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Highly enantioselective organocatalytic α-selenylation of aldehydes using hypervalent iodine compounds

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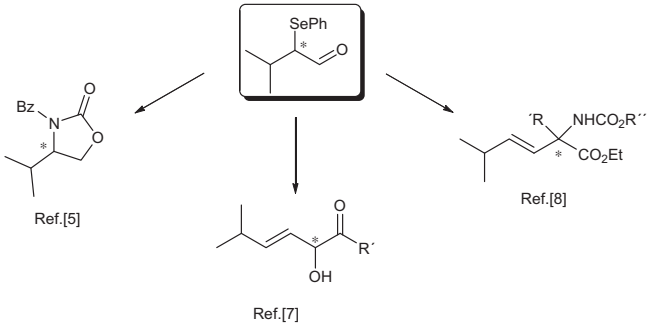
ABSTRACT

The highly enantioselective organocatalytic α-selenylation reaction of aldehydes using a hypervalent iodine compound as an oxidative agent from commercially available phenyl diselenide under mild oxidative conditions is described. This transformation affords α-selenyl aldehydes in good yields and with excellent enantioselectivities. By using hypervalent iodine compounds, it opens up a suitable and alternative way for the preparation of biologically active building blocks such as β-hydroxy alcohols, α-amino acids, and α-hydroxy esters.

1. Introduction

The biochemical role of selenium in mammals and other animals was established in 1973, by the discovery of selenium in the active site of the antioxidant enzyme glutathione peroxidase.[1] General interest in the use of organoselenium compounds in molecular biology intensified after the discovery that organoselenium compounds are much less toxic than inorganic selenium species.[2] There is also a growing interest in organoselenium compounds in other scientific areas, such as enzymology, bioorganic chemistry, and material science, which has led to an increasing demand for organic structures containing selenium atoms.[3] In addition, achiral and chiral organoselenium compounds represent important intermediates in the organic synthesis of other important classes of organic substances. Until now, organic chemists have employed various organoselenium compounds in many useful synthetic transformations, such as cyclization and elimination reactions, as well as sigmatropic rearrangements.[4] The high synthetic utility of α-arylselenylated carbonyl compounds, especially α-arylselenylated aldehydes and ketones that can be readily transformed into valuable building blocks, has attracted the attention of many organic chemists. A number of approaches have been successfully used for the preparation of enantiomerically pure α-arylselenylated carbonyl compounds, but only a limited amount of work dealing with asymmetric selenylation methodologies has been reported to date. Due to the increasing demand for the development of powerful and environmentally friendly methodologies, several examples of organocatalytic transformations affording enantiomerically pure α-arylselenylated compounds or including the formation of those derivatives as key intermediates have been reported. In organocatalysis, successful attempts at the asymmetric α-selenylation reaction of aldehydes were reported by Melchiorre[5] and Córdova[6,7] in 2007, using secondary amine catalysis. In both methodologies, prolinol-derived catalysts and *N*-(phenylseleno)phthalimide were employed as air-stable sources of the phenylselenyl functionality. Recently, two examples of transformations including the organocatalyzed formation of α-selenylated aldehydes were reported on; an asymmetric three-step synthesis of α-hydroxy-(*E*)-β,γ-unsaturated esters developed by Posner[8] and an enantioselective preparation of α-alkyl α-vinyl amino acids reported by Armstrong[9] (Scheme 1).



Scheme 1. α-Selenylated aldehydes as valuable intermediates.

Based on our recent efforts to expand upon this area of asymmetric aminocatalysis[10] and hypervalent iodine chemistry, we herein focus on the development of alternative routes to enantiomerically pure α-selenylated aldehydes using readily-available diselenides in the presence of hypervalent iodine(III) compounds.

