

Supporting Information

Visible-Light Photoredox Synthesis of Chiral α -Selenoamino Acids

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General Procedures

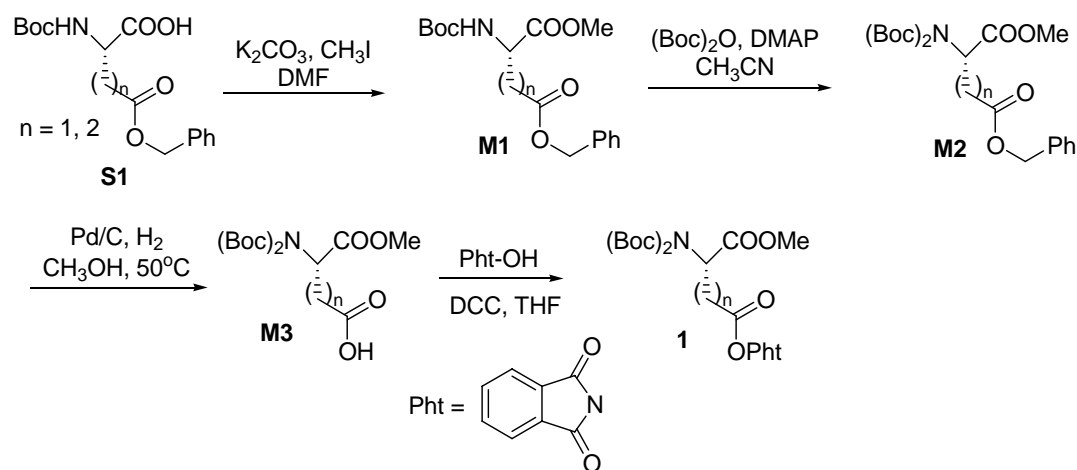
All reactions were carried out in dry solvents. Commercial dichloromethane (DCM) was dried over CaH_2 . Reagents were purchased and used without further purification. Reactions were monitored by thin layer chromatography (TLC), and the products were obtained by column chromatography on silica gel or preparative thin layer chromatography (pTLC). High resolution mass spectra (HRMS) were recorded on a Shimadzu LCMS-IT/TOF quadrupole-time of flight mass spectrometer. NMR spectra were recorded on JOEL JNM-ECA 600, JNM-ECS 400 and JNM-ECA 300 for proton and carbon magnetic resonance spectra (^1H NMR and ^{13}C NMR) using tetramethylsilane (TMS) in the solvent of CDCl_3 as the internal standard (^1H NMR: TMS at 0.00 ppm, CHCl_3 at 7.26 ppm; ^{13}C NMR: CDCl_3 at 77.16 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad.

Abbreviations: DMF: *N,N*-dimethylformamide; DMAP: *N,N*-dimethyl-4-aminopyridine; THF: tetrahydrofuran; EtOAc: ethyl acetate; DCM: dichloromethane; Boc_2O : di-*tert*-butyldicarbonate

Experimental Procedures and Characterization Data

General Procedure for Synthesis of *N*-Bis(Boc)-Asp(OPht)-OMe (1a) and *N*-Bis(Boc)-Glu(OPht)-OMe (1b)

M1, M2, M3 were prepared by following the procedures in the reference.¹



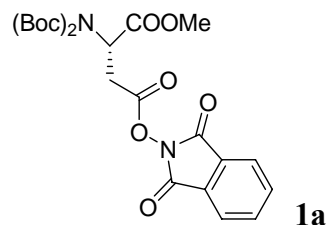
***N*-Boc-Asp(OBn)-OMe (**M1a**).** Boc-Asp(OBzl)-OH (4.8 g, 14.9 mmol) was dissolved in dry DMF (35 mL) in a 100 mL round bottom flask. Finely ground K_2CO_3 (3.0 g, 22 mmol) was added to the solution. The mixture was cooled to 0 °C in an ice bath over five minutes. Methyl iodide (2.0 mL, 30 mmol) was then added to the flask over 30 seconds. The resulting mixture was stirred at 0 °C for 3 hours. A yellow color developed within 20-30 minutes. The ice bath was removed, and H_2O (50 mL) was added, producing a grayish white precipitate. The mixture was extracted with EtOAc (3 \times 50 mL). The organic layers were combined and washed with saturated NaHCO_3 (50 mL) and saturated NaCl (4 \times 50 mL). The organic layer (which was yellow) was dried over Na_2SO_4 , and passed through a plug of silica, eluting with ethylacetate. Evaporation under reduced pressure afforded **M1a** as a white powder, yield: 4.93 g (98 %).

***N*-Boc₂-Asp(OBzl)-OMe (**M2a**).** Di-*tert*-butyl dicarbonate (4.78 g, 22 mmol), DMAP (1.79 g, 14.6 mmol) and **M1a** (4.93 g, 14.6 mmol) were placed into a dry 100 mL round bottom flask. Dry acetonitrile (30 mL) was added to the flask, and the resulting solution was stirred for 24 hours,

during which time the reaction color went from light to dark yellow. Water (50 mL) was added, and the solution became cloudy white. The resulting mixture was extracted with EtOAc (3×50 mL). The combined organic layers were washed with 1 M HCl (50 mL) and saturated NaCl (4×50 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to afford **M2a** as a viscous red oil, yield: 6.17 g (96%).

N-Boc₂-Asp-OMe (M3a). Palladium on activated carbon (1.2 g, 10% by weight) was added to a dry 100 mL round bottom flask charged with **M2a** (6.17 g, 14.0 mmol) and MeOH (30 mL). A H_2 balloon was attached to the reaction vessel equipped with a three way valve. The mixture was degassed by quickly alternating vacuum evacuation and H_2 backfill three times. Then the flask was placed to a 50 °C oil bath for 12 hours. After the reaction completed, the mixture was filtered to remove the Pd/C, and the solvent of the remaining solution was evaporated under reduced pressure to afford **M3a** as a light yellow oil, yield: 4.62 g (95%).

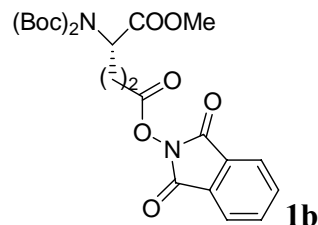
N-Boc₂-Asp(OPht)-OMe (1a). **1a** was synthesized by following the procedure in the reference.² *N*-Hydroxyphthalimide (2.39 g, 14.63 mmol) was added to a 100 mL round bottom flask charged with **M3a** (4.62 g, 13.3 mmol) and dry THF (30 mL). After the mixture was stirred for over 10 minutes, DCC (2.74 g, 13.3 mmol) was added to the flask in portions, and the reaction was performed at room temperature for 24 hours. After the reaction completed, the resulting mixture was filtered, the solvent of the remaining solution was removed under reduced pressure, and the crude product was purified by flash silica gel column chromatography (DCM/EtOAc = 60/1, R_f = 0.52) to give **1a** as a viscous pale yellow oil, yield: 4.9 g (75%).



***N*-Boc₂-Asp(OPht)-OMe (1a).** Viscous pale yellow oil.

¹H NMR (CDCl₃, 400 MHz) δ 7.88 (dd, *J*₁ = 5.5 Hz, *J*₂ = 3.2 Hz, 2H), 7.79 (dd, *J*₁ = 5.5 Hz, *J*₂ = 3.2 Hz, 2H), 5.53 (dd, *J*₁ = 7.5 Hz, *J*₂ = 5.9 Hz, 1H), 3.8 (s, 3H), 3.66 (dd, *J*₁ = 17.1 Hz, *J*₂ = 5.9 Hz, 1H), 3.11 (dd, *J*₁ = 17.1 Hz, *J*₂ = 5.9 Hz, 1H), 1.51 (s, 18H).

¹³C NMR (CDCl₃, 100 MHz) δ 169.5, 167.2, 161.7, 151.5, 134.8, 129.0, 124.0, 84.0, 54.5, 52.9, 33.0, 28.0.



Boc₂-Glu(Pht)-OMe (1b). **1b** was prepared according to the similar procedures above. Eluent: DCM/EtOAc = 60/1, *R*_f = 0.52. Pale yellow solid, mp 45-48 °C.

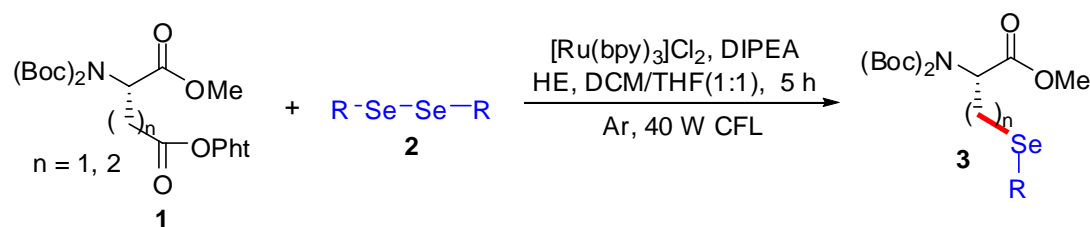
¹H NMR (CDCl₃, 400 MHz) δ 7.88 (dd, *J*₁ = 5.5 Hz, *J*₂ = 3.2 Hz, 2H), 7.79 (dd, *J*₁ = 5.5 Hz, *J*₂ = 3.2 Hz, 2H), 4.99 (dd, *J*₁ = 9.1 Hz, *J*₂ = 5.5 Hz, 1H), 3.7 (s, 3H), 2.87-2.75 (m, 2H), 2.68-2.59 (m, 1H), 2.37-2.27 (m, 1H), 1.51 (s, 18H).

¹³C NMR (CDCl₃, 100 MHz) δ 170.5, 169.0, 161.9, 152.0, 134.8, 128.9, 124.0, 83.7, 57.1, 52.4, 28.0, 27.9, 25.2.

