Palladium-Catalyzed Intramolecular Selenocarbamoylation of Alkynes with Carbamoselenoates: Formation of α -Alkylidene- β -Lactam Framework

Masashi Toyofuku,[†] Shin-ichi Fujiwara,^{*,‡} Tsutomu Shin-ike,[‡] Hitoshi Kuniyasu,[†] Nobuaki Kambe^{*,†}

[†] *Department of Molecular Chemistry, Graduate School of Engineering, Osaka University,
Suita, Osaka 565-0871, Japan*

[‡] *Department of Chemistry, Osaka Dental University,
Hirakata, Osaka 573-1121, Japan*

e-mail: fujiwara@cc.osaka-dent.ac.jp, kambe@chem.eng.osaka-u.ac.jp

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1. Genaral Comments

THF was distilled from benzophenone ketyl just prior to use. 1-Octyne, toluene, and CH_2Cl_2 were distilled from CaH_2 . $\text{Pd}(\text{PPh}_3)_4$ was prepared according to the literature procedure.^{S1} 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.

2. Preparation of Carbamoyl Chlorides

***N*-Butyl-*N*-prop-2-ynylcarbamoyl chloride: Typical Procedure.**^{S2} Into a 200-mL flask were placed triphosgene (8.3 mmol) and CH_2Cl_2 (8 mL) under N_2 . After cooling to $-78\text{ }^\circ\text{C}$, 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, $80\text{ }^\circ\text{C}$) as colorless oil contaminated with a small amount of pyridine hydrochloride and was used without further purification.

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

3. Procedures and Characterization of Reaction Materials

Se-Phenyl *N,N*-dimethylcarbamoseleenoate (**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 Et₂O-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 Et₂O (30 mL X 4), the combined organic phase was dried with MgSO₄. The solvents were removed *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane/Et₂O = 1/1) to afford *Se*-phenyl *N,N*-dimethylcarbamoseleenoate (**1**) in 73% yield: white solid; mp 34 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.98 (s, 6 H), 7.33-7.58 (m, 5 H); ¹³C NMR (100 MHz, CDCl₃) δ 36.7, 37.1, 126.4 (¹*J*_{Se-C} = 91.7 Hz), 128.4, 128.6, 136.2 (²*J*_{Se-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 C₉H₁₁NOSe: 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).

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 1/1); 44% yield as a *s-cis/trans* mixture; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.27 (brs, 1 H), 3.09 (brs, 3 H), 4.22 (brs, 2 H), 7.33-7.60 (m, 5 H); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{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 C₁₁H₁₁NOS₂: 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-ynyl carbamoselenoate (3b).

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 1/1); 59% yield as a *s-cis/trans* mixture; colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{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 C₁₄H₁₇NOS₂: 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).

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 1/1); 29% yield as a *s-cis/trans* mixture; colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{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 C₁₇H₁₅NOS₂: 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).

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 4/1); 54% yield as a *s-cis/trans* mixture; pale yellow oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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]carbamoseleenoate (3e).**

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 5/1); 48% yield as a *s-cis/trans* mixture; pale yellow solid; mp 85 °C; ^1H 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, 688 cm^{-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*-butyl-*N*-pent-4-ynylcarbamosenoate (8a).**

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 3/1); 38% yield as a *s-cis/trans* mixture; colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{Se-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 C₁₆H₂₁NOSe: C, 59.62; H, 6.57; N, 4.35. Found: C, 59.24; H, 6.28; N, 4.41.

***Se*-Phenyl *N*-butyl-*N*-hex-5-ynylcarbamosenoate (8b).**

Purified by silica gel column chromatography (*n*-hexane/Et₂O = 3/1); 39% yield as a *s-cis/trans* mixture; colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{Se-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*-pent-4-ynyl-*N*-prop-2-ynylcarbamosenoate (10).**

Purified by silica gel column chromatography (*n*-hexane/ Et_2O = 3/1); 59% yield as a *s-cis/trans* mixture; 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 ($^1J_{Se-C}$ = 93.2 Hz), 128.7 (two peaks overlapped), 136.3 ($^2J_{Se-C}$ = 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.

***S*-Phenyl *N*-methyl-*N*-prop-2-ynylcarbamothiolate (12).**

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, Et₂O was added to the filtrate and washed with brine, and dried with MgSO₄. Evaporation of the solvent and purification by silica gel column chromatography (*n*-hexane/Et₂O = 3/1) afforded **12** in 66% yield: ¹H NMR (400 MHz, CDCl₃) δ 2.28 (brs, 1 H), 3.12 (brs, 3 H), 4.21 (brs, 2 H) 7.37-7.50 (m, 5 H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₁H₁₁NOS: 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 (**14**).**

Selenol ester **14** was prepared from 2,2-dimethylpent-4-ynoyl chloride^{S3} according to the typical procedure of carbamoselenoates and was purified by silica gel column chromatography (*n*-hexane/Et₂O = 10/1); 34% yield; colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 24.3, 29.3, 52.2, 71.0, 79.9, 125.5, 128.4, 128.8, 135.9 (²*J*_{Se-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 C₁₃H₁₄OSe: C, 58.88; H, 5.32. Found: C, 58.87; H, 5.32.