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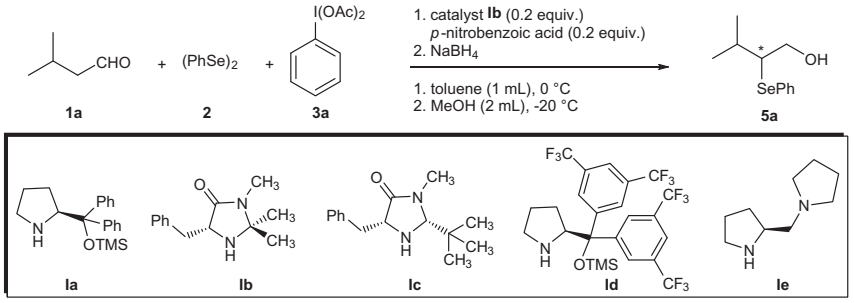
2. Results and discussion

In order to successfully develop an amine-promoted asymmetric α-selenylation of aldehydes, we focused on the use of readily-available diselenides as the source of selenium reagent. Initially we focused on the development of an oxidative system that could serve for the mediation of arylselenium species from symmetrical diselenides. Taking into account the presence of an easily-oxidized aldehyde functionality present in the substrate, and that hypervalent iodine(III) compounds act as mild oxidants,[11] preferentially IBA and other iodine(III) compounds were examined.

At the outset of our studies, we considered the use of iodobenzene diacetate **3a**[12] as a mild oxidant together with phenyl diselenide **2** and *iso*-valeraldehyde **1a** activated with secondary amine catalyst **I** successfully been used for α-selenylations.[5,6] However, while the *O*-TMS-protected diphenylprolinol **Ia** catalyzed α-selenylation of *iso*-valeraldehyde **1a** with good efficiency, only moderate enantioselectivity was obtained (Table 1, entry 1). A significant enhancement of the rate was observed in the presence of an acidic additive (*p*-nitrobenzoic acid). Unsatisfying results were obtained with MacMillan 2nd generation catalyst **Ic** and pyrrolidine-derived catalysts **Id, Id, Ic**. The use of Jorgenseńs catalyst **Id** led to the formation of **5a** in only trace amounts. When catalyst **Ib** was employed, the corresponding α-selenoaldehyde **5a** was obtained in high yield with excellent enantioselectivity (Table 1, entry 2).

Encouraged by these results, we decided to optimize the reaction conditions (solvent, temperature, hypervalent iodine(III) compound, catalyst-loading, Table 2). A solvent screen revealed that imidazolidinone **Ib** catalyzed the formation of **5a** with the highest enantioselectivity at 0 °C in toluene (Table 2, entry 2), while the

Table 1
Screening of catalysts for the α-selenylation of isovaleraldehyde

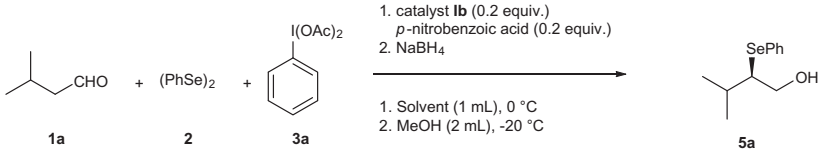


Entry	Catalyst	Temp (°C)	Time (h)	Yield (%)	ee (%)[a]
1	**Ia**	0	70	55	−84
2	**Ib**	0	40	69	98
3	**Ic**	0	40	62	70
4	**Id**	0	70	—	n.d.
5	**Ie**	0	72	51	21

Experimental conditions: a mixture of **1a** (0.25 mmol), catalyst **Ib** and acid (20%), **2** (0.25 mmol), and **3a** (0.25 mmol) in the toluene (1 mL) was stirred at 0 °C for the time shown in the Table. After full conversion and in situ reduction the crude product was purified by column chromatography.

[a] Determined by HPLC (AD 90:10 Hept:*i*PrOH, 0.5 mL).

Table 2
Screening of the solvent and catalyst loading of isovaleraldehyde



Entry	Solvent	Temp (°C)	Time (h)	Conversion (%)	Yield (%)	ee[a] (%)
1	Toluene	25	3	100	69	84
2	Toluene	0	40	100	65	98
3	CH2Cl2	0	24	100	42	82
4	THF	0	72	100	50	77
5	MeCN	0	72	65	33	75
6	Toluene	0	40	100	62	98[b]
7	Toluene	0	140	100	35	92[c]
8	Toluene	0	45	100	61	98[d]

Experimental conditions: a mixture of **1a** (0.25 mmol), catalyst **Ib** and acid (20%), **2** (0.25 mmol), and **3a** (0.25 mmol) in the selected solvent (1 mL) was stirred at 0 °C for the time shown in the Table. After full conversion and in situ reduction the crude product was purified by column chromatography.