General Procedure for Synthesis of Diselenides (2)

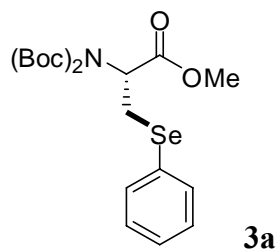
Diselenides were prepared according to the previous literature.³ To a 100 mL three-necked flask, 30 mmol of Mg powder (0.72 g), a stirring bar and a small piece of I₂ were added. The flask was then equipped with a condenser and charged with N₂. Under N₂ protection, anhydrous ether (20 mL) was injected by syringe. A small amount of halogenated hydrocarbon was added, after initiation the rest of the halogenated hydrocarbon (30 mmol) in anhydrous ether (30 mL) was slowly injected with ice-water bath cooling. After the preparation of Grignard reagent, dried selenium powder (30 mmol, 2.4 g) was added slowly. After stirring for 1 h, the mixture was dumped into 100 mL of 1 M HCl solution with ice cooling for acidolysis. The mixture was extracted by ether (3 × 50 mL) and the combined organic layer was dehydrated by anhydrous Na₂SO₄. The solution was charged with O₂ for 24 h and turned orange. Distillation of solvent afforded the crude diselenide, which could be purified by recrystallization with EtOH–H₂O or column chromatography (eluent: petroleum ether).

General Procedure for Synthesis and Characterization of Compounds 3



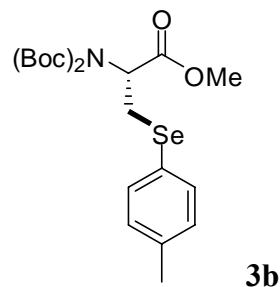
General procedure for synthesis of compounds 3. [Ru(bpy)₃]Cl₂ (1.5 μmol, 1.2 mg), diselenides (2) (0.15 mmol) and Hantzsch ester (HE) (0.225 mmol, 57 mg) were added to a 25-mL Schlenk tube equipped with a Teflon septum and magnetic stir bar. The tube was evacuated and

back-filled with argon for three cycles and then sealed under an atmosphere of argon. *N*-Bis(Boc)-Asp(OPht)-OMe (**1a**) or *N*-Bis(Boc)-Glu(OPht)-OMe (**1b**) (0.15 mmol) (0.15 mmol) and DIPEA (0.375 mmol, 63 μ L, 32.3 mg) were dissolved in mixed solvent of dichloromethane (DCM) (0.5 mL) and tetrahydrofuran (THF) (0.5 mL), and then the solution was added to the tube by syringe. The tube was irradiated with a 40 W fluorescent lamp at room temperature (approximately 2 cm away from the light source). After the complete conversion of the substrates (monitored by TLC), the reaction mixture was diluted with 20 mL of EtOAc, and the solution was filtered by flash chromatography. The filtrate was evaporated by rotary evaporator, and the residue was purified by silica gel column chromatography or preparative thin layer chromatography (pTLC) to give the desired product (**3**).



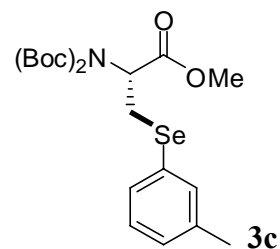
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(phenylselanyl)propanoate (3a). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 56.5 mg (82%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{20}H_{29}NNaO_6Se$ $[M+Na]^+$ m/z 482.1054, found 482.1049.

1H NMR ($CDCl_3$, 400 MHz) δ 7.53 (dd, $J_1 = 7.3$ Hz, $J_2 = 3.21$ Hz, 2H), 7.25-7.24 (m, , 3H), 5.14 (dd, $J_1 = 8.7$ Hz, $J_2 = 4.3$ Hz, 1H), 3.71 (s, 3H), 3.68 (dd, $J_1 = 13.0$ Hz, $J_2 = 5.0$ Hz, 1H), 3.37 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 1.46 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 151.8, 133.0, 130.0, 129.2, 127.3, 83.4, 58.7, 52.5, 28.7, 28.0.



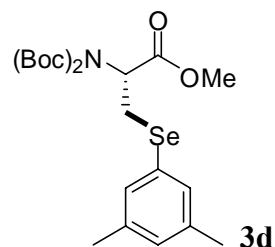
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(*p*-tolylselanyl)propanoate (3b). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 59.6 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₁NNaO₆Se [M+Na]⁺ m/z 496.1210, found 496.1202.

¹H NMR (CDCl₃, 400 MHz) δ 7.43 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 7.7 Hz, 2H), 5.11 (dd, *J*₁ = 9.6 Hz, *J*₂ = 5.5 Hz, 1H), 3.70 (s, 3H), 3.63 (dd, *J*₁ = 13.0 Hz, *J*₂ = 5.5 Hz, 1H), 3.32 (dd, *J*₁ = 13.2 Hz, *J*₂ = 9.6 Hz, 1H), 2.30 (s, 3H), 1.46 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.5, 151.9, 137.4, 133.6, 130.0, 126.2, 83.3, 58.7, 52.5, 29.1, 28.0, 21.1.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(*m*-tolylselanyl)propanoate (3c). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 59 mg (83%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₁NNaO₆Se [M+Na]⁺ m/z 496.1210, found 496.1208.

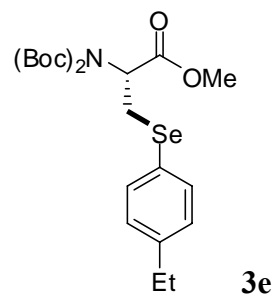
^1H NMR (CDCl_3 , 400 MHz) δ 7.36 (s, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.04 (d, J = 7.3 Hz, 1H), 5.14 (dd, J_1 = 9.6 Hz, J_2 = 5.5 Hz, 1H), 3.71 (s, 3H), 3.67 (dd, J_1 = 13.2 Hz, J_2 = 5.5 Hz, 1H), 3.34 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 2.31 (s, 3H), 1.46 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.5, 151.9, 138.9, 133.7, 130.0, 129.9, 129.0, 128.1, 83.4, 58.7, 52.5, 28.6, 28.0, 21.3.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(3,5-dimethylphenylselanyl) propanoate (3d). Eluent: petroleum ether/ethyl acetate (10:1).

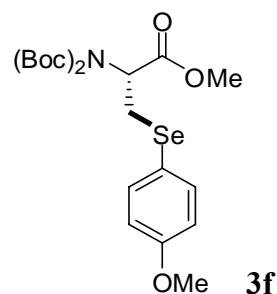
Yield: 61.2 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for $\text{C}_{22}\text{H}_{33}\text{NNaO}_6\text{Se}$ $[\text{M}+\text{Na}]^+$ m/z 510.1367, found 510.1364.

^1H NMR (CDCl_3 , 400 MHz) δ 7.26 (s, 2H), 6.86 (s, 1H), 5.14 (dd, J_1 = 9.6 Hz, J_2 = 5.5 Hz, 1H), 3.72 (s, 3H), 3.67 (dd, J_1 = 12.8 Hz, J_2 = 5.5 Hz, 1H), 3.34 (dd, J_1 = 12.8 Hz, J_2 = 9.1 Hz, 1H), 2.26 (s, 6H), 1.46 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.5, 151.8, 138.6, 130.7, 129.6, 129.1, 83.3, 58.7, 52.5, 28.5, 28.0, 21.2.



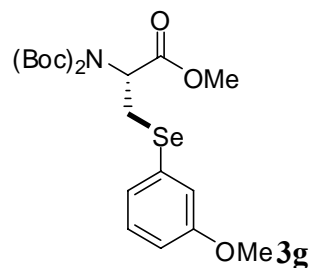
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(4-ethylphenylselanyl)propanoate (3e). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 61.3 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₂H₃₃NNaO₆Se [M+Na]⁺ m/z 510.1367, found 510.1366.

¹H NMR (CDCl₃, 400 MHz) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.12 (dd, *J*₁ = 9.6 Hz, *J*₂ = 5.5 Hz, 1H), 3.70 (s, 3H), 3.67 (dd, *J*₁ = 12.8 Hz, *J*₂ = 5.5 Hz, 1H), 3.34 (dd, *J*₁ = 12.8 Hz, *J*₂ = 9.1 Hz, 1H), 2.6 (q, *J* = 7.8 Hz, 2H), 1.46 (s, 18H), 1.20 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.5, 151.9, 143.7, 133.7, 128.8, 126.5, 83.3, 58.7, 52.5, 29.1, 28.5, 28.0, 15.5.



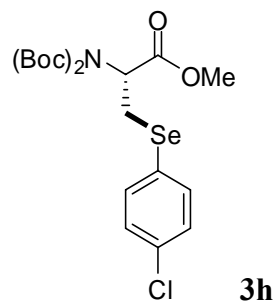
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(4-methoxyphenylselanyl)butanoate (3f). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 63.11 mg (86%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₁NNaO₇Se [M+Na]⁺ m/z 512.1159, found 512.1165.

¹H NMR (CDCl₃, 400 MHz) δ 7.51 (d, *J* = 8.2 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.10 (dd, *J*₁ = 8.7 Hz, *J*₂ = 5.5 Hz, 1H), 3.78 (s, 3H), 3.70 (s, 3H), 3.57 (dd, *J*₁ = 13.2 Hz, *J*₂ = 5.0 Hz, 1H), 3.27 (dd, *J*₁ = 13.2 Hz, *J*₂ = 9.6 Hz, 1H), 1.47 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.5, 159.6, 152.0, 136.1, 120.0, 114.9, 83.3, 58.7, 55.3, 52.5, 30.0, 28.0.



