclization can be successfully applied to thiocarbamoylation and to the construction of a cyclopentenone framework. Intramolecular addition of carbon-selenium bonds to the allene unit takes place selectively, giving rise to the formation of allyl selenides. Although allyl selenides are known to react with transition metals, further reactions such as oligomerization of allenes were not observed in this system.[1,12]

4-4 Experimental Section

Genaral Comments

Toluene was distilled from CaH_2 under N_2. $Pd(PPh_3)_4$[13] was prepared according to the literature procedure. Commercially available dehydrated DMF, CH_2Cl_2 and dioxane (Wako Chemicals) were used without further distillation. Other reagents without citation were purchased from commercial source and used without further purification. By product **7** is a

known compound.[14] Melting points were determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-ALICE-400 (400 MHz and 100 MHz, respectively) spectrometer using Me_4Si (in $CDCl_3$) as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Preparative TLC was conducted by using Wakogel B-5F silica gel (325 mesh). Mass spectra (CI and EI) were taken on a SHIMAZU GCMS-QP2000 operating in the electron impact mode (70 eV) equipped with CBP1-M25-025 column. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus. For the copies of ^{1}H and ^{13}C NMR spectrum of all samples, see Supporting Information of the published paper.[15]

Procedures and Characterization of Reaction Materials

***Se*-Pheny *N*-benzyl-*N*-buta-2,3-dienyl carbamoselenoate (5a, run 1, Table 1): Typical procedure A.**

Into a 300-mL flask equipped with a dropping funnel were placed paraformaldehyde (57.7 mmol), diisopropylamine (57.6 mmol), CuBr (11.6 mmol) and anhydrous dioxane (180 mL) under N_2 and the suspension was stirred at room temperature. A solution of *Se*-phenyl *N*-benzyl-*N*-prop-2-ynyl carbamoselenoate (28.8 mmol, prepared according to the modified literature procedure[16]) in 20 mL of dioxane was added dropwise and the mixture was then heated at reflux for 15 h. After cooling to room temperature, Et_2O was added and filtered through the silica gel pad, volatiles were removed *in vacuo*. The crude product was purified by silica gel column chromatography (*n*-hexane/Et_2O = 5/1) to afford *Se*-phenyl *N*-benzyl-*N*-buta-2,3-dienyl carbamoselenoate **5a** in 54% yield as a *s-cis/trans* mixture; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45-3.50 (br, 2 H), 4.57-4.62 (br, 2 H), 4.78-4.89 (br, 2 H), 5.15 (brs, 1 H), 7.24-7.64 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.7 (minor), 46.5 (major), 50.2 (major), 51.6 (minor), 76.4 (minor), 77.4 (major), 85.7 (minor), 86.0 (major), 126.7, 127.7 (br), 127.9 (br), 128.5 (br), 128.6 (br), 128.8 (br), 128.9, 129.1, 136.7 ($^2J_{Se\text{-}C}$ = 11.0 Hz), 164.8, 209.2; IR (NaCl) 3060, 2929, 1955, 1667 (C=O), 1454, 1394, 1172, 1021, 740, 690 cm^{-1}; MS (CI) m/z (relative intensity, %) 344 (M+1, 100), 186 (54). Anal. Calcd for $C_{16}H_{17}NOSe$: C, 63.16; H, 5.01; N, 4.09. Found: C, 63.29; H, 5.10; N, 4.06.

***Se*-Pheny *N*-buta-2,3-dienyl-*N*-butyl carbamoselenoate (5b, run 2, Table 1).**

5b was prepared from *Se*-phenyl *N*-butyl-*N*-prop-2-ynyl carbamoselenoate according to the typical procedure **A**. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 5/1); 60% yield as a *s-cis/trans* mixture; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89-1.01 (m, 3 H), 1.28-1.55 (m, 2 H), 1.57-1.67 (m, 2 H), 3.30-3.38 (m, 2 H), 3.94-3.99 (m, 2 H), 4.80-4.89

(m, 2 H), 5.15-5.18 (m, 1 H), 7.32-7.61 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 20.0, 29.7 (minor), 30.5 (major), 46.3 (major), 47.6 (minor), 47.9 (minor), 48.3 (major), 76.3 (minor), 77.3 (major), 86.3 (major), 86.6 (minor), 126.7, 128.7, 129.0, 136.6, 163.9 (minor), 164.0 (major), 209.0 (minor), 209.3 (major); IR (NaCl) 2958, 1955, 1674 (C=O), 1397, 1175, 1022, 839, 739 cm^{-1}; MS (CI) m/z (relative intensity, %) 310 (M^++1, 100), 152 (84). Anal. Calcd for $C_{15}H_{19}NOSe$: C, 58.44; H, 6.21; N, 4.54. Found: C, 58.15; H, 6.18; N, 4.51.