[a] Determined by HPLC (AD 90:10 Hept:*i*PrOH, 0.5 mL).

[b] 10% catal. loading

[c] 5% catal. loading

[d] PhIO used instead of $PhI(OAc)_2$.

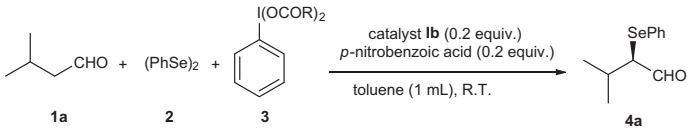
use of $PhI(OAc)_2$ in comparison with PhIO and $PhI(O_2CCF_3)_2$[13] led to higher yields of **5a**. It should be noted that while the enantiocontrol of the studied reaction is highly temperature-dependent (entry 1), only a slight decrease in the enantiocontrol was observed when 5 mol % of catalyst was used (entry 7).

The reaction efficiency was strongly dependent on the catalyst-loading, the reaction temperature (Table 2), the type of iodine compound, the ratios of hypervalent iodine compound **3**, phenyl diselenide **2** and aldehyde **1,** and the presence of an acid (*p*-nitrobenzoic acid) for the formation of enamine intermediate. The results in Table 3 show that $PhI(OAc)_2$ is able to mediate the formation of phenyl selenium from phenyl diselenide but does not oxidize phenyl selenide to phenyl selenium. When an excess of $PhI(OAc)_2$ was used (entry 1), conversion to the corresponding **4a** (50%) as well as the formation of another unidentified product was observed.

In order to study the scope of the α-selenylation reaction, various aldehydes including alkyl, alkenyl, aromatic, and ester moieties were tested (Table 4). When aliphatic aldehydes, such as pentanal and heptanal, were used, the corresponding alcohols **5c**, **5d** were obtained in 67% and 66% yield, respectively, both with excellent enantioselectivity (entries 2 and 3). The formation of diselenylated products was not observed under the optimized reaction conditions, although significant amounts of α,α-diselenylated aldehydes were detected when employing a higher excess of **2** within the α-selenylation reaction. Sterically demanding aldehydes, such as *iso*-valeraldehyde (entry 1) and 3,3-dimethylbutyraldehyde were also well-tolerated for the reported transformations. For example, the reaction between phenyl diselenide, $PhI(OAc)_2$, and 3,3-dimethylbutyraldehyde **1a** gave the corresponding product **5b**, after in situ reduction, in 66% yield with 95% ee (entry 5). The use 3-phenylpropionaldehyde **1f**, as an example of an aromatic aldehyde, led to the formation of the corresponding compound **5f** in 67% yield and 99% ee (entry 6). The use of aldehydes containing an ester group was also successfully examined. In the case of an ester moiety, benzyl 4-formylbutanoate **1g** afforded the corresponding alcohol **5g** in 70% yield with 99% ee (entry 7).

The absolute configuration of α-selenylated aldehydes **4a** was ascertained by chemical correlation. Following the procedure developed by Córdova et al.[6]we prepared the highly enantiopure compound *ent*-**5a**, with an (*S*)-absolute configuration, $\{[\alpha]_D^{25} = -8.5$ (*c* 1.1, $CHCl_3)\}$. Based on our protocol we obtained highly enantiopure compound **5a**, $\{[\alpha]_D^{25} = +9.4$ (*c* 0.6, $CHCl_3)\}$, which clearly indicates that the absolute configuration of the corresponding aldehyde **4a** is (2*R*). Based on the observed results and previous reports, in Scheme 2 we propose a mechanism for

Table 3
Optimization of the reagent ratio of the α-selenylation reaction

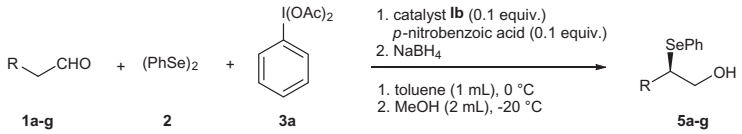


1a 2 3 4a

Entry	R	Ratio 1:2:3	Time (h)	Conversion (%)[a]
1	CH_3	1:0.5:1	12	100[b]
2	CH_3	1:0.5:0.5	16	50[c]
3	CF_3	1:0.5:1	24	30
4	CF_3	1:0.5:0.5	24	50
5	CH_3	1:1:1	2	100

[a] Determined by ^1H NMR.
[B] Formation of **4a** and non-identified highly unstable aldehyde product (ratio 1:1).
[c] 50% Conversion to **4a** was also observed after 72 h.