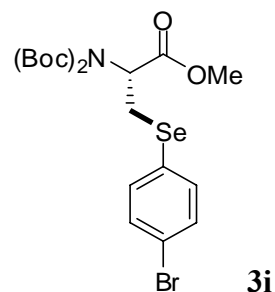
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(*m*-tolylselanyl)propanoate (3g). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 61.61 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{21}H_{31}NNaO_7Se$ $[M+Na]^+$ m/z 512.1159, found 512.1162.

1H NMR ($CDCl_3$, 400 MHz) δ 7.16 (t, $J = 7.8$ Hz, 1H), 7.10 (d, $J = 7.3$ Hz, 1H), 7.09 (s, 1H), 6.78 (d, $J = 6.8$ Hz, 1H), 5.14 (dd, $J_1 = 9.6$ Hz, $J_2 = 5.5$ Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.68 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.5$ Hz, 1H), 3.36 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 1.46 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 159.8, 151.9, 131.0, 130.0, 125.2, 118.2, 113.3, 83.4, 58.7, 55.3, 52.5, 28.6, 28.0.



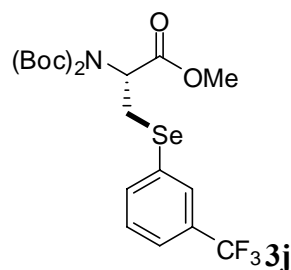
(S)-methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(4-chlorophenylselanyl)propanoate (3h). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 61.38 mg (83%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{20}H_{28}ClNNaO_6Se$ $[M+Na]^+$ m/z 516.0661, found 516.0658.

^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.7 Hz, 2H), 5.11 (dd, J_1 = 8.7 Hz, J_2 = 5.50 Hz, 1H), 3.71 (s, 3H), 3.65 (dd, J_1 = 13.2 Hz, J_2 = 5.0 Hz, 1H), 3.35 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 1.47 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.3, 152.0, 134.6, 133.6, 129.3, 128.2, 83.5, 58.7, 52.6, 29.1, 28.0.



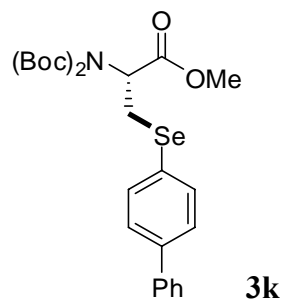
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(4-chlorophenylselanyl)propanoate (3i). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 56.38 mg (70%). Yellow oil. HRMS (ESI-TOF): calculated for $\text{C}_{20}\text{H}_{28}\text{BrNNaO}_6\text{Se}$ $[\text{M}+\text{Na}]^+$ m/z 560.0156, found 560.0150.

^1H NMR (CDCl_3 , 400 MHz) δ 7.40 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 5.10 (dd, J_1 = 8.7 Hz, J_2 = 5.50 Hz, 1H), 3.71 (s, 3H), 3.65 (dd, J_1 = 13.2 Hz, J_2 = 5.0 Hz, 1H), 3.36 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 1.46 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.3, 152.0, 134.8, 132.2, 129.0, 121.7, 83.5, 58.6, 52.6, 29.0, 28.0.



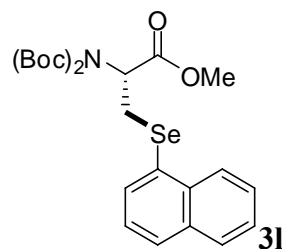
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(3-(trifluoromethyl)phenylselanyl)propanoate (3j). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 35.57 mg (45%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{21}H_{28}F_3NNaO_6Se$ $[M+Na]^+$ m/z 550.0927, found 550.0926.

1H NMR ($CDCl_3$, 400 MHz) δ 7.78 (s, 1H), 7.71 (d, $J = 7.8$ Hz, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 7.37 (t, $J = 7.8$ Hz, 1H), 5.14 (dd, $J_1 = 9.6$ Hz, $J_2 = 5.5$ Hz, 1H), 3.75–3.72 (m, 4H), 3.39 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 1.46 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 151.9, 136.1, 131.6, 131.4, 131.3, 129.5, 125.1, 124.1, 123.2, 122.4, 83.6, 58.6, 52.6, 28.9, 28.0.



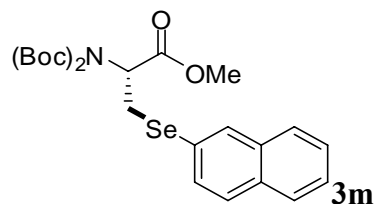
(S)-Methyl 3-(biphenyl-4-ylselanyl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate (3k). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 62.61 mg (78%). Light yellow oil. HRMS (ESI-TOF): calculated for $C_{26}H_{33}NNaO_6Se$ $[M+Na]^+$ m/z 558.1367, found 558.1367.

^1H NMR (CDCl_3 , 400 MHz) δ 7.60 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 6.8 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.42 (t, J = 6.4 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 5.17 (dd, J_1 = 8.7 Hz, J_2 = 5.5 Hz, 1H), 3.74-3.69 (m, 4H), 3.40 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 1.46 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.4, 151.9, 140.5, 140.3, 133.5, 129.1, 128.9, 127.8, 127.5, 127.0, 83.5, 58.7, 52.5, 28.8, 28.0.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(naphthalen-1-ylselanyl)propanoate (3l). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 61.1 mg (80%). Yellow oil. HRMS (ESI-TOF): calculated for $\text{C}_{24}\text{H}_{31}\text{NNaO}_6\text{Se}$ $[\text{M}+\text{Na}]^+$ m/z 532.1210, found 532.1208.

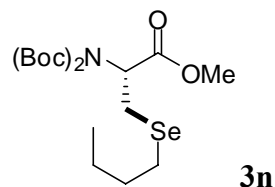
^1H NMR (CDCl_3 , 400 MHz) δ 8.38 (d, J = 8.7 Hz, 1H), 7.85-7.78 (m, 3H), 7.57-7.48 (m, 2H), 7.36 (t, J = 7.3 Hz, 1H), 5.19 (dd, J_1 = 8.7 Hz, J_2 = 5.5 Hz, 1H), 3.72-3.67 (m, 4H), 3.39 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 1.40 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.4, 151.8, 134.2, 134.1, 132.9, 129.2, 128.8, 128.7, 127.7, 126.8, 126.3, 125.8, 83.4, 58.7, 52.5, 28.3, 27.9.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(naphthalen-2-ylselanyl)propanoate (3m). Eluent: petroleum ether/ethyl acetate (10:1).

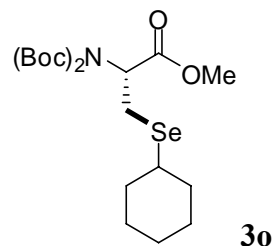
Yield: 61.85 mg (81%). Yellow oil. HRMS (ESI-TOF): calculated for $C_{24}H_{31}NNaO_6Se$ $[M+Na]^+$ m/z 532.1210, found 532.1210.

1H NMR ($CDCl_3$, 400 MHz) δ 8.01 (s, 1H), 7.78-7.70 (m, 3H), 7.59 (m, $J = 8.7$ Hz, 1H), 7.48-7.42 (m, 2H), 5.19 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.77 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.0$ Hz, 1H), 3.71 (s, 3H), 3.46 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 1.42 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 151.9, 133.9, 132.4, 131.8, 130.4, 128.5, 127.7, 127.5, 127.4, 126.5, 126.1, 83.4, 58.8, 52.5, 28.6, 27.9.



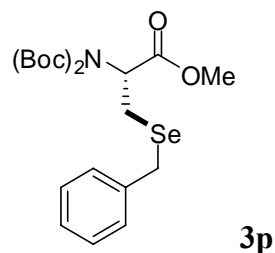
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(butylselanyl)propanoate (3n). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 54.0 mg (82%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{18}H_{33}NNaO_6Se$ $[M+Na]^+$ m/z 462.1366, found 462.1362.

1H NMR ($CDCl_3$, 400 MHz) δ 5.08 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.72 (s, 3H), 3.31 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.0$ Hz, 1H), 3.01 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 2.62-2.55 (m, 2H), 1.66-1.59 (m, 2H), 1.50 (s, 18H), 1.43-1.34 (m, 2H), 0.90 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 152.0, 83.3, 58.9, 52.5, 32.5, 28.1, 24.6, 23.8, 23.0, 13.7.



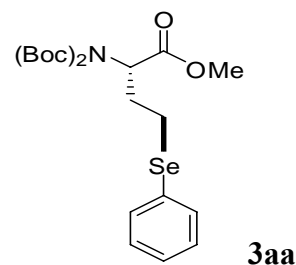
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-3-(cyclohexylselanyl)propanoate (3o). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 50.22 mg (72%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₀H₃₅NNaO₆Se [M+Na]⁺ m/z 488.1523, found 488.1522.

¹H NMR (CDCl₃, 400 MHz) δ 5.08 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.72 (s, 3H), 3.31 (d, $J = 8.2$ Hz, 1H), 3.04 (t, $J = 10.0$ Hz, 1H), 2.93 (s, 1H), 2.04-1.97 (m, 2H), 1.76-1.70 (m, 2H), 1.61-1.54 (m, 2H), 1.50-1.45 (m, 20H), 1.34-1.24 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.6, 152.0, 83.3, 59.3, 52.5, 39.1, 34.4, 28.1, 26.9, 25.9, 22.3.



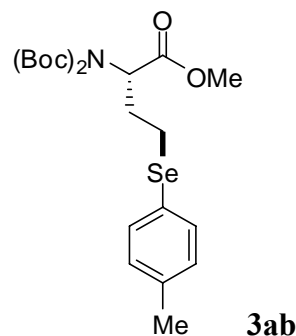
(S)-Methyl 3-(benzylselanyl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate (3p). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 60.30 mg (85%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₁NNaO₆Se [M+Na]⁺ m/z 496.1210, found 496.1209.