***Se*-Pheny *N*-buta-2,3-dienyl-*N*-(1-phenethyl) carbamoselenoate (5c, run 3, Table 1).**

5c was prepared from *Se*-phenyl *N*-(1-phenylethyl)-*N*-prop-2-ynyl carbamoselenoate according to the typical procedure **A**. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 3/1); 43% yield as a *s-cis/trans* mixture; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 3.83-3.93 (m, 2 H), 4.52-4.59 (m, 2 H), 4.73-4.84 (m, 2 H), 5.07-5.13 (m, 1 H), 7.20-7.63 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 45.6 (minor), 46.4 (major), 50.1 (major), 51.5 (minor), 61.4, 76.4 (minor), 77.4 (major), 85.7 (minor), 126.7, 127.2 (br), 127.5 (br), 127.6 (br), 127.8 (br), 128.4 (br), 128.6, 128.7, 128.8, 129.0, 135.5, 136.6 ($^2J_{Se\text{-}C}$ = 11.3 Hz), 164.6, 209.1 (major), 209.5 (minor); IR (NaCl) 3060, 2931, 1955, 1674 (C=O), 1395, 1174, 1144, 1021, 740 cm^{-1}; MS (CI) m/z (relative intensity, %) 358 (M^++1, 94), 200 (100). Anal. Calcd for $C_{19}H_{19}NOSe$: C, 64.04; H, 5.37; N, 3.93. Found: C, 64.31; H, 5.55; N, 4.08.

***S*-Pheny *N*-benzyl-*N*-buta-2,3-dienyl carbamothioate (5d, run 4, Table 1).**

5d was prepared from *S*-phenyl *N*-benzyl-*N*-prop-2-ynyl carbamothioate according to the typical procedure **A**. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1); 88% yield as a *s-cis/trans* mixture; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 3.95-3.98 (m, 2 H), 4.64 (brs, 2 H), 4.74-4.95 (m, 2 H), 5.16 (brs, 1 H), 7.27-7.55 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.6 (major, minor), 50.0 (major), 50.7 (major), 76.4 (minor), 77.2 (major), 85.9 (major, minor), 127.7 (br), 128.5 (br), 128.7 (br), 129.0, 129.2, 135.7, 167.2, 209.4 (major), 209.5 (minor); IR (NaCl) 3062, 2927, 1955, 1666 (C=O), 1398, 1186, 1024, 750 cm^{-1}; MS (EI) m/z (relative intensity, %) 295 (M^+, 2), 186 (13), 162 (22), 109 (10), 91 (100). Anal. Calcd for $C_{18}H_{17}NOS$: C, 73.19; H, 5.80; N, 4.74. Found: C, 72.90; H, 5.72; N, 4.72.

***Se*-Pheny *N*-benzyl-*N*-penta-3,4-dienyl carbamoselenoate (5e, run 5, Table 1): Typical procedure B.[16]**

Into a 20-mL flask were placed elemental selenium (3.3 mmol) and THF (4.0 mL) under N_2 and the suspension was cooled to 0 °C. PhLi (0.90 M in Et_2O-cyclohexane, 3.7 mL, 3.3 mmol) was added slowly to prepare PhSeLi and the stirring was continued for 5 min. To the pale yellow solution of PhSeLi was then added *N*-benzyl-*N*-penta-3,4-dienylcarbamoyl chloride (3.0 mmol) in 4.0 mL of THF at the same temperature, and the mixture was warmed up to

