The use of chiral diferrocenyl diselenides for highly selective asymmetric intramolecular selenocyclisation

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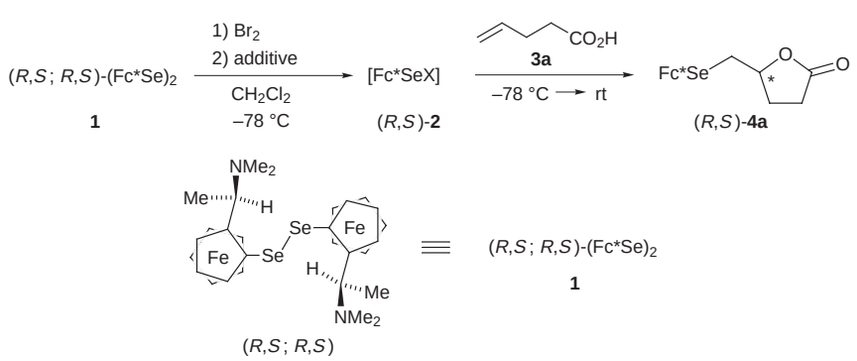
Asymmetric intramolecular selenocyclisation of alkenoic acids, alkenols and alkenyl urethanes using chiral 2-[1-(dimethylamino)ethyl]ferrocenylselenenyl cations proceeds smoothly to give the corresponding organoselenenyl moiety-containing lactones, cyclic ethers and N-heterocycles, respectively, in good to excellent chemical yields (up to 97%) with very high diastereoselectivities (up to 98% de). The nature of the counter anions of the selenenylating agents affected remarkably the diastereoselectivity of the cyclisation, PF_6^- and BF_4^- being revealed to be the best for alkenoic acids and alkenols, and alkenyl urethanes, respectively. A plausible reaction scheme for the cyclisation is presented where a chiral selenenylating agent approaches the carbon–carbon double bond of the substrate from the less sterically-congested direction to afford a chiral episelenonium ion followed by an intramolecular back side attack of a nucleophile.

Introduction

A variety of organoselenium compounds have been proven to be quite useful for organic synthesis over several decades.[1] Recent interest in this field has focused on the synthesis of optically active organoselenium compounds and their application to highly selective asymmetric synthesis.[2–15] The compounds employed for this purpose are mostly the stable optically active diselenides which can be used as electrophilic and nucleophilic chiral selenenylating reagents[2–13] and also as chiral ligands for transition metal-catalysed asymmetric synthesis.[14] Electrophilic heteroatom cyclisations, which are the addition of internal heteroatom nucleophiles such as O, N and S to carbon–carbon double bonds initiated by some external electrophiles are well known to generate the corresponding heterocyclic compounds.[16] The organoselenium compounds have been used as one of these electrophilic species to afford heterocyclic compounds such as lactones, cyclic ethers, lactams and N-heterocycles which contain an organoselenium moiety at the side chain.[17] Recently, the asymmetric version of this intramolecular selenocyclisation has been explored using a variety of optically active organoselenium reagents.[6a,b,7a,c,8a,9a,c] We have also succeeded in highly diastereoselective selenocyclisation of alkenes using optically active ferrocenylselenenyl bromide prepared *in situ* easily from diferrocenyl diselenide and bromine.[12] Herein, the details of the approach are reported for producing the selenium-containing optically active lactones, cyclic ethers and N-heterocyclic compounds from the corresponding alkenoic acids, alkenols and alkenyl urethanes, respectively, in good to excellent chemical yields with very high diastereoselectivities. The nature of the counter anions of the selenenylating agents affected remarkably the diastereoselectivity of the cyclisation, PF_6^- and BF_4^- being revealed to be the best for alkenoic acids and alkenols, and alkenyl urethanes, respectively. A plausible reaction scheme for the cyclisation is presented where a chiral selenenylating agent approaches the carbon–carbon double bond of the substrate from the less sterically-congested direction to afford a chiral episelenonium ion followed by an intramolecular back side attack of a nucleophile.