¹H NMR (CDCl₃, 400 MHz) δ 7.29 (d, $J = 8.7$ Hz, 2H), 7.26 (t, $J = 7.3$ Hz, 2H), 7.22-7.18 (m, 1H), 5.11 (dd, $J_1 = 8.7$ Hz, $J_2 = 4.35$ Hz, 1H), 3.80 (s, 2H), 3.72 (s, 3H), 3.22 (dd, $J_1 = 13.0$ Hz, $J_2 = 5.0$ Hz, 1H), 2.95 (dd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, 1H), 1.50 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.4, 152.0, 139.0, 129.0, 128.6, 126.8, 83.5, 58.5, 52.5, 28.1, 27.7, 24.0.



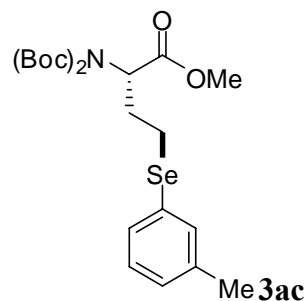
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(phenylselanyl)butanoate (3aa). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 56.8 mg (80%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₁NNaO₆Se [M+Na]⁺ m/z 496.1210, found 496.1214.

¹H NMR (CDCl₃, 400 MHz) δ 7.49 (d, *J* = 7.8 Hz, 2H), 7.25-7.22 (m, , 3H), 5.06 (dd, *J*₁ = 8.7 Hz, *J*₂ = 4.3 Hz, 1H), 3.69 (s, 3H), 2.98-2.87 (m, 2H), 2.56-2.47 (m, 1H), 2.27-2.18 (m, 1H), 1.47 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.9, 151.9, 132.8, 129.8, 129.1, 127.0, 83.4, 58.0, 52.3, 31.0, 28.0, 24.4.



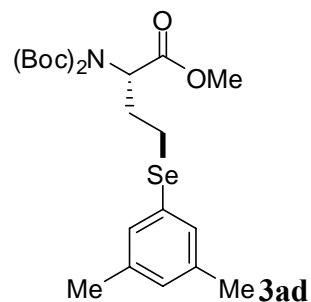
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(*p*-tolylselanyl)butanoate (3ab). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 61.37 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₂H₃₃NNaO₆Se [M+Na]⁺ m/z 510.1367, found 510.1370.

^1H NMR (CDCl_3 , 400 MHz) δ 7.40 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 7.8 Hz, 2H), 5.05 (dd, J_1 = 8.2 Hz, J_2 = 5.5 Hz, 1H), 3.69 (s, 3H), 2.93-2.82 (m, 2H), 2.53-2.42 (m, 1H), 2.30 (s, 3H), 2.24-2.13 (m, 1H), 1.47 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.0, 152.0, 137.2, 133.5, 130.0, 125.8, 83.4, 58.0, 52.3, 31.0, 28.0, 24.8, 21.1.



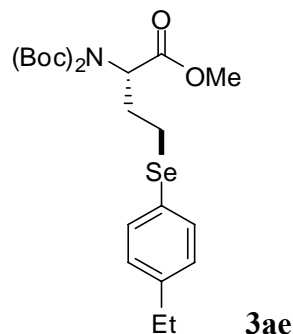
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(*m*-tolylselanyl)butanoate (3ac). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 60.6 mg (83%). Colorless oil. HRMS (ESI-TOF): calculated for $\text{C}_{22}\text{H}_{33}\text{NNaO}_6\text{Se}$ $[\text{M}+\text{Na}]^+$ m/z 510.1367, found 510.1369.

^1H NMR (CDCl_3 , 400 MHz) δ 7.32 (s, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 7.3 Hz, 1H), 5.05 (dd, J_1 = 8.7 Hz, J_2 = 5.5 Hz, 1H), 3.70 (s, 3H), 2.96-2.88 (m, 2H), 2.54-2.47 (m, 1H), 2.31 (s, 3H), 2.27-2.18 (m, 1H), 1.47 (s, 18H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.9, 151.9, 138.9, 133.4, 129.8, 129.6, 128.9, 127.9, 83.4, 58.0, 52.3, 31.0, 28.0, 24.3, 21.3.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(*m*-tolylselanyl)butanoate (3ad). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 63.88 mg (85%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₃H₃₅NNaO₆Se [M+Na]⁺ *m/z* 524.1523, found 524.1517.

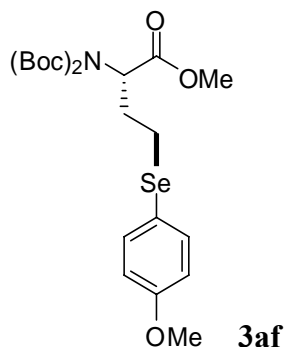
¹H NMR (CDCl₃, 400 MHz) δ 7.26 (s, 2H), 6.85 (s, 1H), 5.05 (dd, *J*₁ = 8.7 Hz, *J*₂ = 5.5 Hz, 1H), 3.70 (s, 3H), 2.96-2.85 (m, 2H), 2.55-2.46 (m, 1H), 2.27 (s, 3H), 2.25-2.17 (m, 1H), 1.47 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.9, 151.9, 138.7, 130.4, 129.4, 128.9, 83.4, 58.0, 52.3, 31.1, 28.0, 24.2, 21.2.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(4-ethylphenylselanyl)butanoate (3ae). Eluent: petroleum ether/ethyl acetate (10:1). Yield:

61.37 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{23}H_{35}NNaO_6Se$ $[M+Na]^+$ m/z 524.1523, found 524.1520.

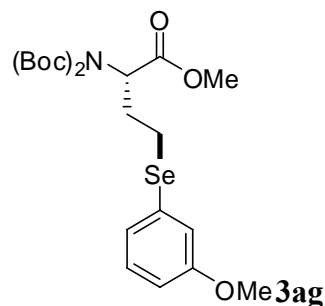
1H NMR ($CDCl_3$, 400 MHz) δ 7.44 (d, $J = 8.2$ Hz, 2H), 7.09 (d, $J = 7.8$ Hz, 2H), 5.05 (dd, $J_1 = 8.2$ Hz, $J_2 = 5.5$ Hz, 1H), 3.69 (s, 3H), 2.92-2.85 (m, 2H), 2.60 (q, $J = 7.8$ Hz, 2H), 2.54-2.43 (m, 1H), 2.25-2.16 (m, 1H), 1.47 (s, 18H), 1.21 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 151.9, 143.5, 133.5, 128.8, 126.1, 83.3, 57.9, 52.2, 31.0, 28.5, 28.0, 24.7, 15.5.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(4-methoxyphenylselanyl)butanoate (3af). Eluent: petroleum ether/ethyl acetate (10:1).

Yield: 64.14 mg (85%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{22}H_{33}NNaO_7Se$ $[M+Na]^+$ m/z 526.1316, found 526.1317.

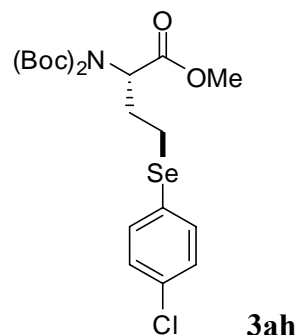
1H NMR ($CDCl_3$, 400 MHz) δ 7.47 (d, $J = 8.7$ Hz, 2H), 6.80 (d, $J = 8.7$ Hz, 2H), 5.05 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.78 (s, 3H), 3.69 (s, 3H), 2.84-2.77 (m, 2H), 2.50-2.38 (m, 1H), 2.21-2.12 (m, 1H), 1.47 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 159.5, 152.0, 136.0, 119.4, 114.8, 83.4, 57.9, 55.3, 52.3, 30.9, 28.0, 25.5.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(3-methoxyphenylselanyl)butanoate (3ag). Eluent: petroleum ether/ethyl acetate (10:1).

Yield: 63.4 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{22}H_{33}NNaO_7Se$ $[M+Na]^+$ m/z 526.1316, found 526.1319.

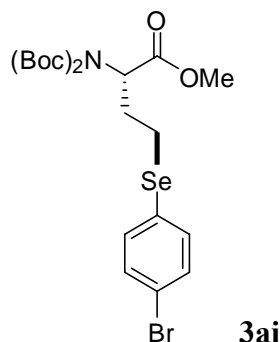
1H NMR ($CDCl_3$, 400 MHz) δ 7.16 (s, t, $J = 7.8$ Hz, 1H), 7.06 (d, $J = 7.3$ Hz, 1H), 7.05 (s, 1H), 6.77 (d, $J = 7.8$ Hz, 1H), 5.06 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.00-2.89 (m, 2H), 2.56-2.50 (m, 1H), 2.28-2.18 (m, 1H), 1.48 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 159.8, 152.0, 130.8, 129.9, 124.8, 117.9, 112.9, 83.4, 58.0, 55.3, 52.3, 31.1, 28.0, 24.3.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(4-chlorophenylselanyl)butanoate (3ah). Eluent: petroleum ether/ethyl acetate (10:1). Yield:

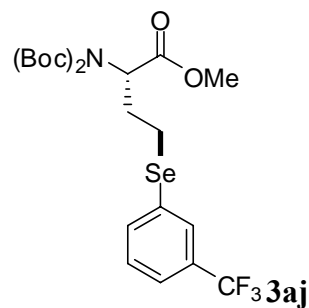
63.14 mg (83%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₁H₃₀ClNNaO₆Se [M+Na]⁺ m/z 530.0818, found 530.0818.