room temperature and stirred for 4 h. After the mixture was poured into brine (15 mL) and extracted with Et_2O (10 mL X 4), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 3/1) to afford *Se*-phenyl *N*-benzyl-*N*-penta-3,4-dienyl carbamoselenoate **5e** in 72% yield as a *s-cis/trans* mixture; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29-2.38 (m, 2 H), 3.39-3.48 (m, 2 H), 4.60-4.80 (m, 4 H), 5.07-5.15 (m, 1 H), 7.24-7.70 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1 (minor), 26.8 (major), 47.0 (minor), 47.3 (major), 50.3 (major), 52.4 (minor), 75.2 (minor), 75.7 (major), 86.1 (major), 86.3 (minor), 126.6 (br), 127.0 (br), 127.4 (br), 127.7 (br), 127.9 (br), 128.5 (br), 128.6, 128.8, 135.6 (br), 136.5 ($^2J_{Se\text{-}C}$ = 11.0 Hz), 164.4, 208.7; IR (NaCl) 3030, 2930, 1955, 1671 (C=O), 1397, 1175, 1022, 740 cm^{-1}; MS (CI) m/z (relative intensity, %) 358 (M^++1, 100), 200 (73). Anal. Calcd for $C_{19}H_{19}NOSe$: C, 64.04; H, 5.37; N, 3.93. Found: C, 63.96; H, 5.42; N, 3.81.

***Se*-Phenyl 4,5-Hexadienecarboselenoate (5f, run 6, Table 1).**

Into a 50-mL flask were placed Ph_2Se_2 (13 mmol), CH_2Cl_2 (23 mL) and 4,5-hexadienoic acid[17] (8.6 mmol) under N_2 and then $^nBu_3P$ (13 mmol) and CH_2Cl_2 (3 mL) were added cooling with ice-bath, and the stirring was continued for 5 h at room temperature. After the mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (30 mL x 3) and Et_2O (30 mL x 2), the combined organic phase was dried with $MgSO_4$. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et_2O = 30/1) to afford *Se*-phenyl 4,5-hexadienecarboselenoate **5f** in 52% yield as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33-2.40 (m, 2 H), 2.83 (t, *J* = 7.1 Hz, 2 H), 4.73-4.77 (m, 2 H), 5.16 (tt, *J* = 6.6 Hz, 6.4 Hz, 1 H), 7.35-7.40 (m, 3 H), 7.49-7.52 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 46.4, 76.4, 88.2, 126.4, 128.9, 129.3, 135.8, 199.5, 208.4; IR (NaCl) 3058, 2913, 1956, 1716 (C=O), 1579, 1477, 1051, 851, 738 cm^{-1}; MS (EI) m/z (relative intensity, %) 252 (M^+, 21), 171 (24), 158 (31), 95 (91), 67 (100). HRMS (EI) calcd for $C_{12}H_{12}OSe$: 252.0053. Found 252.0046.

***Se*-Pheny *N*-hexa-4,5-dienyl-*N*-(1-phenethyl) carbamoselenoate (5g, eq 3).**

5g was prepared from *N*-hexa-4,5-dienyl-*N*-(1-phenylethyl)carbamoyl chloride according to the typical procedure **B**. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 3/1); 30% yield as a *s-cis/trans* mixture; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68-1.82 (m, 2 H), 1.95-2.08 (m, 2 H), 2.87-3.03 (m, 2 H), 3.21-3.41 (m, 2 H), 3.49-3.58 (m, 2 H), 4.66-4.75 (m, 2 H), 5.07-5.16 (m, 1 H), 7.17-7.65 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2 (major), 25.3 (minor), 27.0 (minor), 27.8 (minor), 34.2 (major), 35.5 (minor), 47.9 (minor), 49.0 (minor), 50.4 (major), 51.0 (minor), 75.4 (minor), 75.8 (major), 88.7 (minor), 89.0 (major), 126.4, 126.8 (br), 128.7 (br), 128.8, 129.0 (br), 136.7 (two peaks overlapped),

136.8, 138.0, 138.7, 163.8, 208.5; IR (NaCl) 3060, 2935, 1955, 1682 (C=O), 1398, 1154, 1022, 846, 740 cm^{-1}; MS (CI) m/z (relative intensity, %) 386 (M^++1, 100), 228 (95). Anal. Calcd for $C_{21}H_{23}NOSe$: C, 65.62; H, 6.03; N, 3.64. Found: C, 65.33; H, 6.02; N, 3.87.

