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Chiral phenylselenyl derivatives of pyrrolidine and *Cinchona* alkaloids: nitrogen–selenium donating ligands in palladium-catalyzed asymmetric allylic alkylation

Mariola Zielińska-Błajet, Renata Siedlecka and Jacek Skarżewski*

Department of Organic Chemistry, Faculty of Chemistry, Wrocław University of Technology, 50-370 Wrocław, Poland

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Abstract—Enantiomeric pyrrolidine alcohols and *Cinchona* alkaloids reacted with $PhSeCN/Bu_3P$ in toluene at 0–25 °C to give the corresponding phenyl selenides with complete inversion of configuration at the substitution centers. Thus, the chiral selenoethers obtained were tested in the Pd-catalyzed allylic alkylation of dimethyl malonate with *rac*-1,3-diphenyl-2-propenyl acetate. When chiral selenium pyrrolidine derivatives were applied, the enantioselectivity observed was improved versus the respective sulfur pyrrolidine derivatives up to over 98% ee. The results suggest that the pyrrolidine selenoethers served as the effective N(sp^3), Se-donating chiral ligands. The selenoethers obtained from *Cinchona* alkaloids also gave the allylic alkylation product with a higher ee over those for the corresponding thioethers. The results are in agreement with nucleophilic attack directed at the allylic carbon located *trans* to the chalcogen atom in the intermediate η^3-allylpalladium complex.

1. Introduction

Properly designed chiral ligands offer great potential in the synthetic application of catalytic asymmetric reactions.[1] The most valuable ligands (*privileged catalysts*) are effective in various, often mechanistically different, enantioselective transformations.[2] To this class of catalysts belong the derivatives of natural cyclic amino acids and *Cinchona* alkaloids. Many successful chiral ligands have already been found for the palladium-catalyzed allylic nucleophilic alkylation, a powerful tool for enantioselective C–C bond formation.[3] Nevertheless, this reaction is still used for testing new catalysts for transition-metal catalyzed processes, since its mechanism is well understood and the enantioselectivity of products is determined by both steric and stereoelectronic properties of the chiral ligand coordinated to the palladium atom.[3] Thus, due to the *trans* effect,[4] an attacking nucleophile favorably approaches the complexed allylic system from the opposite site to the more π-accepting ligand center. According to this, in the case of bidentate C=N (imine)—chalcogen ether ligands, the nucleophile approaches *trans* to the more π-accepting imine donor,[4] while for strongly σ-donating (sp^3)-nitrogen and weakly π-accepting chalcogen atoms, the *trans* direction to chalcogen is generally preferred (Fig. 1).[5]

Within our investigation program to explore the preparation and use of chiral organochalcogen compounds in asymmetric catalysis, we have developed the synthesis of new sulfur–nitrogen mixed donor chelate ligands suitable for this purpose. Among them, we obtained the sulfur derivatives of chiral pyrrolidine alcohols[6] and *Cinchona* alkaloids.[7] On the other hand, nitrogen-containing selenoethers have already been reported as successful catalysts in the Pd-catalyzed allylic substitutions.[8] This subject has recently been reviewed by Braga et. al.[9] Encouraged by the reported results, we have elaborated upon an easy

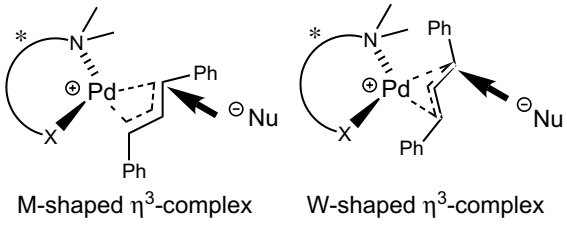

Figure 1.

* Corresponding author. Tel.: +48 71 320 2464; fax: +48 71 328 4064; e-mail: jacek.skarzewski@pwr.wroc.pl

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preparation of the respective phenyl selenides derived from the chiral amino alcohols belonging to the *privileged catalysts* class. Herein, we report their syntheses and catalytic use as new enantioselective N, Se-ligands, easily available in both enantiomeric forms. We also compare their catalytic performance to the results obtained for the respective N,S-analogues.