4. Procedures and Characterization of Reaction Products

(Z)-N,N-Dimethy-3-(phenylseleno)non-2-enamide (2): Intermolecular

Selenocarbamoylation

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(PPh₃)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/Et₂O = 5/1) to give (Z)-N,N-dimethy-3-(phenylseleno)non-2-enamide (**2**) in 40% yield: brown oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{Se-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 (NMe₂) 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 C₁₇H₂₅NOSe: 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**(7a):****Intramolecular****Selenocarbamoylation**

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3a** (0.4 mmol), toluene (0.5 mL), and Pd(PPh₃)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 CHCl₃) to provide (Z)-1-methyl-3-phenylselenomethyleneazetidin-2-one (**7a**) in 74% yield: white solid; mp 93 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.97 (s, 3 H), 3.72 (s, 2 H), 6.70 (s, 1 H), 7.32-7.57 (m, 5 H); ¹³C NMR (100 MHz, CDCl₃) δ 28.9, 50.8, 119.6 (¹J_{Se-C} = 121.7 Hz), 127.7, 129.2, 130.1, 132.6 (²J_{Se-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 C₁₁H₁₁NOSe: 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 (7b).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3b** (0.4 mmol), toluene (0.5 mL), and Pd(PPh₃)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 ¹H NMR (85%, *E/Z* = 2/98), the crude product was purified by preparative recycling HPLC (eluted with CHCl₃) to provide 1-*n*-butyl-3-phenylselenomethyleneazetidin-2-one (**7b**) 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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (¹*J*_{Se-C} = 121.2 Hz (*Z*)), 127.7, 128.2, 129.2, 129.3, 130.2, 132.6 Hz (²*J*_{Se-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 C₁₄H₁₇NOSe: 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 (7c).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3c** (0.4 mmol), toluene (2 mL), and Pd(PPh₃)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*. After the NMR yield and the *E/Z* ratio were determined by ¹H NMR (84%, *E/Z* = 3/97), the crude product was purified by preparative recycling HPLC (eluted with CHCl₃) to provide 1-benzyl-3-phenylselenomethylene azetidin-2-one (**7c**) in 59% yield. Pure (*Z*)-**7c** was obtained by recrystallization from *n*-hexane/CHCl₃ = 1/1: white solid; mp 88 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 46.1, 48.4, 120.6 (¹*J*_{Se-C} = 122.6 Hz), 127.4, 127.6, 127.8, 128.4, 129.0, 129.9, 132.6 (²*J*_{Se-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 C₁₇H₁₅NOSe: 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 (7d).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3d** (0.4 mmol), toluene (0.5 mL), and Pd(PPh₃)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*. After the NMR yield and the *E/Z* ratio were determined by ¹H NMR (93%, *E/Z* = 3/97), the crude product was purified by preparative recycling HPLC (eluted with CHCl₃) to provide 1-benzyl-3-(1-phenylseleno)propylideneazetidin-2-one (**7d**) in 88% yield. Pure (Z)-**7d** was obtained by recrystallization from *n*-hexane/CHCl₃ = 1/1: white solid; mp 102 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (²*J*_{Se-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 C₁₉H₁₉NOSe: 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 (7e).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **3e** (0.4 mmol), toluene (4 mL), and Pd(PPh₃)₄ (0.020 mmol) at room temperature under Ar and the solution turned immediately red. After the mixture was refluxed for 20 h, toluene was removed *in vacuo*. The crude product was purified by preparative recycling HPLC (eluted with CHCl₃) to provide 1-methyl-3-[(p-chlorophenyl)phenylselenomethylene]azetidin-2-one (**7e**) in 76% yield. After the *E/Z* ratio was determined by ¹H NMR (*E/Z* = 11/89), pure (*Z*)-**7e** was obtained by recrystallization from *n*-hexane/CHCl₃ = 1/1: pale yellow solid; mp 128 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.01 (s, 3 H), 3.91 (s, 2 H), 7.06-7.32 (m, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 28.9, 51.1, 127.4, 128.2, 128.3, 128.6, 129.7, 129.9, 133.9 (²*J*_{Se-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 C₁₇H₁₄ClNOS₂: C, 56.29; H, 3.89; N, 3.86. Found: C, 56.26; H, 3.75; N, 3.86. The structure of (*Z*)-**7e** was confirmed by X-ray analysis (**Figure S1**).