***Se*-Pheny *N*-benzyl-*N*-hepta-5,6-dienyl carbamoselenoate (5h, eq 4).**

5h was prepared from *N*-benzyl-*N*-hepta-5,6-dienylcarbamoyl chloride according to the typical procedure **B**. Purified by silica gel column chromatography (*n*-hexane/Et_2O = 3/1); 58% yield as a *s-cis/trans* mixture; pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25-1.50 (m, 2 H), 1.53-1.76 (m, 2 H), 1.91-2.11 (m, 2 H), 3.17-3.40 (m, 2 H), 4.43-4.73 (m, 4 H), 5.00-5.14 (m, 1 H), 7.17-7.72 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 26.2, 26.8, 27.6, 27.7, 27.8, 47.6 (minor), 47.9 (minor), 50.3 (major), 52.4 (minor), 74.9 (minor), 75.2 (major), 89.4 (minor), 89.6 (major), 126.8 (br), 126.9 (br), 127.3, 127.6, 127.9, 128.1, 128.7, 128.8, 129.1, 164.4 (major), 164.6 (minor), 208.5; IR (NaCl) 3060, 2935, 1955, 1674 (C=O), 1399, 1175, 1074, 845, 740 cm^{-1}; MS (CI) m/z (relative intensity, %) 386 (M^++1, 100), 228 (63), 174 (13). Anal. Calcd for $C_{21}H_{23}NOSe$: C, 65.62; H, 6.03; N, 3.64. Found: C, 65.40; H, 6.03; N, 3.61.

Procedures and Characterization of Reaction Products

1-Benzyl-3-phenylselenomethyl-1,5-dihydro-pyrrol-2-one (6a, run 1, Table 1): Typical procedure.

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **5a** (0.4 mmol), DMF (0.4 mL) and $Pd(PPh_3)_4$ (0.005 mmol) at room temperature under N_2 and the solution turned immediately red. After the mixture was heated at 80 °C for 5 h, filtered through the celite pad with Et_2O, volatiles were removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/Et_2O = 1/1) to afford 1-benzyl-3-phenylseleno-1,5-dihydro-pyrrole-2-one **6a** in 90% yield as blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 3.65 (s, 2 H), 3.75 (s, 2 H), 4.62 (s, 2 H), 6.47 (s, 1 H) 7.19-7.51 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 46.4, 50.0, 127.4, 127.6, 128.0, 128.7, 129.0, 130.0, 133.7, 136.4, 136.5, 137.2, 170.1; IR (NaCl) 3060, 2917, 1682(C=O), 1452, 1244, 1077, 817, 738, 693 cm^{-1}; MS (EI) m/z (relative intensity, %) 343 (M^+, 2), 185 (40), 91 (100). HRMS (EI) calcd for $C_{18}H_{17}NOSe$: 343.0475. Found 343.0478.

1-Butyl-3-phenylselenomethyl-1,5-dihydro-pyrrol-2-one (6b, run 2, Table 1).

Purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/1) to afford 1-butyl-3-phenylseleno-1,5-dihydro-pyrrole-2-one **6b** in 76% yield as blow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 1.26-1.37 (m, 2 H), 1.51-1.58 (m, 2 H), 3.44 (t, J = 7.2 Hz, 2 H), 3.72 (s, 2 H), 3.77 (s, 2 H), 6.50 (s, 1 H), 7.21-7.28 (m, 3 H), 7.48-7.51 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.9, 21.1, 30.5, 42.0, 50.3, 127.2, 128.8, 130.0, 133.4

($^2J_{Se\text{-}C}$ = 10.0 Hz), 135.7, 136.6, 169.9; IR (NaCl) 3055, 2929, 1682(C=O), 1578, 1456, 1410, 1244, 1022, 737 cm^{-1}; MS (EI) m/z (relative intensity, %) 309 (M^+, 61), 228 (100), 152 (73), 96 (90), 53 (63). Anal. Calcd for $C_{15}H_{19}NOSe$: C, 58.44; H, 6.21; N, 4.54. Found: C, 58.21; H, 6.22; N, 4.48.

1-Phenethyl-3-phenylselenomethyl-1,5-dihydro-pyrrol-2-one (6c, run 3, Table 1).
Purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/2) to afford 1-phenylethyl-3-phenylseleno-1,5-dihydro-pyrrole-2-one **6c** in 85% yield as blow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.90 (t, *J* = 7.3 Hz, 2 H), 3.56 (s, 2 H), 3.70 (t, *J* = 7.3 Hz, 2 H), 6.37 (s, 1 H), 7.18-7.49 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 34.9, 44.0, 51.2, 126.4, 127.3, 128.5, 128.7, 128.9, 130.0, 133.6 ($^2J_{Se\text{-}C}$ = 10.1 Hz), 135.9, 136.6, 138.8, 169.9; IR (NaCl) 3058, 2926, 1682(C=O), 1578, 1455, 1409, 1247, 1022, 739, 693 cm^{-1}; MS (EI) m/z (relative intensity, %) 357 (M^+, 12), 266 (16), 199 (35), 108 (100). HRMS (EI) calcd for $C_{19}H_{19}NOSe$: 357.0632. Found 357.0626.