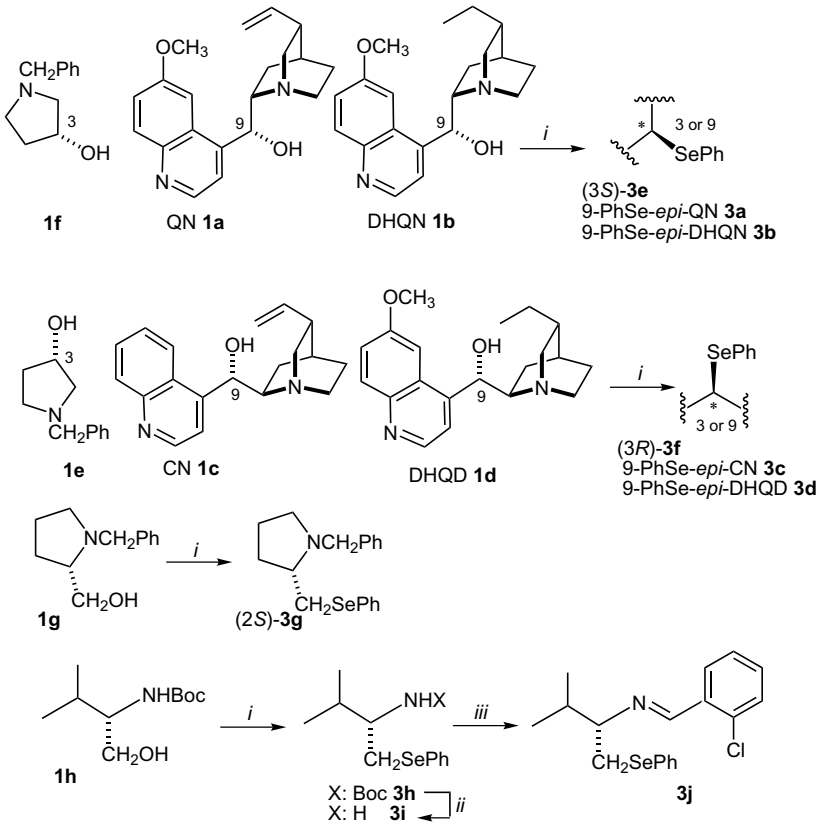
2. Results and discussion

The unknown chiral phenyl selenides were synthesized directly from the easily available enantiomeric alcohols **1a**–**h** via nucleophilic substitution with phenyl selenocyanate and tributylphosphine.[10] Analogously to the Mitsunobu reaction, the hydroxy groups were activated as the oxophosphonium salts generated from tributylphosphine oxidized with phenyl selenocyanate. The intermediates that formed, underwent an S_N2 reaction with the phenylselenoate anion generated, thus bringing about the desired conversion of alcohols into phenyl selenides. For the secondary alcohols, an inversion of configuration at the stereogenic centers took place.

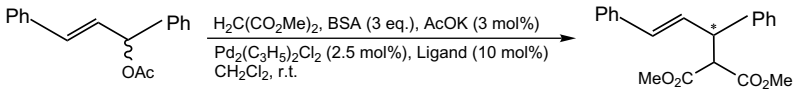
$$PhSeCN + Bu_3P \rightarrow Bu_3P^+SePh\cdot CN^-$$
$$Bu_3P^+SePh\cdot CN^- + ROH \rightarrow Bu_3P^+OR + HCN + PhSe^-$$
$$Bu_3P^+OR + PhSe^- \rightarrow RSePh + Bu_3P{=}O\ (S_N2)$$