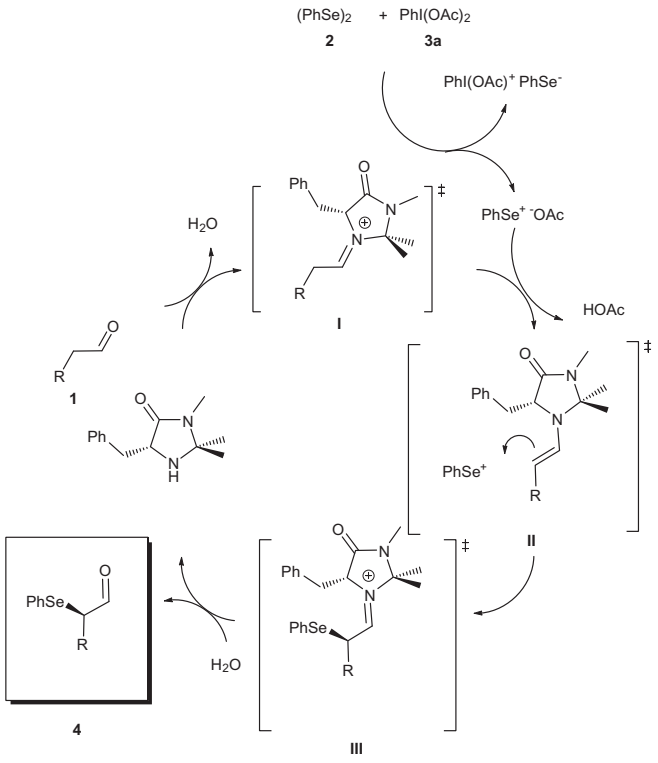
Table 4
Substrate scope of the organocatalytic α-selenylation of aldehydes



1a-g 2 3a 5a-g

Entry	R	Temp. (°C)	Time (h)	Yield (%)	ee (%)[a]
1	*i*Pr	0	40	69	98
2	*n*-Pentyl	0	50	66	99
3	*n*-Propyl	0	50	67	99
4	*n*-Allyl	0	48	51	99
5	*t*-Butyl	0	40	66	95
6	Bn	0	20	67	99
7	CH_2CO_2Bn	0	20	70	99

Experimental conditions: a mixture of **1a–g** (0.25 mmol), catalyst **Ib** and acid (20%), **2** (0.25 mmol), and **3a** (0.25 mmol) in toluene (1 mL) was stirred at 0 °C for the time shown in the Table. After full conversion and in situ reduction the crude product was purified by column chromatography.
[a] Determined by HPLC. Absolute configuration of compounds **5b–5g** was assigned by analogy to absolute configuration of **5a**.



Scheme 2. Proposed mechanism of the α-phenylselenylation of aldehydes.

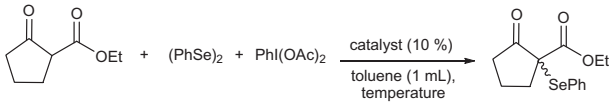
our α-selenylation methodology, whereby the hypervalent iodine species **3a** plays a crucial role as the phenyl selenium mediator, which avoids oxidation of the aldehyde functionality.

Next, we decided to extend our methodology to β-keto esters.[14,15] The treatment of ester **7** with phenyl diselenide and $PhI(OAc)_2$ in the presence of cinchona alkaloid derivatives as catalysts (10 mol %) led to the formation of the corresponding α-selenylated product **8** (Table 5). Despite the high efficiency of the above mentioned methodology (yields of **8** up to 93%), further optimization of the reaction conditions (solvent, catalyst, temperature) revealed limited enantiocontrol, affording only slightly enantioenriched α-selenylated products (up to 36% ee, Table 5). Other β-keto esters with more bulky alkyl groups showed similar results in terms of efficiency and selectivity of the reaction. Nevertheless, the aforementioned results represent the first high yielding report in the area of selenylation reaction of β-keto esters, which are valuable building blocks in the synthesis of structurally diverse organic molecules.[16]