1-Benzyl-3-phenylthiomethyl-1,5-dihydro-pyrrol-2-one (6d, run 4, Table 1).
Purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/2) to afford 1-benzyl-3-phenylthio-1,5-dihydro-pyrrole-2-one **6d** in 70% yield as blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 2 H), 3.83 (s, 2 H), 4.63 (s, 2 H), 6.73 (s, 1 H) 7.15-7.34 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 46.4, 50.2, 126.3, 127.6, 128.0, 128.7, 128.9, 129.4, 135.7, 135.8, 137.1, 137.5, 170.2; IR (NaCl) 3030, 2919, 1674(C=O), 1439, 1246, 1078, 1026, 982, 821, 741, 693 cm^{-1}; MS (EI) m/z (relative intensity, %) 295 (M^+, 59), 91 (100). HRMS (EI) calcd for $C_{18}H_{17}NOS$: 295.1031. Found 295.1048.

1-Benzyl-3-phenylselenomethyl-5,6-dihydro-1*H*-pyridin-2-one (6e, run 5, Table 1).
Purified by silica gel column chromatography (*n*-hexane/Et_2O = 1/2) to afford 1-Benzyl-3-phenylseleno-5,6-dihydro-1*H*-pyridin-2-one **6e** in 82% yield as blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 2.15-2.20 (m, 2 H), 3.21 (t, *J* = 7.1 Hz, 2 H), 3.78 (s, $^2J_{Se\text{-}H}$ = 12.2 Hz, 2 H), 4.65 (s, 2 H), 6.05 (t, *J* = 4.4 Hz, 1 H) 7.21-7.53 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.9, 27.9, 44.7, 50.1, 127.3, 127.4, 128.0, 128.6, 128.9, 130.4, 132.4, 134.3, 134.6, 137.4, 164.3; IR (NaCl) 3058, 2938, 1661(C=O), 1622, 1480, 1446, 1218, 1022, 740 cm^{-1}; MS (CI) m/z (relative intensity, %) 385 (M^++1, 100). HRMS (CI) calcd for $C_{19}H_{20}NOSe$: 358.0710. Found 358.0704.

2-Phenylselenomethyl-cyclopent-2-enone (6f, run 6, Table 1).
Purified by preparative TLC (*n*-hexane/Et_2O = 5/1) to afford 2-Phenylselenomethyl-cyclopent-2-enone **6f** in 88% yield as pale yellow oil; ^1H NMR (400

MHz, $CDCl_3$) δ 2.39-2.42 (m, 2 H), 2.48-2.51 (m, 2 H), 3.62 (s, 2 H), 7.15 (s, 1 H), 7.25-7.28 (m, 3 H), 7.46-7.50 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 26.3, 34.4, 127.4, 129.0, 130.0, 133.7 ($^2J_{Se-C}$ = 10.1 Hz), 142.8, 158.9, 207.8; IR (NaCl) 3053, 2921, 1702(C=O), 1437, 1341, 1200, 1000, 927, 739, 692 cm^{-1}; MS (EI) m/z (relative intensity, %) 252 (M^+, 100), 171 (31), 158 (42), 95 (49). Anal. Calcd for $C_{12}H_{12}OSe$: C, 57.38; H, 4.82. Found: C, 57.16; H, 4.83.

1-Phenethyl-3-phenylselenomethyl-1,5,6,7-tetrahydro-azepin-2-one (6g, eq 3)
and
1-Phenethyl-3-(1-phenylselenovinyl)-piperidin-2-one (15g, eq 3)

NMR yields of **6g/15g** were 72%/7%. Separated by preparative TLC (*n*-hexane/Et_2O = 1/1) to afford pure 1-phenethyl-3-phenylselenomethyl-1,5,6,7-tetrahydro-azepin-2-one **6g** and impurities-contained 1-phenethyl-3-(1-phenylselenovinyl)-piperidin-2-one **15g**, respectively.