Practically, we adopted the Grieco protocol,[10] using toluene as the solvent instead of the originally used THF or pyridine. This simple procedure gave the required products in good to reasonable yields (Scheme 1). Commercially available primary amino alcohols *N*-Boc-L-valinol **1h** and (*S*)-1-benzyl-2-pyrrolidinemethanol **1g** as well as the unhindered secondary ones (*S*)- and (*R*)-1-benzyl-3-hydroxypyrrolidines **1e** and **1f** reacted smoothly, while the *Cinchona* alcohols **1a**–**d**, namely, quinine (QN), dihydroquinine (DHQN), cinchonine (CN), and dihydroquinidine (DHQD) required longer reaction time and the yield was lower. It was observed before that the phenylsulfanyl derivatives of *Cinchona* alkaloids **2** of the same 8,9-configurations (i.e., 8*R*,9*R* or 8*S*,9*S*) gave in the Pd-catalyzed allylic substitution much higher enantioselectivities than those of *unlike* configurations,[7] the selenium compounds of the *like*-type were only prepared. All the respective selenylated products were obtained as a single enantio- or diastereoisomer. It is noteworthy that the direct substitution of the hydroxy group, even if not high yielding, gave pure phenyl selenide along with the easily separable unchanged substrate. When the substitution of QN-tosylate with $PhSe^-Na^+$ in DMF was attempted, the desired product could not be separated from the resulting mixture.

Thus, the chiral selenides obtained were applied in the Pd-catalyzed allylic alkylation. The previously prepared corresponding sulfides **2a**–**g** previously prepared had also been tested in this reaction model.[6,7] We studied the alkylation of dimethyl malonate with *rac*-1,3-diphenyl-2-propenyl acetate, using *N*,*O*-bis(trimethylsilyl)acetamide (BSA)—potassium acetate (3 mol %) as a base, $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$



Scheme 1. Reagents and conditions: (i) PhSeCN, Bu_3P, toluene; (ii) TFAA, CH_2Cl_2; (iii) 2-ClC_6H_4CHO, $CH_2Cl_2/MgSO_4$.



Scheme 2.

(2.5 mol %) as the palladium pre-catalyst and the respective selenide or sulfide as the chiral ligand (10 mol %). The reaction was carried out in methylene chloride at 25 °C for 3–10 days (Scheme 2). In the absence of a ligand, no product could be detected after this period of time.

The obtained results are presented in Table 1. The configuration of product obtained in the reaction was the same for the corresponding sulfur and selenium derivatives.

As can be seen from the results, for all sterically congested *Cinchona* derivatives **3a**–**d**, the yield of the product was less for the more sterically demanding Se-ligand than for the respective S-ligands **2a**–**d**. This steric crowding is supported by the highly deshielded ^{77}Se NMR signals observed for **3a**–**d** (δ ca. 500 ppm) as opposed to ca. 400 ppm observed for **3e** and **3f**.[12] Since there was no reaction in the absence of ligand, we believed that the substitution of sulfur by selenium in the *Cinchona* derivatives could lead to the less favorable complexation of palladium. Nevertheless, for compounds the softer donating selenium still increases enantioselectivity versus the corresponding sulfur ligands (cf. Table 1, entries 1 and 2). The selenium ligands of opposite configuration (8*R*,9*R*) demonstrated worse results and gave a less ee than their sulfur analogues. The examination of molecular models for the [Pd$^+$ (8*S*,9*S*)-**3a** η^3-1,3-diphenylallyl] cation shows that the M-shaped complex is clearly favored. The nucleophilic attack at the allylic carbon, located *trans* to the selenium atom in the M complex, lead to the product of (*R*)-configuration (cf. Fig. 1), that is observed.

Contrary to the results for the *Cinchona*-derived ligands, in all cases of the pyrrolidine derivatives **3e**–**g**, the exchange of sulfur into selenium gave the catalysts of excellent yield and clearly increased enantioselectivity. Also the selenium derivative of valinol **3j** gave a higher ee than the respective sulfur compound. As before, the stereochemistry of the product was the same as observed for the corresponding sulfur ligands.[6,7,11] The stereochemical outcomes are again in agreement with the *trans* effect, directing the nucleophile along the Se–Pd–C axis for **3e**–**g** and along N–Pd–C axis for **3j**. In the case of selenium pyrrolidine derivatives, the palladium atom fits into the coordination space, thus easily forming the complexes. Due to the stronger electron-donating ability (softness) of selenium, the corresponding Pd-complexes are more stable than those of sulfur ligands. As a consequence, a higher yield of the allylic substitution product was observed. The malonate anion attack on the η^3-allylpalladium complex intermediate is directed to the allylic carbon, located *trans* to the more π-accepting selenium center, resulting in a higher enantioselectivity for N, Se-ligands.