3. Conclusion

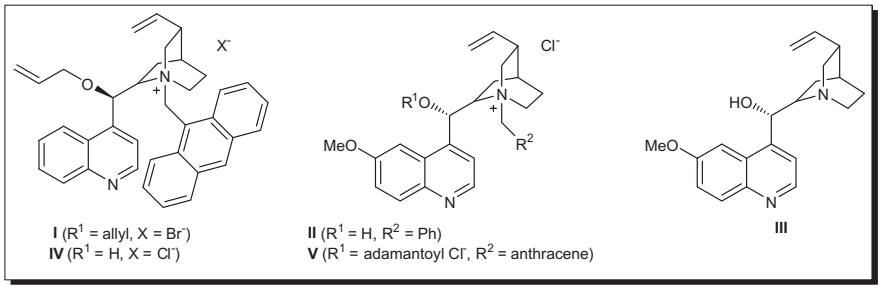
In conclusion, we have reported on a highly enantioselective organocatalytic α-selenylation reaction of aldehydes using a hypervalent iodine compound as an oxidative agent from commercially available starting materials under mild oxidative conditions. This transformation affords α-selenyl aldehydes in good yields and with excellent enantioselectivities. By using hypervalent iodine compounds, we have opened up a suitable and alternative route for the preparation of biologically active building blocks such as β-hydroxy alcohols,[8] α-amino acids,[9,17] α-hydroxy esters,[18] and

Table 5
Screening results for the α-selenylation of ester **7**



Entry	Solvent	Catalyst	Time (h)	Temperature (°C)	Yield (%)	ee (%)[a]
1	Toluene	**I**	1	25	93	36
2	Toluene	**II**	1	25	35	−3
3	Toluene	**III**	1	25	42	8
4	Toluene	**IV**	1	25	64	18
5	Toluene	**V**	1	25	58	8
6	Toluene	**I**	16	0	94	28
7	THF	**I**	10	0	94	36
8	THF	**I**	2	25	87	30
9	DCM	**I**	2	25	85	22

Experimental conditions: a mixture of **7** (0.1 mmol), catalyst (10%), **2** (0.2 mmol), and **3a** (0.2 mmol) in toluene (1 mL) was stirred at rt for the time shown in the Table. After full conversion the crude product was purified by column chromatography.
[a] Determined by HPLC (IB 95:5 Hept:*i*PrOH, 1 ml).



allylic amines.[19] Mechanistic studies and further applications of hypervalent iodine compounds are currently ongoing in our laboratory.

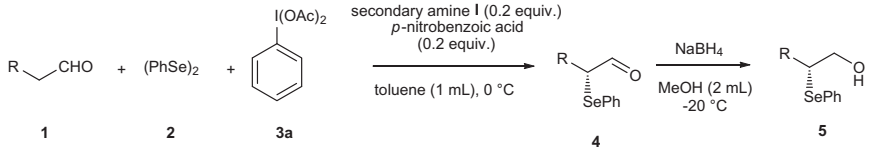
4. Experimental

4.1. General

Chemicals and solvents were either purchased (puriss p.A.) from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used, and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g), $Ce(SO_4)_2{\cdot}H_2O$ (10 g), concd H_2SO_4 (60 mL), and H_2O (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), concd H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

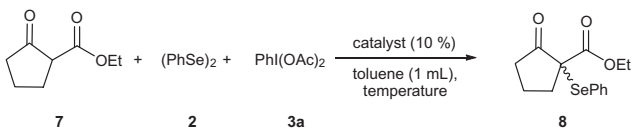
Flash chromatography was performed by using silica gel Merck 60 (particle size 0.040–0.063 mm). ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded with Bruker AVANCE III 600 or Varian VNMRs 300 instruments. Chemical shifts are given in ppm relative and coupling constants *J* are given in Hz. The spectra were recorded in $CHCl_3$-d_1 as solvent at room temperature which served as internal standard (δ = 7.26 ppm) for ^{1}H NMR and (δ = 77.0 ppm) for ^{13}C NMR. Chiral HPLC was carried out using a LCP 5020 Ignos liquid chromatography pump with LCD 5000 spectrophotometric detector with column Daicel Chiralpak® AD. High-resolution mass spectra were recorded with a LTQ Orbitrap XL spectrometer. IR DRIFT spectras were recorded with Nicolet AVATAR 370 FT-IR in cm^{-1}.