6g : 66% yield; blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.55-1.61 (m, 2 H), 1.92-1.97 (m, 2 H), 2.89 (t, J = 7.3 Hz, 2 H), 2.97 (t, J = 6.3 Hz, 2 H), 3.68 (t, J = 7.3 Hz, 2 H), 3.86 (s, 2 H), 5.80 (t, J = 7.0 Hz, 2 H), 7.18-7,50 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 29.0, 30.7, 35.0, 46.7, 49.6, 126.3, 127.0, 128.4, 128.9 (two peaks overlapped), 130.1, 130.3, 133.2, 136.3, 139.1, 169.9; IR (NaCl) 3026, 2929, 2860, 1651(C=O), 1437, 1436, 1369, 737 cm^{-1}; MS (CI) m/z (relative intensity, %) 386 (M^++1, 100), 228 (10). Anal. Calcd for $C_{21}H_{23}NOSe$: C, 65.62; H, 6.03; N, 3.64. Found: C, 65.33; H, 6.03; N, 3.82.

15g : blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.65-1.72 (m, 1 H), 1.80-1.90 (m, 2 H), 1.98-2.03 (m, 1 H), 2.89 (t, J = 7.4 Hz, 2 H), 3.06-3.11 (m, 1 H), 3.16-3.22 (m, 1 H), 3.33 (t, J = 6.7 Hz, 1 H), 3.44-3.51 (m, 1 H), 3.65-3.73 (m, 1 H), 5.37 (s, 1 H), 5.60 (s, 1 H), 7.18-7.61 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 27.5, 33.5, 48.8, 49.8, 51.2, 121.6, 126.3 , 127.5; 128.5, 128.9, 129.3, 130.1, 133.8, 139.2, 141.9, 168.8. IR (NaCl) 3058, 2932, 2860, 1645(C=O), 1634, 1488, 1436, 1352, 1198, 1022, 741, 700 cm^{-1}. MS (CI) m/z (relative intensity, %) 386 (M^++1, 100), 230 (25). HRMS(CI) calcd for $C_{21}H_{24}NOSe$: 386.1023. Found 386.1029.

1-Benzyl-3-phenylselenomethyl-5,6,7,8-tetrahydro-1*H*-azocin-2-one (6h, eq 4)
and
1-Benzyl-3-(1-phenylselenovinyl)-azepan-2-one (15h, eq 4)

Separated by preparative TLC (*n*-hexane/Et_2O = 2/1) to afford 1-benzyl-3-phenylselenomethyl-5,6,7,8-tetrahydro-1*H*-azocin-2-one **6h** and 1-benzyl-3-(1-phenylselenovinyl)-azepan-2-one **15h**, respectively.

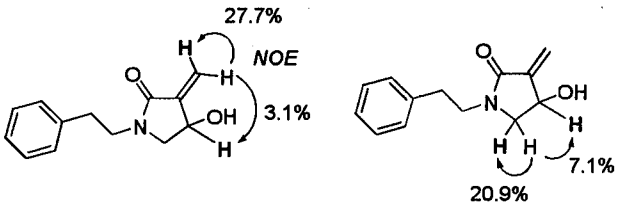
6h : 26% yield; blown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13-1.21 (m, 1 H), 1.37-1.42 (m, 1 H), 1.57-1.67 (m, 2 H), 2.00-2.08 (m, 1 H), 2.13-2.21 (m, 1 H), 2.93 (d, J = 15.0 Hz, 1 H), 3.44

(t, J = 13.4 Hz, 2 H), 3.79 (d, J = 12.2 Hz, 1 H), 4.00 (d, J = 14.9 Hz, 1 H), 4.10 (d, J = 11.5 Hz, 1 H), 5.37 (d, J = 14.9 Hz, 1 H), 5.69 (t, J = 7.3 Hz, 1 H), 7.20-7.47 (m, 10 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 22.2, 26.1, 28.0, 32.9, 45.9, 47.9, 127.0, 127.2 , 127.9, 128.5, 129.0, 130.1, 131.4, 131.8, 132.8, 137.0, 170.0. IR (NaCl) 3058, 2929, 1652(C=O), 1622, 1477, 1436, 1203, 1078, 737, 693 cm^{-1}. MS (CI) m/z (relative intensity, %) 386 (M^++1, 100). Anal. Calcd for $C_{21}H_{23}NOSe$: C, 65.62; H, 6.03; N, 3.64. Found: C, 65.45; H, 6.05; N, 3.73.