3. Conclusion

In conclusion, the catalytic activity and enantioselectivity of the chiral pyrrolidine phenyl selenides in the Pd-catalyzed allylic alkylation not only rivals but generally outperforms that of the corresponding sulfur analogues. The practical advantages of the selenium-based catalysts include their straightforward synthesis, high activity and enantioselectivity.

4. Experimental

4.1. General

Melting points were determined using a Boetius hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1600 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker CPX (^{1}H, 300 MHz) spectrometer using TMS as an internal standard. ^{77}Se NMR spectra were recorded at 115 MHz on a Bruker Avance™ 600 MHz spectrometer using dimethyl selenide as an external standard. Optical rotations at 589 nm were measured using an Optical Activity Ltd. Model AA-5 automatic polarimeter. Separations of the products by chromatography were performed on silica gel 60 (230–400 mesh) purchased from Merck. TLC was performed using silica gel 60 precoated plates (Merck). All procedures with PhSeCN were carried out under dry argon.

Table 1. Pd-catalyzed alkylation of dimethyl malonate with 1,3-diphenyl-2-propenyl acetate in the presence of N,Se- and N,S-donating ligands[a]

Entry	Ligand **3**	Yield (%)	ee (%)	Sulfur analogue **2**		Configuration of product
				Yield	ee (%)	
1	9-PhSe-*epi*-QN **3a**	23	66	46	56	(+)-*R*
2	9-PhSe-*epi*-DHQN **3b**	17	60	67	46	(+)-*R*
3	9-PhSe-*epi*-CN **3c**	20	62	22	76	(−)-*S*
4	9-PhSe-*epi*-DHQD **3d**	16	48	22	62	(−)-*S*
5	3*R*-**3e**	93	>98	73	90	(+)-*R*
6	3*S*-**3f**	90	95	75	90	(−)-*S*
7	2*S*-**3g**	80	86	78	79	(+)-*R*
8	*S*-**3j**	80	>98	87	94	(+)-*R*

[a] The results for the sulfur compounds were taken from Ref. 7 (**2a**–**d**), Ref. 6 (**2e**–**g**), and Ref. 11 (**2j**).

4.2. Ligand synthesis

4.2.1. General procedure for the synthesis of selenium compounds 3. To a solution of alkaloids or appropriate pyrrolidine alcohols (1 mmol) and PhSeCN (0.219 g, 1.2 mmol) in toluene (5 mL) stirred at 0 °C under an argon atmosphere a solution of Bu_3P (0.176 g, 1.2 mmol) in toluene (1 mL) was added by syringe for 10 min. The mixture was allowed to warm to rt and it was further stirred for 2.5–3.5 h (pyrrolidine alcohols) or overnight (alkaloids). Thereafter the mixture was diluted with Et_2O (4 mL) and washed with 5% NaOH (4 mL). The organic phase was washed with water (2×4 mL) and then 1 M HCl (3×4 mL). The combined acid layer was alkalinized to pH >7 with 10% NaOH and extracted with Et_2O (3×4 mL). The ether solution was washed with water, brine, dried over Na_2SO_4, and the solvent was evaporated. Chromatography of the residue on silica gel using $CHCl_3$/*t*-BuOMe, 1:1 gave selenide as a yellow oil or crystals.