¹H NMR (CDCl₃, 400 MHz) δ 7.47 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H), 5.03 (dd, *J*₁ = 8.7 Hz, *J*₂ = 5.5 Hz, 1H), 3.70 (s, 3H), 2.95-2.88 (m, 2H), 2.54-2.45 (m, 1H), 2.24-2.14 (m, 1H), 1.47 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.3, 152.0, 134.6, 133.6, 129.3, 128.2, 83.5, 58.7, 52.6, 29.1, 28.0, 24.7.



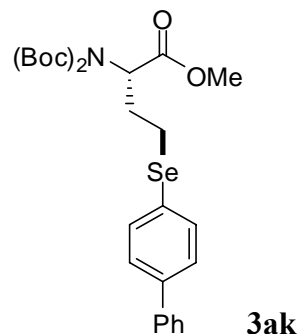
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(4-bromophenylselanyl)butanoate (3ai). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 56.38 mg (70%). Yellow oil. HRMS (ESI-TOF): calculated for C₂₁H₃₀BrNNaO₆Se [M+Na]⁺ m/z 574.0312, found 574.0309.

¹H NMR (CDCl₃, 400 MHz) δ 7.36 (s, 4H), 5.03 (dd, *J*₁ = 8.7 Hz, *J*₂ = 5.5 Hz, 1H), 3.70 (s, 3H), 2.95-2.88 (m, 2H), 2.54-2.45 (m, 1H), 2.24-2.14 (m, 1H), 1.47 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.9, 152.0, 134.5, 132.2, 128.7, 121.3, 83.5, 57.9, , 52.4, 31.0, 28.0, 24.7.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(3-(trifluoromethyl)phenylselanyl)butanoate (3aj). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 63.4 mg (84%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{22}H_{30}F_3NNaO_6Se$ $[M+Na]^+$ m/z 564.1084, found 564.1081.

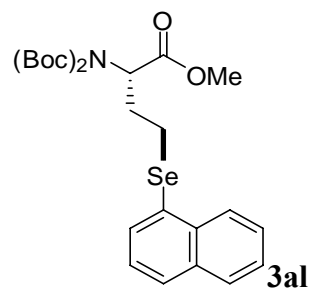
1H NMR ($CDCl_3$, 400 MHz) δ 7.78 (s, 1H), 7.71 (d, $J = 7.8$ Hz, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 7.37 (t, $J = 7.8$ Hz, 1H), 4.99 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.70 (s, 3H), 2.52-2.45 (m, 3H), 2.20-2.18 (m, 1H), 1.48 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 151.9, 136.1, 131.6, 131.4, 131.3, 129.5, 125.1, 124.1, 123.2, 122.4, 83.4, 58.1, 52.3, 31.0, 28.0, 26.1.



(S)-Methyl 4-(biphenyl-4-ylselanyl)-2-(bis(*tert*-butoxycarbonyl)amino)butanoate (3ak). Eluent: petroleum ether/ethyl acetate (10:1). Yield:

64.25 mg (78%). Yellow oil. HRMS (ESI-TOF): calculated for $C_{27}H_{35}NNaO_6Se$ $[M+Na]^+$ m/z 572.1524, found 572.1520.

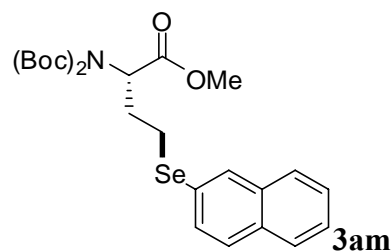
1H NMR ($CDCl_3$, 400 MHz) δ 7.58-7.55 (m, 4H), 7.50-7.41 (m, 4H), 7.34 (t, $J = 7.9$ Hz, 1H), 5.08 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.70 (s, 3H), 3.00-2.91 (m, 2H), 2.60-2.51 (m, 1H), 2.30-2.20 (m, 1H), 1.48 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 152.0, 140.5, 140.1, 133.2, 128.9, 128.8, 127.9, 127.5, 127.0, 83.5, 58.0, 52.3, 31.1, 28.0, 24.5.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(naphthalen-1-ylselanyl)butanoate (3al). Eluent: petroleum ether/ethyl acetate (10:1). Yield:

62.78 mg (80%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{25}H_{33}NNaO_6Se$ $[M+Na]^+$ m/z 546.1367, found 546.1368.

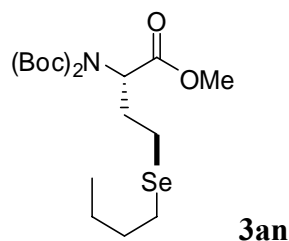
1H NMR ($CDCl_3$, 400 MHz) δ 8.37 (d, $J = 8.2$ Hz, 1H), 7.83-7.71 (m, 3H), 7.56-7.47 (m, 2H), 7.36 (t, $J = 7.8$ Hz, 1H), 5.07 (dd, $J_1 = 8.6$ Hz, $J_2 = 5.5$ Hz, 1H), 3.67 (s, 3H), 2.53-2.45 (m, 1H), 2.27-2.15 (m, 1H), 1.44 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 152.0, 134.4, 134.1, 132.5, 129.0, 128.7, 128.5, 127.6, 126.7, 126.3, 125.9, 83.4, 58.0, 52.3, 31.0, 28.0, 24.5.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(naphthalen-2-ylselanyl)butanoate (3am). Eluent: petroleum ether/ethyl acetate (10:1).

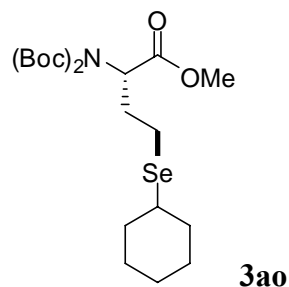
Yield: 62.76 mg (80%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{25}H_{33}NNaO_6Se$ $[M+Na]^+$ m/z 546.1367, found 546.1370.

1H NMR ($CDCl_3$, 400 MHz) δ 7.97 (s, 1H), 7.79-7.71 (m, 3H), 7.56 (d, $J = 8.2$ Hz, 1H), 7.48-7.44 (m, 2H), 5.09 (dd, $J_1 = 8.6$ Hz, $J_2 = 5.5$ Hz, 1H), 3.69 (s, 3H), 3.06-2.96 (m, 2H), 2.60-2.51 (m, 1H), 2.30-2.21 (m, 1H), 1.45 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 152.0, 134.0, 132.3, 131.4, 130.2, 128.5, 127.8, 127.3, 126.5, 126.0, 83.5, 58.0, 52.3, 31.1, 28.0, 24.4.



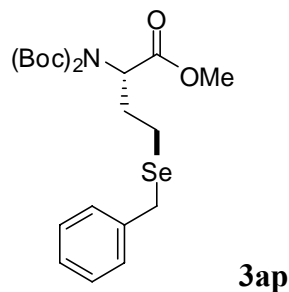
(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(butylselanyl)butanoate (3an). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 55.74 mg (82%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{19}H_{35}NNaO_6Se$ $[M+Na]^+$ m/z 476.1523, found 476.1521.

^1H NMR (CDCl_3 , 400 MHz) δ 5.02 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.72 (s, 3H), 2.60-2.52 (m, 4H), 2.51-2.43 (m, 1H), 2.26-2.18 (m, 1H), 1.67-1.60 (m, 2H), 1.50 (s, 18H), 1.44-1.34 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.1, 152.0, 83.3, 58.1, 52.3, 32.7, 31.3, 28.1, 23.7, 23.1, 20.1, 13.7.



(S)-Methyl 2-(bis(*tert*-butoxycarbonyl)amino)-4-(cyclohexylselanyl)butanoate (3ao): Eluent: petroleum ether/ethyl acetate (10:1). Yield: 51.75 mg (72%). Colorless oil. HRMS (ESI-TOF): calculated for $\text{C}_{21}\text{H}_{37}\text{NNaO}_6\text{Se}$ $[\text{M}+\text{Na}]^+$ m/z 502.1680, found 502.1682.

^1H NMR (CDCl_3 , 400 MHz) δ 5.01 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.71 (s, 3H), 2.95-2.88 (m, 1H), 2.64-2.53 (m, 2H), 2.52-2.43 (m, 1H), 2.27-2.17 (m, 1H), 2.02-1.98 (m, 2H), 1.75-1.70 (m, 2H), 1.50 (s, 20H), 1.35-1.21 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.0, 152.0, 139.2, 128.8, 128.5, 126.7, 83.3, 58.1, 52.3, 30.9, 28.4, 28.0, 26.9, 20.3.

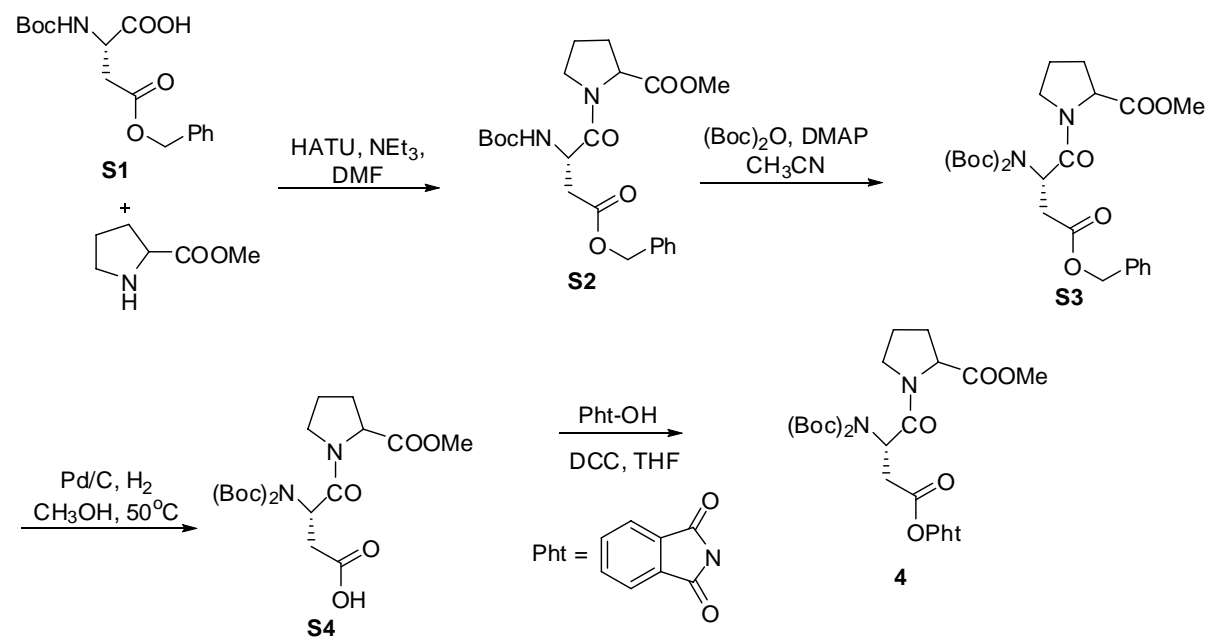


(S)-Methyl 4-(benzylselanyl)-2-(bis(*tert*-butoxycarbonyl)amino)butanoate (3ap). Eluent: petroleum ether/ethyl acetate (10:1). Yield: 62.10 mg (85%). Colorless oil. HRMS (ESI-TOF): calculated for $C_{22}H_{33}NNaO_6Se$ $[M+Na]^+$ m/z 510.1367, found 510.1368.