15h : 19% yield; blown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23-1.32 (m, 1 H), 1.51-1.65 (m, 2 H), 1.89-1.98 (m, 3 H), 3.17-3.22 (m, 1 H), 3.28-3.34 (m, 1 H), 3.59 (dd, J = 8.7 Hz, 2.8 Hz, 1 H), 4.44 (d, J = 14.4 Hz, 1 H), 4.76 (d, J = 14.7 Hz, 1 H), 5.40 (s, 1 H), 5.70 (s, 1 H), 7.24-7.61 (m, 10 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 27.4, 28.6, 30.5, 47.9, 51.3, 53.4, 120.0, 127.3, 127.4, 128.4, 128.5, 129.1, 131.5, 134.0, 137.7, 143.1, 174.3. IR (NaCl) 3066, 2928, 1634(C=O), 1477, 1435, 1261, 1212, 998, 902, 742, 694 cm^{-1}. MS (CI) m/z (relative intensity, %) 386 (M^++1, 100). Anal. Calcd for $C_{21}H_{23}NOSe$: C, 65.62; H, 6.03; N, 3.64, Found: C, 65.85; H, 6.19; N, 3.83.

4-Hydroxy-3-methylene-1-phenethyl-pyrrolidin-2-one (8, eq 2)

Into a flame-dried 30-mL flask equipped with a dropping funnel were placed allyl selenide **6c** (0.27 mmol) and anhydrous CH_2Cl_2 (2 mL) under N_2. A solution of *m*-CPBA (0.32 mmol) in 2 mL of CH_2Cl_2 was added dropwise at -78 °C (acetone/CO_2) and the mixture was stirred at same temperature. After 1 h, saturated $NaHCO_3$aq and Et_2O were added and washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et_2O = 5/1 to 3/1 to Et_2O, then EtOAc) afforded **8** in 63% yield as a white solid; mp 90.0-91.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (t, J = 7.6 Hz, 2 H), 3.16 (dd, J = 2.2 Hz, 14.5 Hz, 1 H), 3.48-3.66 (m, two peaks overlapped, 4 H), 4.72 (brs, 1 H), 5.65 (s, 1 H), 6.09 (s, 1 H), 7.20-7.31 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.6, 44.4, 54.5, 65.7, 119.4, 126.6, 128.6, 128.7, 138.4, 143.7, 166.5; NOE experiments (summary of the results are shown below): irradiation of the vinyl singlet at δ 5.65 resulted in 27.7% and 3.1% enhancements of the singlet at δ 6.09 (geminal vinyl-H) and the broad singlet at δ 4.72 (-C*H*C(OH)-), respectively. Irradiation of the multiplet at δ 3.50 resulted in 20.9% and 7.1% enhancements of the double-doublet at δ 3.16 (geminal diastereotopic-H) and the broad singlet at δ 4.72 (-C*H*C(OH)-), respectively.; IR (KBr) 3302(O-H), 2934, 1676(C=O), 1483, 1296, 1095, 1031, 952, 754, 704 cm^{-1}; MS (EI), m/z (relative intensity, %) 217 (M^+, 23), 126 (100), 104 (25), 96 (55). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.58; H, 6.90; N, 6.27.



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[6] Solvent effect was examined by using **5b** as a substrate. NMR yields of **6b** obtained in 5 h are as follows: 38% (toluene, reflux), 14% (toluene, 80 °C), 35% (cyclopentyl methyl ether (CPME), 80 °C), 60% (THF, reflux), 83% (PhCN, 80 °C), 86% (DMF, 80 °C). Dielectronic constants (ε_r, 25 °C) of the solvents: toluene (2.38), CPME (4.76), THF (7.58), PhCN (25.20), DMF (36.71), see: (a) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed; Wiley-VCH; Weinheim, 2003. (b) Kadish, K. M.; Anderson, J. E.; *Pure*

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[7] When the reaction of **5a** was conducted in toluene-d_8 at 110 °C, no deuterium-incorporated products was detected. When one equiv of fluorene or H_2O were added as possible H-sources, product selectivities (**7** v.s. **6a**) were not changed. From these results, allylic hydrogens in the ring (α-hydrogens of the nitrogen atom) of the products would be the H-source forming **7**. Selective formation of **6e** and **6f** from **5e** and **5f** in toluene reflux conditions (entries 5 and 6), where allylic hydrogens in the ring of **6e** and **6f** locate at the β-carbon, not at the α-carbon, from the nitrogen atom, also support this hypothesis.

[8] Allyl selenides are recognized not only as versatile synthetic intermediates (ref 9) but also as potential mimetics of enzyme and precursors of DNA radicals (ref 10).