Figure S1. ORTEP Drawing of (Z)-7e

(Z)-1-Butyl-3-phenylselenomethylenepiperidin-2-one (9a).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **8a** (0.4 mmol), toluene (0.5 mL), and Pd(PPh₃)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 TLC (*n*-hexane/Et₂O = 3/1) to provide (Z)-1-butyl-3-phenylselenomethylenepiperidin-2-one (**9a**) in 75% yield: colorless oil; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 14.0, 20.3, 22.9, 29.3, 31.2, 47.4, 48.2, 125.1, 127.2, 128.7, 132.9 (²*J*_{Se-C} = 9.2 Hz), 134.9, 137.3 (¹*J*_{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 $\text{C}_{16}\text{H}_{21}\text{NOSe}$: C, 59.62; H, 6.57; N, 4.35. Found: C, 59.52; H, 6.51; N, 4.31.

(Z)-1-Butyl-3-phenylselenomethyleneazepan-2-one (9b).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **8b** (0.4 mmol), toluene (2 mL), and $\text{Pd}(\text{PPh}_3)_4$ (0.020 mmol) at room temperature under Ar and the solution turned immediately red. After the mixture was refluxed for 12 h, toluene was removed *in vacuo*. The crude product was purified by preparative TLC (*n*-hexane/ Et_2O = 2/1) to provide (Z)-1-butyl-3-phenylselenomethyleneazepan-2-one (**9b**) in 74% yield: colorless oil; ^1H 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 $\text{C}_{17}\text{H}_{23}\text{NOSe}$: C, 60.71; H, 6.89; N, 4.16. Found: C, 60.56; H, 6.93; N, 4.21.

1-Pent-4-ynyl-3-phenylselenomethyleneazetidin-2-one (11a).

and

1-Prop-2-ynyl-3-phenylselenomethylenepiperidin-2-one (11b).

Into a 3-mL flask equipped with a reflux condenser were placed carbamoselenoate **10** (0.85 mmol), toluene (4 mL), and Pd(PPh₃)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/Et₂O = 2/1) to provide colorless oil of **11a** (50%, *E/Z* = 5/95) and white solid of **11b** (10%, *E/Z* = 11/89). The following spectra and analytical data were obtained from *E/Z* mixtures.

11a: ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 (¹*J*_{Se-C} = 122.2 Hz, (*Z*)), 127.6, 128.1, 129.0, 129.1, 129.9, 132.5 (²*J*_{Se-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.

11b: mp 78 °C; 1H 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 ($^2J_{Se-C} = 9.2$ Hz, (*Z*)), 134.4, 139.1 ($^1J_{Se-C} = 133.2$ 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.

(Z)-1-Methyl-3-phenylthiomethyleneazetidin-2-one (13, eq. 5).

Into a 3-mL flask equipped with a reflux condenser were placed carbamothioate **12** (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 silica gel column chromatography (*n*-hexane/ $Et_2O = 3/1$) to provide (Z)-1-methyl-3-phenylthiomethyleneazetidin-2-one (**13**) in 72% yield: pale yellow solid; mp 128 °C; 1H 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 $\text{C}_{11}\text{H}_{11}\text{NOS}$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.08; H, 5.31; N, 6.80.

2,2-Dimethyl-4-phenylselenomethylenecyclobutanone (15).

Into a 3-mL flask equipped with a reflux condenser were placed selenol ester **14** (0.96 mmol), toluene (1.25 mL), and $\text{Pd}(\text{PPh}_3)_4$ (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 ^1H 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*)-**15**.

(*Z*)-**15**: yellow solid: mp 39 $^\circ\text{C}$; ^1H 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 ($^2J_{\text{Se-C}}$ = 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 $\text{C}_{13}\text{H}_{14}\text{OSe}$: 266.0210. Found

266.0204.

(*E*)-**15**: pale yellow solid: mp 67 °C; ^1H 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 ($^2J_{\text{Se-C}} = 10.6$ 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 $\text{C}_{13}\text{H}_{14}\text{OSe}$: 266.0210. Found 266.0219. The structure of (*E*)-**15** was confirmed by X-ray analysis (**Figure S2**).

Figure S2. ORTEP Drawing of (*E*)-**15**

5. References and Notes

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- S2) Eckert, H.; Forster, B. *Angew. Chem., Int. Ed. Engl.* **1987**, 26, 894.
- S3) 2,2-Dimethylpent-4-ynoyl chloride was prepared from the corresponding ethyl ester by hydrolysis with KOH/EtOH and subsequent chlorination with $(\text{COCl})_2$: Magnus, P.; Slater, M. J.; Principe, L. M. *J. Org. Chem.* **1989**, 54, 5148.