1H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.25 (m, 4H), 7.20 (t, $J = 8.2$ Hz, 1H), 5.00 (dd, $J_1 = 8.7$ Hz, $J_2 = 5.5$ Hz, 1H), 3.77 (s, 2H), 3.71 (s, 3H), 2.54-2.42 (m, 3H), 2.24-2.16 (m, 1H), 1.48 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 152.0, 83.3, 58.2, 52.2, 38.6, 34.6, 34.5, 31.8, 28.3, 28.0, 26.9, 25.8, 18.7.

General Procedure for Synthesis and Characterization of Compounds 4 and 5

Synthesis of *N*-Bis(Boc)-Asp(OPht)-Pro-OMe (4)

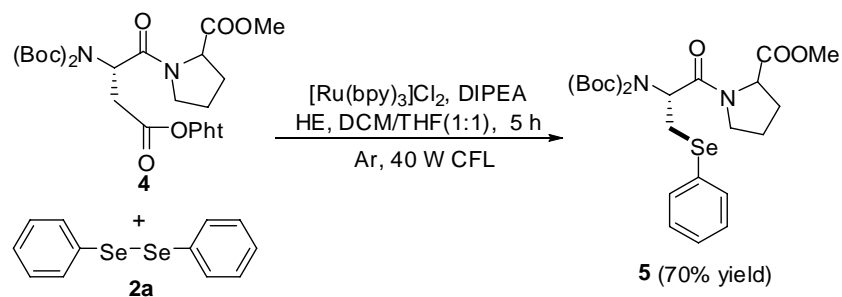


Boc-Asp(OBzl)-Pro-OMe (**S2**) was prepared according to the previous reference.⁴ Boc-Asp(OBzl)-OH (**S1**) (5 mmol, 1.61 g) was dissolved in dry DMF (35 mL) in a 100 mL round bottom flask. HATU (*O*-(7-azabenzotriazol-1-yl)uronium hexafluoro-phosphate) (5 mmol, 1.91g) was added to the solution. After stirring for 30 min, methyl L-prolinate hydrochloride (5 mmol, 0.83g) and NEt_3 (12.5 mmol, 1.75 mL) were added, and the solution was stirred over night. Water (50 mL) was added to the resulting solution, and the mixture was extracted with DCM (3×50 mL). The combined organic layer was washed with 1M HCl (50 mL), saturated NaHCO_3 aqueous solution, and dried over anhydrous Na_2SO_4 . Removal of solvent in the solution under reduced pressure provided Boc-Asp(OBzl)-Pro-OMe (**S2**) (2.06 g, 95%).

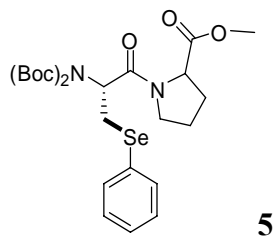
Boc-Asp(OBzl)-Pro-OMe (**S2**) (2.06 g) was dissolved in 30 mL of anhydrous CH_3CN , and di-*tert*-butyl dicarbonate (7.5 mmol, 1.08 g), DMAP

(5 mmol, 0.61 g) was added to the solution. After stirring for 24 hours, water (50 mL) was added, and the solution became cloudy white. The resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic layer was washed with 1 M HCl (50 mL) and saturated NaCl (4 × 50 mL). The organic layer was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to afford **S3** as a viscous red oil, yield: 2.44 g (96%). **S3** was dissolved in CH₃OH (35 mL), palladium on activated carbon (0.4 g, 10% by weight) was added, and a H₂ balloon was attached to the reaction vessel equipped with a three way valve. The mixture was degassed by quickly alternating vacuum evacuation and H₂ backfill three times. Then the flask was placed to a 50 °C oil bath for 12 hours. After the reaction completed, the mixture was filtered to remove the Pd/C, and the solvent of the remaining solution was evaporated under reduced pressure to afford **S4** as a light yellow oil, yield: 1.93 g (95%). *N*-Bis(Boc)-Asp(OPht)-Pro-OMe (**4**) was synthesized by following the procedure in the reference.² *N*-Hydroxyphthalimide (4 mmol, 0.72 g) was added to a 100 mL round bottom flask charged with **S4** (4 mmol, 1.44 g) and dry THF (30 mL). After the mixture was stirred for over 10 minutes, DCC (4 mmol, 0.825 g) was added to the flask in portions, and the reaction was performed at room temperature for 24 hours. After the reaction completed, the resulting mixture was filtered, the solvent of the remaining solution was removed under reduced pressure, and the crude product was purified by flash silica gel column chromatography (DCM/EtOAc = 15/1, R_f = 0.52) to give **4** as a pale yellow solid, yield: 1.65 g (70%). ¹H NMR (CDCl₃, 400 MHz) δ 7.88-7.86 (m, 2H), 7.79-7.77 (m, 2H), 5.52 (t, *J*₁ = 6.8 Hz, 1H), 4.42 (t, *J* = 5.5 Hz, 1H), 3.72 (s, 3H), 3.77-3.61 (m, 3H), 3.40-3.34 (m, 1H), 2.13-1.92 (m, 4H), 1.46 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 172.5, 167.4, 166.8, 161.6, 151.3, 134.9, 134.7, 129.0, 123.9, 84.1, 60.2, 54.8, 52.4, 46.5, 32.7, 28.7, 29.9, 24.9.

Synthesis and Characterization of Compound 5



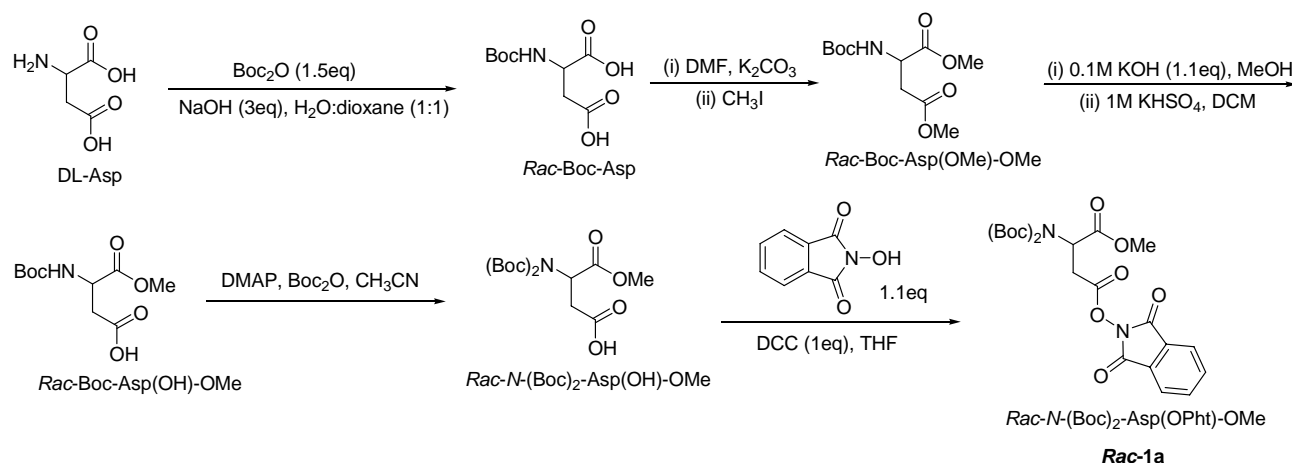
$[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ (1.5 μmol , 1.2 mg), *N*-Bis(Boc)-Asp(OPht)-Pro-OMe (**4**) (0.15 mmol, 88.5mg), diphenyl diselenide (**2a**) (0.15 mmol, 47mg) and Hantzsch ester (HE) (0.225 mmol, 57 mg) were added to a 25-mL Schlenk tube equipped with a Teflon septum and magnetic stir bar. The tube was evacuated and back-filled with argon for three cycles and then sealed under an atmosphere of argon. DIPEA (0.375 mmol, 63 μL , 32.3 mg) was dissolved in mixed solvent of dichloromethane (DCM) (0.5 mL) and tetrahydrofuran (THF) (0.5 mL), and then the solution was added to the tube by syringe. The tube was irradiated with a 40 W fluorescent lamp at room temperature (approximately 2 cm away from the light source). After the complete conversion of the substrates (monitored by TLC), the reaction mixture was diluted with 20 mL of EtOAc, and the solution was filtered by flash chromatography. The filtrate was evaporated by rotary evaporator, and the residue was purified by silica gel column chromatography or preparative thin layer chromatography (pTLC) to give the desired product (**5**).