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[15] *Se*-Phenyl-*N*-alkyl-*N*-prop-2-ynyl carbamoselenoates were readily prepared from the corresponding carbamoyl chlorides according to the typical procedure **B**. For the synthesis of the carbamoyl chlorides, see ref 4a. These carbamoyl chlorides were easily purified by the simple extraction of the crude product with CH_2Cl_2 and 1N HClaq.

[16] Under preparation.

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Summary

In this thesis, the studies on group 10 metal-catalyzed cleavage of carbon-chalcogen bonds and addition to unsaturated hydrocarbons leading to the construction of carbon skeletons were described. These aspects would be good representations showing great potential of organochalcogenides for various catalytic transformations in organic chemistry.

In chapter 1, $Pd(PPh_3)_4$-catalyzed intramolecular carboselenation of alkynes to form four- to eight-membered lactams and four- to six-membered cycloalkanones was described. In this system, four-membered lactam formation is faster than five- and six-membered lactams. It was suggested that facile formation of five-membered palladacycle by *thio-* or *selenopalladation* of an alkyne moiety was a key to the effective construction of four-membered ring skeletons.

In chapter 2, $Pt(PPh_3)_4$-catalyzed intramolecular vinylchalcogenation of internal alkynes with vinyl chalcogenides giving rise to the highly-conjugated δ-lactam frameworks was described. Introduction of electron withdrawing groups to β-position on vinyl moiety may be a key to develop a new type of catalytic reaction using vinyl heteroatom compounds.

In chapter 3, it was revealed that 1,2-addition of selenol esters onto allenes proceeded with excellent regioselectivity and high stereoselectivity in the presence of Pd(0)-PPh_3 catalyst, producing functionalized allyl selenides. A reaction pathway accounting for the observed regio- and stereoselectivity is proposed based on the results of DFT calculations.

In chapter 4, intramolecular selenocarbamoylation of allenes in the presence of Pd(0) catalyst producing α,β-unsaturated γ- and δ-lactams was described. This cyclization can be successfully applied to thiocarbamoylation and to the construction of a cyclopentenone framework.

List of Publications

(1) "Palladium-Catalyzed Intramolecular Selenocarbamoylation of Alkynes with Carbamoselenoates: Formation of α-Alkylidene-β-lactam Frameworks"
Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2005**, *127*, 9706.

(2) "Platinum-Catalyzed Intramolecular Vinylchalcogenation of Alkynes with β-Phenylchalcogeno Conjugated Amides"
Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2008**, *130*, 10504.

(3) "Palladium-Catalyzed Selenoacylation of Allenes Leading to the Regioselective Formation of Functionalized Allyl Selenides"
Toyofuku, M.; Murase, E.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *Org. Lett.* **2008**, *10*, 3957.

(4) "Palladium-Catalyzed Intramolecular Selenocarbamoylation of Allenes with Carbamoselenoates: Regioselective Formation of α,β-Unsaturated Lactam Frameworks"
Toyofuku, M.; Murase, E.; Nagai, H.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *in preparation*

(5) "Palladium-Catalyzed Intramolecular Carboselenation of Alkynes: Construction of α-Alkylidenelactam and α-Alkylidenecycloalkanone Frameworks"
Toyofuku, M.; Fujiwara, S.; Murase, E.; Okada, A.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *in preparation*

Supplementary List of Publications

(1) "Product Class 7: Acyclic Dialkyl Sulfide (R-S-R)"
Fujiwara, S.; Toyofuku, M. In *Science of Synthesis*; Kambe, N. Ed.; Thieme, **2007**, *39*, 469.

(2) "A new entry for the construction of α-alkylidene-β-lactam framework by 4-*exo-dig* cyclization of carbamoyl radicals"
Fujiwara, S.; Shimizu, Y.; Imahori, Y.; Toyofuku, M.; Shin-ike, T.; Kambe, N. *in preparation*

(3) "Palladium-Catalyzed Carbonylation of $TiCl_4$-Mediated Morita-Baylis Hillman Adducts Leading to 5-Methylene-2(5H)-furanone Framework"
Fujiwara, S.; Okada, A.; Toyofuku, M.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *in preparation*

(4) "Palladium-Catalyzed Intramolecular Tellurocarbamoylation of Alkynes with Carbamotelluroates"
Fujiwara, S.; Nagai, H.; Toyofuku, M.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *in preparation*

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