4.2.2. (1*S*,3*R*,4*S*,8*S*,9*S*)-6′-Methoxy-9-phenylselenylcinchonine (9-phenylselenyl-*epi*-quinine, 9-PhSe-*epi*-QN) 3a. Yield 35%, yellow oil; $[\alpha]_D = -46.7$ (*c* 1.20, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.72–0.78 (m, 1H), 1.60–1.70 (m, 4H), 2.28–2.37 (m, 1H), 2.89–2.96 (m, 2H), 3.35–3.45 (m, 3H), 3.87 (s, 3H, OMe), 5.02–5.08 (m, 2H, CH_2=), 5.23 (d, $J = 11.3$ Hz, 1H, C^9H), 5.80–5.92 (m, 1H, CH=), 6.82 (t, $J = 7.5$ Hz, 3H, SePh), 6.94–7.01 (m, 2H, SePh), 7.10 (d, $J = 7.1$ Hz, 2H, ArH), 7.31 (d, $J = 4.7$ Hz, 1H, ArH), 7.86 (t, $J = 9.2$ Hz, 1H, ArH), 8.63 (d, $J = 4.7$ Hz, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.9, 28.1, 28.8, 39.2, 41.1, 44.4, 55.5, 56.5, 60.1, 101.4, 114.5, 120.2, 120.9, 127.9, 128.1, 128.8, 131.6, 136.9, 141.6, 142.2, 144.4, 144.5, 147.4, 157.4; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 506.4; IR (film): 3071, 2940, 2883, 1621, 1584, 1508, 1474, 1234, 1032, 915, 831, 740, 693 cm^{-1}. $R_f = 0.19$ ($CHCl_3$/*t*-BuOMe, 1:1). Anal. Calcd for $C_{26}H_{28}N_2OSe$ (M = 463.46): C, 67.38; H, 6.09; N, 6.04. Found: C, 67.25; H, 6.13; N, 6.00.

4.2.3. (1*S*,3*R*,4*S*,8*S*,9*S*)-10,11-Dihydro-6′-methoxy-9-phenylselenylcinchonine (9-phenylselenyl-*epi*-dihydroquinine, 9-PhSe-*epi*-DHQN) 3b. Yield 49%, yellow oil; $[\alpha]_D = -73.3$ (*c* 1.80, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, $J = 7.2$ Hz, 3H, Me), 1.24–1.65 (m, 8H), 2.55–2.63 (m, 1H), 2.84–2.94 (m, 1H), 3.32–3.50 (m, 3H), 3.88 (s, 3H, OMe), 5.25 (d, $J = 11.3$ Hz, 1H, C^9H), 6.81 (t, $J = 7.5$ Hz, 2H, SePh), 6.94–7.02 (m, 3H, SePh), 7.10 (d, $J = 7.1$ Hz, 2H, ArH), 7.35 (d, $J = 4.7$ Hz, 1H, ArH), 7.86 (t, $J = 9.2$ Hz, 1H, ArH), 8.64 (d, $J = 4.7$ Hz, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.1, 25.7, 27.6, 28.6, 28.8, 37.0, 41.2, 44.5, 55.5, 58.2, 60.1, 101.4, 120.3, 120.9, 128.0, 128.1, 128.9, 131.5, 136.8, 142.3, 144.4, 144.7, 147.4, 157.4; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 506.3; IR (film): 3070, 2932, 2862, 1621, 1584, 1508, 1474, 1238, 1032, 852, 833, 740, 693 cm^{-1}. $R_f = 0.32$ ($CHCl_3$/*t*-BuOMe, 1:1). Anal. Calcd for $C_{26}H_{30}N_2OSe$ (M = 465.50): C, 67.09; H, 6.49; N, 6.02. Found: C, 66.98; H, 6.38; N, 5.96.