Methyl 1-((*S*)-2-(bis(*tert*-butoxycarbonyl)amino)-3-(phenylselanyl)propanoyl)pyrrolidine-2-carboxylate (5). Eluent: petroleum ether/ethyl acetate (4:1). Yield: 58.4 mg (70%). Colorless oil. HRMS (ESI-TOF): calculated for C₂₅H₃₇N₂O₇Se [M+H]⁺ m/z 557.1762, found 557.1765.

¹H NMR (CDCl₃, 400 MHz) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.26-7.22 (m, 3H), 5.14 (dd, *J*₁ = 9.1 Hz, *J*₂ = 5.9 Hz, 1H), 4.38 (t, *J* = 4.1 Hz, 1H), 3.72 (s, 3H), 3.77-3.61 (m, 3H), 3.40-3.34 (m, 1H), 2.13-1.92 (m, 4H), 1.45 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 172.6, 168.0, 151.8, 132.8, 130.9, 129.0, 127.0, 83.5, 59.8, 58.4, 52.3, 46.4, 29.4, 28.7, 27.9, 24.9.

Synthesis and Characterization of *Rac*-3a



D,L-Aspartic acid (1.33 g, 10 mmol) and dioxane (20 mL) were added to a 100mL round bottom glass bottle equipped with a magnetic stir bar, then 3 M NaOH (20 mL) was added to the mixture. After the mixture was stirred for 20 min, Boc₂O (3.28 g, 15 mmol) in dioxane was added dropwise, and the mixture was stirred at room temperature overnight. Solvent was evaporated under reduced pressure, and the remained aqueous

was washed with Et₂O (2 × 50 mL) and the organic phase is extracted with saturated NaHCO₃ (2 × 50 mL). The combined aqueous was acidified with 1M KHSO₄ and extracted with ethyl acetate (3 × 100 mL), and the combined organic phase was dried over Na₂SO₄ and evaporated to give Boc-Asp as a white solid, yield 2.3 g (98%). The white solid was dissolved in DMF (30mL), and a well grounded K₂CO₃ (6 g) was added. After the mixture was changed into a white suspension, CH₃I (4 mL) was added dropwise, and the mixture was stirred at room temperature for over 8 h. Water (50 mL) was added, and the aqueous solution was extracted with ethyl acetate (3 × 100 mL). The combined organic phase was washed with water (3 × 50 mL), brine, dried over Na₂SO₄, evaporated under reduced pressure to give *Rac*-Boc-Asp(OMe)-OMe as a colorless oil, yield 2.48 g (97%). According to the previous procedures,² *Rac*-Boc-Asp(OMe)-OMe (1.3 g, 5 mmol) in 55 mL of methanol was added to a 55 mL of 0.1M KOH solution. The mixture was stirred at room temperature overnight, and methanol was evaporated. Remained aqueous solution was acidified with 1 M HCl (6 mL), and extracted with CH₂Cl₂ (2 × 30 mL), and the combined organic phase dried over Na₂SO₄, evaporated under reduced pressure to provide the desired product *Rac*-Boc-Asp(OH)-OMe as a white solid, yield 1.04g (85%). The solid was dissolved in 30 mL dry acetonitrile, and DMAP (1.037 g, 8.5 mmol) was added. Boc₂O (1.40 g, 6.4 mmol) was added to the mixture in one portion. After stirring at room temperature overnight, water 50 mL was added to the mixture to lead to a white suspension appearing, and then a solution of 1M HCl (10.2 mL) was added. The resulting solution was extracted with ethyl acetate (3 × 50 mL), and the combined organic washed with saturated NH₄Cl (2 × 40 mL), dried with Na₂SO₄, and evaporated. The residue was purified by silica gel column chromatography to give a light brown oil *Rac*-*N*-(Boc)₂-Asp(OH)-OMe, yield 1.18g (80%). *Rac*-*N*-(Boc)₂-Asp(OPht)-OMe was synthesized using the similar procedures as described above as synthesis of *N*-(Boc)₂-Asp(OPht)-OMe. *Rac*-*N*-(Boc)₂-Asp(OH)-OMe (1g, 2.9mmol) was added to a solution of *N*-hydroxyphthalimide (0.52 g, 3.2 mmol) in dry THF (10mL). After the mixture was stirred for over 10 minutes, DCC (0.6 g, 2.9 mmol) was added to the flask in

portions, and the reaction was performed at room temperature for 24 hours. After the reaction completed, the resulting mixture was filtered, the solvent of the remaining solution was removed under reduced pressure, and the crude product was purified by flash silica gel column chromatography (DCM/EtOAc = 60/1, R_f = 0.52) to give *Rac-N*-(Boc)₂-Asp(OPht)-OMe (*Rac-1a*) as a viscous pale yellow oil, yield 0.97 g (68%). ¹H NMR (CDCl₃, 400 MHz) δ 7.88 (dd, J_1 = 5.5 Hz, J_2 = 3.2 Hz, 2H), 7.79 (dd, J_1 = 5.5 Hz, J_2 = 3.2 Hz, 2H), 5.53 (dd, J_1 = 7.6 Hz, J_2 = 6.0 Hz, 1H), 3.8 (s, 3H), 3.66 (dd, J_1 = 17.2 Hz, J_2 = 5.95 Hz, 1H), 3.11 (dd, J_1 = 17.2 Hz, J_2 = 6.0 Hz, 1H), 1.51 (s, 18H). ¹³C NMR (CDCl₃, 100 MHz) δ 169.5, 167.2, 161.7, 151.5, 134.8, 129.0, 124.0, 84.0, 54.5, 52.9, 33.0, 28.0.

Synthesis of *Rac-3a*. [Ru(bpy)₃]Cl₂ (1.5 μmol, 1.2 mg), diphenylselenide (**2a**) (0.15 mmol) and Hantzsch ester (HE) (0.225 mmol, 57 mg) were added to a 25-mL Schlenk tube equipped with a Teflon septum and magnetic stir bar. The tube was evacuated and back-filled with argon for three cycles and then sealed under an atmosphere of argon. *Rac-N*-Bis(Boc)-Asp(OPht)-OMe (*Rac-1a*) (0.15 mmol) and DIPEA (0.375 mmol, 63 μL, 32.3 mg) were dissolved in mixed solvent of dichloromethane (DCM) (0.5 mL) and tetrahydrofuran (THF) (0.5 mL), and then the solution was added to the tube by syringe. The tube was irradiated with a 40 W fluorescent lamp at room temperature (approximately 2 cm away from the light source). After the conversion of the substrates (monitored by TLC), the reaction mixture was diluted with 20 mL of EtOAc, and the solution was filtered by flash chromatography. The filtrate was evaporated by rotary evaporator, and the residue was purified by silica gel column chromatography or preparative thin layer chromatography (pTLC) to give the desired product (*Rac-3a*) in 79% (54.4 mg) yield as a pale yellow oil.

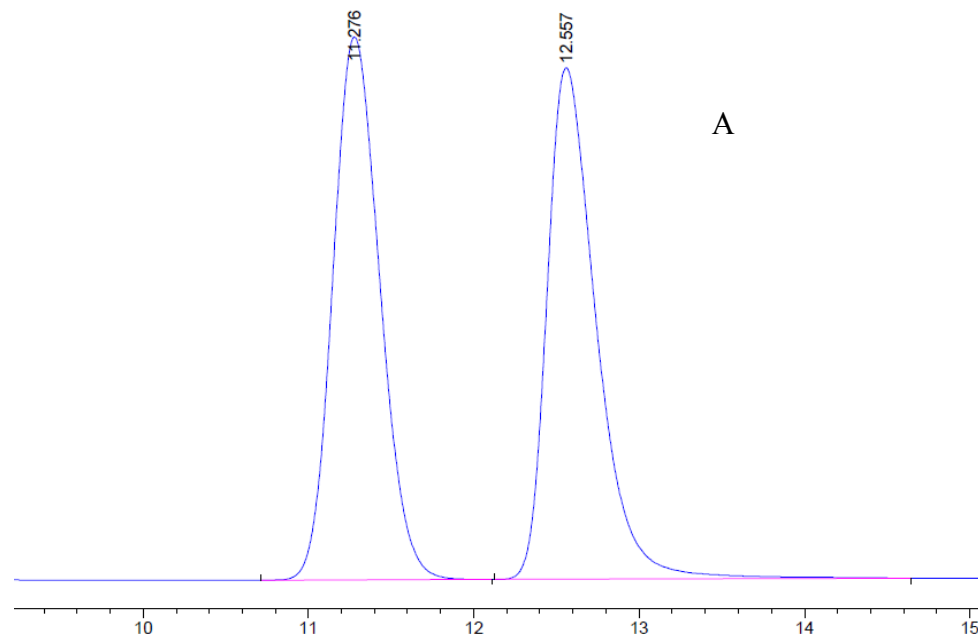
Data for *Rac-3a*: ¹H NMR (CDCl₃, 400 MHz) δ 7.53 (dd, J_1 = 7.3 Hz, J_2 = 3.21 Hz, 2H), 7.25-7.24 (m, , 3H), 5.14 (dd, J_1 = 8.7 Hz, J_2 = 4.3 Hz, 1H), 3.71 (s, 3H), 3.68 (dd, J_1 = 13.0 Hz, J_2 = 5.0 Hz, 1H), 3.37 (dd, J_1 = 13.2 Hz, J_2 = 9.6 Hz, 1H), 1.46 (s, 18H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.4,

151.8, 133.0, 130.0, 129.2, 127.3, 83.4, 58.7, 52.5, 28.7, 28.0.