4.2. General procedure for the organocatalytic asymmetric α-selenylation of aldehydes



In a vial equipped with a teflon-coated stirrer bar, catalyst **Ib** (0.05 mmol, 12 mg, 20 mol %) and *p*-$NO_2C_6H_4CO_2H$ (0.05 mmol, 8 mg, 20 mol %) were dissolved in toluene (1 mL). After the addition of aldehyde **2** (0.25 mmol, 1.0 equiv), the solution was stirred for ca 10 min at 0 °C, then diphenyl diselenide (0.25 mmol, 78 mg, 1 equiv) and iodobenzene diacetate **3a** (0.25 mmol, 80 mg, 1 equiv) were added and the mixture was stirred at the same temperature for an appropriate time (40 h). After completion of the reaction, the mixture was diluted in cooled MeOH (2 mL, −20 °C). Solid $NaBH_4$ (excess) was then added in one portion. After completion of the reaction the solution was poured into a cooled mixture of EtOAc/1 M HCl (−20 °C). The water layer was extracted with EtOAc and the combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by chromatography to give the desired α-seleno alcohol derivatives **5**.

4.3. General procedure for organocatalytic α-selenylation of β-keto ester 7



In a vial equipped with a teflon-coated stirrer bar, catalyst **IIa** (0.01 mmol, 5 mg, 10 mol %) was dissolved in toluene (1 mL). After the addition of ester **7** (0.1 mmol, 16 mg, 1 equiv), the solution was stirred for ca. 10 min at rt, then phenyl diselenide (0.2 mmol, 62 mg, 2 equiv) and iodobenzene diacetate **3a** (0.2 mmol, 64 mg, 1 equiv) were added and the mixture was stirred at the same temperature for an appropriate time. After completion of the reaction (TLC monitoring), the mixture was purified by chromatography to give the desired α-selenylated compound **8**.

4.4. (*R*)-3-Methyl-2-(phenylselanyl)butan-1-ol 5a

Colorless oil, 69% yield, 98% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (90/10 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 230 nm, t_{major} = 12.1 min, t_{minor} = 13.5 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.58–7.56 m, 2H), δ = 7.28–7.23 (m, 3H), δ = 3.74 (dd, *J* = 5.46 Hz, *J*′ = 11.76 Hz, 1H), δ = 3.66 (dd, *J* = 7.26 Hz, *J*′ = 11.76 Hz, 1H), δ = 3.16 (dt, *J* = 7.3 Hz, *J*′ = 5.5 Hz, 1H), δ = 2.23 (br s, OH), δ = 2.06–2.00 (m, 1H), δ = 1.06 (dd, *J* = 6.7 Hz, *J*′ = 13.86 Hz, 6H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 134.57 (2C), 129,11 (3C), 127.55, 63.30, 60.02, 29.94, 21.14, 20.48 ppm; $[\alpha]_D^{25} = +9.4$ (*c* 0.6, $CHCl_3$); IR (KBr): ν = 3354, 3072, 3055, 3013, 2956, 2926, 2869, 1945, 1873, 1808, 1715, 1580, 1473, 1437, 1069, 1021, 740, 692 cm^{-1}; HRMS (TOF) *m*/*z* calcd for $[M+H]^+$ = 245.0439, found = 245.0448.

4.5. (*R*)-3,3-Dimethyl-2-(phenylselanyl)butan-1-ol 5b

Colorless oil, 66% yield, 95% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (90/10 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 230 nm, t_{major} = 5.9 min, t_{minor} = 6.6 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.61–7.60 (m, 2H), δ = 7.27–7.25 (m, 3H), δ = 3.88 dd, *J* = 4,02 Hz, *J*′ = 11.94 Hz, 1H), δ = 3.63 Hz (dd, *J* = 8.7 Hz, *J*′ = 11.94 Hz, 1H), δ = 3.13 Hz (dd, *J* = 4.08 Hz, *J*′ = 8.76 Hz, 1H), δ = 2.45 (br s, OH), δ = 1.10 (s, 9H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 134.06 (2C), 130.60, 129.15 (2C), 127.36, 67.55, 62.11, 34.85, 28.77 ppm; $[\alpha]_D^{25} = -2.7$ (*c* 1.1, $CHCl_3$); IR (KBr): ν = 3440, 3072, 3058, 3016, 2959, 2902, 2869, 1945, 1873, 1796, 1736, 1577, 1476, 1437, 1392, 1368, 1242, 1072, 1042, 743, 689 cm^{-1}; HRMS (TOF) *m*/*z* calcd for $[M+H]^+$ = 259.0596, found = 259.0592.