4.2.4. (1*S*,3*R*,4*S*,8*R*,9*R*)-9-Phenylselenylcinchonine (9-phenylselenyl-*epi*-cinchonine, 9-PhSe-*epi*-CN) 3c. Yield 31%, yellow oil; $[\alpha]_D = +69.1$ (*c* 0.98, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09–1.16 (m, 1H), 1.56–1.62 (m, 2H), 1.66–1.70 (m, 2H), 2.29–2.36 (m, 1H), 3.03–3.20 (m, 5H), 5.05–5.12 (m, 2H, CH_2=), 5.46 (d, $J = 11.2$ Hz, 1H, C^9H), 5.80–5.92 (m, 1H, CH=), 6.79 (t, $J = 7.5$ Hz, 2H, SePh), 6.90–6.95 (m, 1H, SePh), 7.08–7.11 (m, 2H, SePh), 7.38–7.44 (m, 2H, ArH), 7.59 (d, $J = 7.6$ Hz, 1H, ArH), 7.86 (d, $J = 8.5$ Hz, 1H, ArH), 7.95 (d, $J = 8.5$ Hz, 1H, ArH), 8.75 (d, $J = 4.7$ Hz, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.5, 27.9, 28.0, 39.7, 43.4, 47.5, 49.7, 60.3, 114.7, 120.2, 122.5, 126.2, 127.9, 128.1, 128.8, 129.2, 130.1, 131.6, 136.7, 140.7, 146.3, 148.2, 149.8; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 506.2; IR (film): 3067, 2941, 2875, 1592, 1508, 1455, 1111, 995, 905, 762, 634 cm^{-1}. $R_f = 0.18$ ($CHCl_3$/*t*-BuOMe, 1:1). Anal. Calcd for $C_{25}H_{26}N_2Se$ (M = 433.46): C, 69.27; H, 6.05; N, 6.46. Found: C, 69.19; H, 6.12; N, 6.30.

4.2.5. (1*S*,3*R*,4*S*,8*R*,9*R*)-10,11-Dihydro-6′-methoxy-9-phenylselenylcinchonine (9-phenylselenyl-*epi*-dihydroquinidine, 9-PhSe-*epi*-DHQD) 3d. Yield 46%, yellow crystals, mp 147.5–149 °C; $[\alpha]_D = +160.4$ (*c* 0.96, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, $J = 7.2$ Hz, 3H, Me), 1.02–1.10 (m, 1H), 1.26–1.60 (m, 7H), 2.72–2.79 (m, 1H), 3.00–3.19 (m, 3H), 3.38–3.48 (m, 1H), 3.88 (s, 3H, OMe), 5.34 (d, $J = 11.2$ Hz, 1H, C^9H), 6.82 (t, $J = 7.5$ Hz, 2H, SePh), 6.88–7.05 (m, 3H, SePh), 7.11 (d, $J = 7.0$ Hz, 2H, ArH), 7.38 (d, $J = 4.7$ Hz, 1H, ArH), 7.86 (t, $J = 9.2$ Hz, 1H, ArH), 8.63 (d, $J = 4.7$ Hz, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 26.0, 26.2, 27.3, 27.8, 37.7, 43.8, 49.5, 49.9, 55.4, 60.5, 100.9, 120.4, 121.2, 127.9, 128.1, 128.9, 131.6, 136.6, 142.5, 144.4, 144.8, 147.4, 157.5; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 500.6; IR (KBr): 3058, 2933, 2868, 1619, 1586, 1505, 1472, 1219, 1029, 848, 826, 739, 694 cm^{-1}. Anal. Calcd for $C_{26}H_{30}N_2OSe$ (M = 465.50): C, 67.09; H, 6.49; N, 6.02. Found: C, 66.92; H, 6,47; N, 6.01.

4.2.6. (+)-(*R*)-1-Benzyl-3-phenylselenylpyrrolidine 3e. Yield 60%, light yellow oil; $[\alpha]_D = +17.6$ (*c* 0.82, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90–1.97 (m, 1H), 2.34–2.41 (m, 1H), 2.55–2.63 (m, 2H), 2.66–2.71 (m, 1H), 3.11 (dd, $J_1 = 10.0$ Hz, $J_2 = 7.2$ Hz, 1H), 3.61 and 3.68 (AB_q, $J = 12.9$ Hz, 2H, CH_2Ph), 3.74–3.80 (m, 1H), 7.23–7.32 (m, 8H, ArH), 7.49–7.53 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.8, 38.0, 53.4, 60.1, 61.3, 127.0, 127.1, 128.3, 128.8, 129.1, 130.7, 133.4, 138.9; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 399.8; IR (film): 3060, 3027, 2960, 2791, 1579, 1477, 1437, 1375, 1346, 1145, 1073, 1023, 736, 698 cm^{-1}. $R_f = 0.46$ ($CHCl_3$/*t*-BuOMe, 1:1). Anal. Calcd for $C_{17}H_{19}NSe$ (M = 316.31): C, 64.55; H, 6.06; N, 4.43. Found: C, 64.41; H, 6.00; N, 4.37.