HPLC Analysis of *Rac*-**3a**, **3a** and Mixture of *Rac*-**3a** and **3a** with Different Ratios

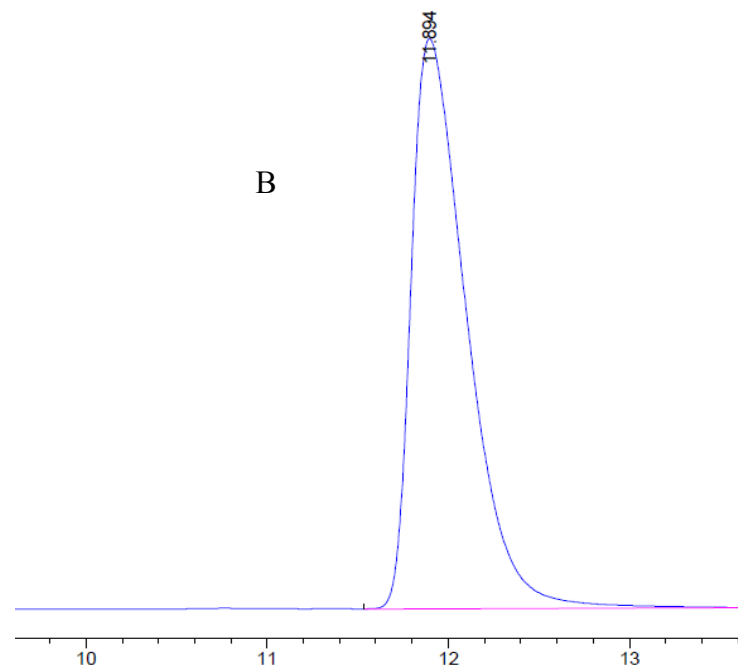
The samples were determined by HPLC with ID-H chiral column using *n*-hexane/isopropanol (90:10) as the mobile phase (column pressure = 40 bar, flow rate = 1 ml/min).

(A) HPLC of *Rac*-**3a** with concentration of 2 mg/mL (Peak area ratio of (*S*)-**3a**/*(R)*-**3a** = 50.34 : 49.66)



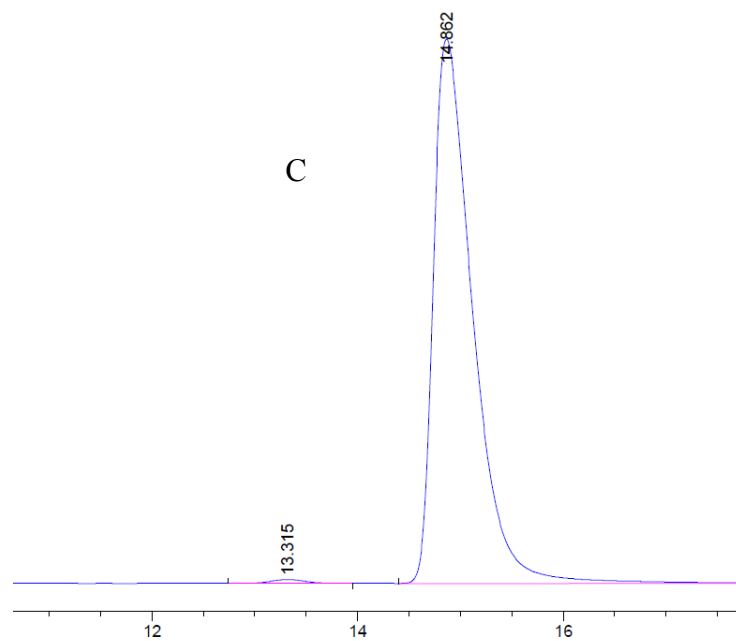
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	11.276	BB	0.3077	1.34090e4	678.49896	50.3415
2	12.557	BB	0.3156	1.32271e4	639.45135	49.6585

(B) HPLC of **3a** with concentration of 2 mg/mL



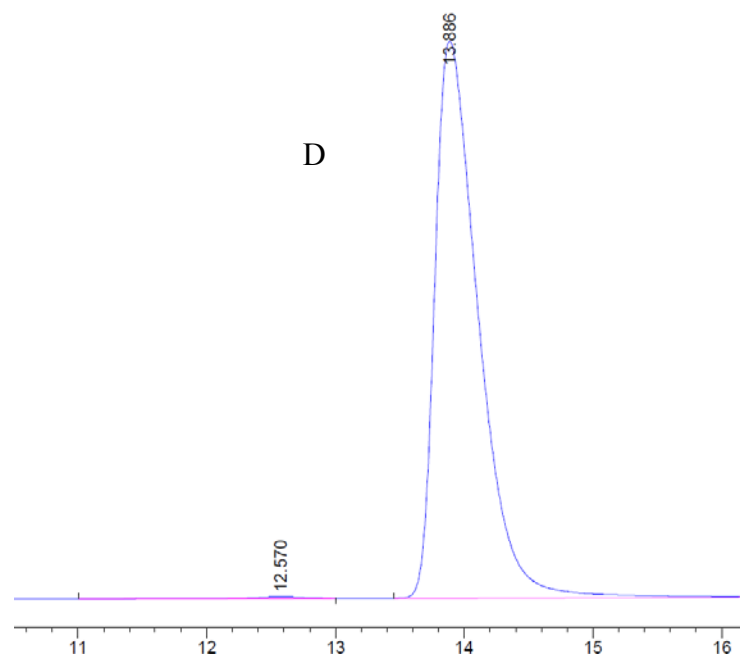
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	11.894	BB	0.3252	2.86945e4	1349.56030	100.0000

(C) HPLC of mixture *Rac*-**3a** and **3a** (molar ratio of *Rac*-**3a**/**3a** = 0.01:1) (Peak area ratio of (*S*)-**3a**/*(R)*-**3a** = 0.62 : 99.38)



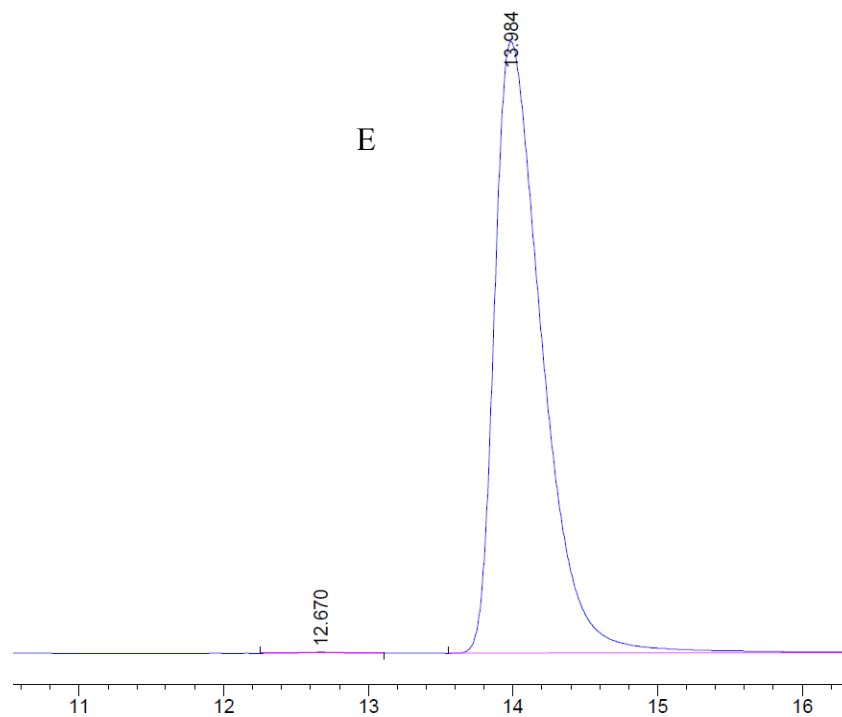
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	13.315	BB	0.3620	182.26784	7.86787	0.6246
2	14.862	BB	0.4033	2.89980e4	1090.90613	99.3754

(D) HPLC of mixture *Rac-3a* and **3a** (molar ratio of *Rac-3a*/**3a** = 0.005:1) (Peak area ratio of (*S*)-**3a**/*(R)*-**3a** = 0.31 : 99.69)



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	12.570	BB	0.3684	83.87241	3.37692	0.3137
2	13.886	BB	0.3565	2.66495e4	1136.84338	99.6863

(E) HPLC of mixture *Rac*-**3a** and **3a** (molar ratio of *Rac*-**3a**/**3a** = 0.001:1) (Peak area ratio of (*S*)-**3a**/*(R)*-**3a** = 0.16 : 99.84)



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	12.670	BB	0.2991	39.76816	2.02454	0.1628
2	13.984	BB	0.3476	2.43901e4	1063.85950	99.8372

References

- (1) Englund, E. A.; Gopi, H. N.; Appella, D. H. *Org. Lett.* **2004**, 6, 213-215.
- (2) Kachkovskiy, G.; Faderl, C.; Reiser, O. *Adv. Synth. Catal.* **2013**, 355, 2440-2248.
- (3) Yu, L.; Wang, J.; Wang, Y.; Xu, Q. *Appl. Organometal. Chem.* **2014**, 28, 652-656.
- (4) Kolyasnikova, K. N.; Vichuzhanin, M. V.; Gudasheva T. A. *Pharm. Chem. J.* **2012**, 46, 96-102.
- (5) Denmark, S. E.; Montgomery, J. I. *J. Org. Chem.* **2006**, 71, 6211.
- (6) Adams, L. A.; Aggarwal V. K.; Boonert R. V.; Bressel B.; Cox R. J.; Shepherd J.; Vincente J.; Walter M.; Whittingham W. G.; Winn C. L. *J. Org. Chem.* **2003**, 68, 9433.

The NMR Spectra of Compounds **3**, **5** and *Rac*-**3a**