4.6. (*R*)-2-(Phenylselanyl)pentan-1-ol 5c

Colorless oil, 67% yield, 99% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (98/2 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 230 nm, t_{major} = 18.6 min, t_{minor} = 19.8 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57–7.56 (m, 2H), δ = 7.32–7.26 (m, 3H), δ = 3.62 (dd, *J* = 4.86 Hz, *J*′ = 11.64 Hz, 1H), δ = 3.53 (dd, *J* = 6.78 Hz, *J*′ = 11.64 Hz, 1H), δ = 3.27–3.23 (m, 1H), δ = 2.27 (br s, OH), δ = 1.66–1.47 (m, 4H), δ = 0.93 (t, 4H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 135.38 (2C), 129.06 (2C), 127.91, 127.41, 64.25, 50.27, 33.77, 20.99, 13.78 ppm; $[\alpha]_D^{25} = +19.3$ (*c* 0.6, $CHCl_3$); IR (KBr): ν = 3363, 3072, 3058, 3013, 2959, 2926, 2866, 1948, 1876, 1799, 1715, 1577, 1461, 1473, 1437, 1024, 737, 692 cm^{-1}; HRMS (TOF) *m*/*z* calcd for $[M+H]^+$ = 245.0439, found = 245.0450.

4.7. (*R*)-2-(Phenylselanyl)heptan-1-ol 5d

Colorless oil, 66% yield, 99% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (95/5 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 190 nm, t_{major} = 14.9 min, t_{minor} = 16.8 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57–7.56 (m, 2H), δ = 7.34–7.26 (m, 3H), δ = 3.62 (dd, J = 4.86 Hz, J' = 11.64 Hz, 1H), δ = 3.52 (dd, J = 6.78 Hz, J' = 11.64 Hz, 1H), δ = 3.26–3.21 (m, 1H), δ = 2.20 (br s, OH), δ = 1.69–1.64 (m, 1H), δ = 1.61–1.55 (m, 2H), δ = 1.48–1.44 (m, 1H), δ = 1.33–1.26 (m, 4H), δ = 0.89 (t, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 135.40 (2C), 129.07 (2C), 127.93, 127.43, 64.25, 50.60, 31.62, 31.53, 27.48, 22.49, 14.01 ppm; $[\alpha]_D^{25} = +15.4$ (c 0.7, $CHCl_3$); IR (KBr): ν = 3351, 3069, 3058, 3013, 2953, 2932, 2866, 2863, 1942, 1876, 1802, 1733, 1580, 1479, 1464, 1060, 1039, 1024, 1000, 743, 692 cm^{-1}; HRMS (TOF) m/z calcd for $[M+H]^+$ = 273.0752, found = 272.0750.

4.8. (*R*)-2-(Phenylselanyl)pent-4-en-1-ol 5e

Colorless oil, 51% yield, 99% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (95/5 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 190 nm, t_{major} = 19.9 min, t_{minor} = 21.8 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.59−7.57 m, 2H), d = 7.32–7.27 (m, 3H), δ = 5.92–5.85 (m, 1H), δ = 5.14–5.10 (m, 2H), δ = 5.14–5.10 (m, 2H), δ = 3.66 (dd, J = 5.16 Hz, J' = 11.64 Hz, 1H), δ = 3.58 (dd, J = 6.3 Hz, J' = 11.64 Hz, 1H), δ = 3.33–3.28 (m, 1H), δ = 2.46 (dt, J = 5.7 Hz, J' = 1.26 Hz, 2H), δ = 2.16 (br s, OH) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 135.48, 135.37 (2C), 129.13 (2C), 128.03, 127.34 117.37, 63.88, 48.65, 48.65, 36.25 ppm; $[\alpha]_D^{25} = +14.0$ (c 0.3, $CHCl_3$); IR (KBr): ν = 3357, 3069, 3055, 2995, 2977, 2929, 2872, 1951, 1882, 1829, 1715, 1577, 1479, 1437, 1075, 1021, 997, 740, 689 cm^{-1}; HRMS (TOF) m/z calcd for $[M+H]^+$ = 243.0283, found = 243.0289.