4.2.7. (−)-(*S*)-1-Benzyl-3-phenylselenylpyrrolidine 3f. Yield 63%, yellow oil; $[\alpha]_D = -16.9$ (*c* 0.94, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.87–1.96 (m, 1H), 2.33–2.40 (m, 1H), 2.53–2.61 (m, 2H), 2.64–2.70 (m, 1H), 3.09 (dd, $J_1 = 10.0$ Hz, $J_2 = 7.2$ Hz, 1H), 3.59 and 3.67 (AB_q, $J = 12.9$ Hz, 2H, CH_2Ph), 3.71–3.79 (m, 1H), 7.22–7.30 (m, 8H, ArH), 7.46–7.52 (m, 2H, ArH). $R_f = 0.46$ ($CHCl_3$/*t*-BuOMe, 1:1).

4.2.8. (−)-(*S*)-1-Benzyl-2-(phenylselenylmethyl)pyrrolidine 3g. Yield 73%, light yellow oil; $[\alpha]_D = -70.2$ (*c* 0.94, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 1.67–1.83 (m, 3H), 1.97–2.20 (m, 2H), 2.36–2.42 (m, 1H), 2.76–2.86 (m, 1H), 2.91–3.04 (m, 1H), 3.10–3.12 (m, 1H), 3.28 and 4.02 (AB_q, $J = 12.9$ Hz, 1H, CH_2Ph), 3.47 and 3.90 (AB_q, $J = 13.1$ Hz, 1H, CH_2Ph), 7.18–7.35 (m, 8H, ArH), 7.44–7.50 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.5, 23.5, 31.0, 54.5, 58.7, 63.2, 126.5, 127.2, 128.2, 128.4, 128.7, 128.9, 134.4, 139.1; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 255.5; IR (film): 3061, 3027, 2966, 2796, 1579, 1495, 1454, 1355, 1124, 1073, 1028, 738, 699 cm^{-1}. $R_f = 0.62$ ($CHCl_3$/*t*-BuOMe, 1:1). Anal. Calcd for $C_{18}H_{21}NSe$ (M = 330.34): C, 65.45; H, 6.41; N, 4.24. Found: C, 65.23; H, 6.23; N, 4.30.

4.2.9. (*S*)-*N*-2′-Chlorobenzylidene-2-amino-3-methyl-1-phenylselenylbutane 3j. Schiff base **3j** was prepared from aminoselenide **3i**, obtained from N-protected by Boc group selenium compound **3h**.

Selenium compound **3h** was prepared from N-Boc-L-valinol (1 mmol) similarly as described above. Yield 40%, oil, $R_f = 0.49$ (*t*-BuOMe/$CHCl_3$/hexane, 2.5:2.0:14.0). ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (dd, $J_1 = 6.8$ and $J_2 = 3.1$ Hz, 6H), 1.42 (s, 9H), 1.80–1.91 (m, 1H), 3.07 (d, $J = 4.9$ Hz, 2H), 3.62–3.67 (m, 1H), 4.56 (d, $J = 7.2$ Hz, 1H), 7.22–7.27 (m, 3H, ArH), 7.50–7.56 (m, 2H, ArH).

4.2.9.1. Removing the Boc-group. The N-protected selenium compound **3h** (0.4 mmol) was added to an equimolar mixture of CF_3COOH (40 mmol, 3.06 mL) and CH_2Cl_2 (40 mmol, 2.66 mL). The solution was stirred at room temperature for 1.5 h. The reaction was monitored by TLC. The solvent was evaporated and 3 M NaOH (5 mL) then added to the residue. The solution was extracted with chloroform (4 × 5 mL). The organic layers were collected, washed with brine, and dried over Na_2SO_4 to afford 98 mg of pure **3i** as a crystallizing oil (95% yield). $R_f = 0.13$ (*t*-BuOMe/$CHCl_3$, 5:4), $[\alpha]_D = +70.9$ (*c* 1.98, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 0.92 (dd, $J_1 = 6.8$ and $J_2 = 3.2$ Hz, 6H), 1.39 (br s, 2H), 1.65–1.76 (m, 1H), 2.67–2.73 (m, 1H), 2.79 (dd, $J_1 = 11.6$ and $J_2 = 9.3$ Hz, 1H), 3.15 (dd, $J_1 = 11.6$ and $J_2 = 3.1$ Hz, 1H), 7.22–7.26 (m, 3H), 7.49–7.53 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 17.7, 19.3, 33.6, 35.3, 56.3, 126.9, 129.1, 130.3, 132.7; IR (film): 3366, 3071, 3057, 2958, 2929, 2871, 1579, 1478, 1437, 736, 691 cm^{-1}.

4.2.9.2. Preparation of 3j. Equimolar amounts of aminoselenide **3i** (0.34 mmol, 83 mg) and 2-chlorobenzaldehyde (0.34 mmol, 48 mg) were dissolved in 1.5 mL of dry CH_2Cl_2. Anhyd $MgSO_4$ (220 mg) was added and the solution was stirred at room temperature for 24 h. The solution was filtrated and evaporated to afford 108 mg of **3j** as yellow oil (87% yield). $R_f = 0.75$ (*t*-BuOMe/$CHCl_3$, 5:4), $[\alpha]_D = +119.8$ (*c* 1.06, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.95 (dd, $J_1 = 7.5$ and $J_2 = 7.0$ Hz, 6H), 2.02 (m, 1H), 3.15–3.18 (m, 2H), 3.32–3.35 (m, 1H), 7.19–7.36 (m, 6H, ArH), 7.47–7.50 (m, 2H, ArH), 7.94 (dd, $J_1 = 7.5$ and $J_2 = 1.7$ Hz, 1H, ArH), 8.57 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$): δ 18.7, 19.8, 32.6, 33.4, 76.9, 126.7, 126.9, 128.8, 129.0, 129.7, 130.6, 131.4, 132.6, 133.3, 135.1, 157.7; ^{77}Se NMR (115 MHz, $CDCl_3$): δ 274.0; IR (film): 3067, 2960, 2874, 1636, 1579, 1473, 1439, 1383, 1052, 736, 693 cm^{-1}. Anal. Calcd for $C_{18}H_{20}NClSe$ (M = 364.78): C, 59.27; H, 5.53; N, 3.84. Found: C, 59.50; H, 5.38; N, 3.84.

4.3. Catalytic reaction procedure

A solution of the allylpalladium chloride dimer (4 mg, 0.01 mmol) and ligand (0.04 mmol) in dry dichloromethane (1.0 mL) was stirred under argon atmosphere at room temperature for 15 min before a solution of the corresponding substrate (0.4 mmol) in dichloromethane (1.5 mL) was added. The resulting yellow solution was treated successively with dimethyl malonate (1.2 mmol, 0.159 g, 0.137 mL), *N*,*O*-bis(trimethylsilyl)acetamide (1.2 mmol, 0.244 g, 0.296 mL), and anhydrous potassium acetate (1.2 mg, 0.012 mmol). The reaction was carried out at room temperature for 3–8 days until conversion was complete according to TLC analysis. The reaction mixture was diluted with ether (10 mL) and quenched with satd NH_4Cl. The organic layer was washed with brine and dried over $MgSO_4$. The product was purified by column chromatography (hexane/ethyl acetate, 5:1). The enantiomeric excess was determined by ^1H NMR using the chiral shift reagent Eu(hfc)$_3$ (0.5 equiv). Observed $\Delta\delta = 11$ Hz downfield for the dextrorotatory (*R*)-enantiomer. The assignment of the absolute configuration was based on the specific rotation according to the literature data.

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