4.9. (*R*)-3-Phenyl-2-(phenylselanyl)propan-1-ol 5f

Colorless oil, 67% yield, 99% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (95/5 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 230 nm, t_{major} = 24.8 min, t_{minor} = 27.1 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51−7.49 m, 2H), δ = 7.27–7.17 (m, 8H), δ = 3.58 (dd, J = 4.44 Hz, 1H), δ = 3.53–3.45 (m, 2H), d = 3.01–2.94 (m, 2H), δ = 3.13 (br s, OH) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 139.01, 135.26 (2C), 129.12 (2C), 129.07 (2C), 128.45 (2C), 128.00, 127.56, 126.55, 63.10, 50.55, 38.16 ppm; $[\alpha]_D^{25} = +14.1$ (c 0.7, $CHCl_3$); IR (KBr): ν = 3380, 3102, 3058, 3028, 2998, 2932, 2869, 1951, 1879, 1805, 1736, 1601, 1580, 1476, 1455, 1431, 1066, 1021, 1000, 743, 698 cm^{-1}; HRMS (TOF) m/z calcd for $[M+H]^+$ = 292.0366, found = 292.0373.

4.10. (*R*)-Benzyl 4-hydroxy-3-(phenylselanyl)butanoate 5g

Colorless oil, 70% yield, 99% ee. The ee was determined by HPLC analysis using Chiralpak AD-H column (95/5 heptane/*i*-PrOH, flow rate 0.5 mL/min; λ = 190 nm, t_{major} = 30.3 min, t_{minor} = 32.6 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.47 d, J = 7.2 Hz, 2H), δ = 7.26–7.16 (m, 8H), δ = 5.05 (d, J = 3.54 Hz, 2H), δ = 3.60–3.50 (m, 3H), δ = 2.73 (dd, J = 6.72 Hz, J' = 16.26 Hz, 1H), δ = 2.62 (dd, J = 7.14 Hz, J' = 16.26 Hz, 1H), δ = 2.15 (br s, OH) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 171.43, 135.71 (2C), 135.56, 129.21 (2C), 128.57 (2C), 128.35 (3C), 126.70, 66.72, 64.39, 43.13, 37.37 ppm; $[\alpha]_D^{25}$ == +6.8 (c 1.2, $CHCl_3$); IR (KBr): ν = 3443, 3058, 3028, 2947, 2878, 1954, 1885, 1727, 1577, 1476, 1458, 1434, 1299, 1213, 1174, 1135, 1000, 743, 692 cm^{-1}; HRMS (ESI) m/z calcd for $[M+Na]^+$ = 373.0319, found = 373.0312.

4.11. Ethyl 2-oxo-1-(phenylselanyl)cyclopentanecarboxylate 8

Colorless oil, 93% yield, 36% ee. The ee was determined by HPLC analysis using Chiralpak IB column (95/5 heptane/*i*-PrOH, flow rate 1 mL/min; λ = 190 nm, t_{major} = 7.9 min, t_{minor} = 8.5 min); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.64−7.62 m, 2H), δ = 7.41–7.38 (m, 1H), δ = 7.33–7.30 (m, 2H), δ = 4.19 (q, J = 7.14 Hz, 2H), δ = 2.55–2.50 (m, 1H), δ = 2.45–2.39 (m, 1H), δ = 2.33–2.27 (m, 1H), δ = 2.09–2.05 (m, 1H), δ = 2.00–1.90 (m, 2H), δ = 1.24 (t, J = 7.2 Hz, 3H), ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 207.57, 169.55, 137.55 (2C), 129.74, 129.00 (2C), 126.49, 62.13, 58.86, 36.91, 34.27, 19.11, 14.00 ppm; $[\alpha]_D^{25} = -63.5$ (c 1.2, $CHCl_3$); IR (KBr): ν = 3075, 3055, 2977, 2935, 2899, 1751, 1730, 1715, 1577, 1476, 1257, 1230, 1141, 1018 cm^{-1}; HRMS (ESI) m/z calcd for $[M+Na]^+$ = 335.01561, found = 335.01561.

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