Results and discussion

As chiral organoselenium compounds, we employed (*R*,*S*;*R*,*S*)- and (*S*,*R*;*S*,*R*)-bis{2-[1-(dimethylamino)ethyl]ferrocenyl} diselenides (**1a** and **1b**, respectively) which have been prepared from optically active amino-substituted ferrocene by the reported method.[13] Preliminary experiments were carried out under various conditions with pent-4-enoic acid (**3a**) using (*R*,*S*)-ferrocenylselenenyl bromide (**2a**), which was prepared *in situ* from **1a** and bromine in CH_2Cl_2 at −78 °C, to establish the optimal condition for cyclisation (Scheme 1, Table 1).[18] First, it was found that the reaction did not proceed at all under stirring at −78 °C for 1 h and then at room temperature for 20 h, but it proceeded smoothly when an excess amount of Et_3N was added (Table 1, entries 2 and 3). The product was exclusively (*R*,*S*)-ferrocenylselenenylmethyl-γ-lactone (*R*,*S*)-**4a** which was



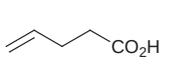
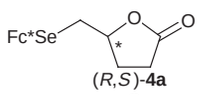
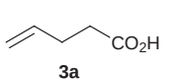
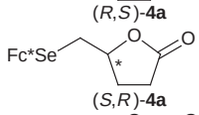
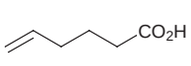
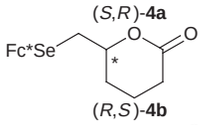
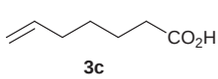
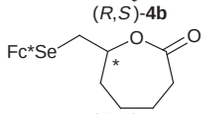
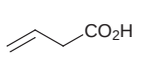
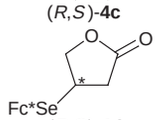
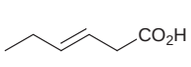
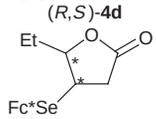
Scheme 1

Table 1 Cyclisation of pent-4-enoic acid (**3a**) using various (*R*,*S*)-Fc*SeX [(*R*,*S*)-**2**]

Entry	Additive	X		*T*/°C (*t*/h)	Yield (%)[a]	De (%)[b]
1	none	Br	(*R*,*S*)-**2a**	−78 (1)→rt (20)	0	—
2	Et_3N	Br	(*R*,*S*)-**2a**	−78 (1)→rt (20)	47	96
3	Et_3N	Br	(*R*,*S*)-**2a**	0 (1)→rt (20)	91	85
4	AgOTf	OTf	(*R*,*S*)-**2b**	−78 (1)→rt (20)	76	96
5	$AgBF_4$	BF_4	(*R*,*S*)-**2c**	−78 (1)→rt (20)	84	92
6	$AgPF_6$	PF_6	(*R*,*S*)-**2d**	−78 (1)→rt (20)	91[c]	97

[a] Measured by ^{1}H NMR of the crude product. [b] Measured by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group of the crude product. [c] Isolated yield.

Table 2 Cyclisation of alkenoic acids using (*R*,*S*)-Fc*$SePF_6$ [(*R*,*S*)-**2d**][a]

Entry	Substrate **3**	Product **4**	Yield (%)[b]	De (%)[c]
1	 **3a**	 (*R*,*S*)-**4a**	91[d]	97
2[e]	 **3a**	 (*S*,*R*)-**4a**	77[d,e]	95
3	 **3b**	 (*R*,*S*)-**4b**	87	89
4	 **3c**	 (*R*,*S*)-**4c**	46	15
5	 **3d**	 (*R*,*S*)-**4d**	76	33
6	 **3e**	 (*R*,*S*)-**4e**	93	95

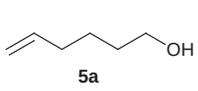
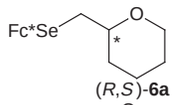
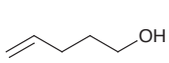
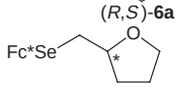
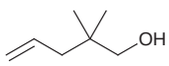
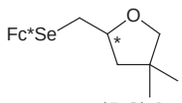
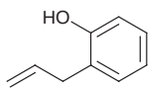
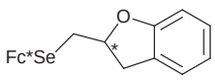
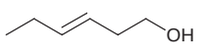
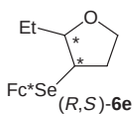
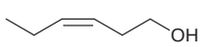
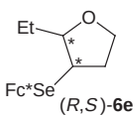
[a] All reactions were performed in CH_2Cl_2 at −78 °C for 1 h and then at 25 °C for 20 h. [b] Measured by ^{1}H NMR. [c] Measured by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group of the crude product. [d] Isolated yield. [e] (*S*,*R*)-**2d** was employed.

isolated by column chromatography (Al_2O_3) in a moderate chemical yield with an excellent diastereoselectivity. The diastereomeric excess of (*R*,*S*)-**4a** was determined by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group in its crude product. When the reaction was carried out at 0 °C for 1 h and then at room temperature for 20 h, (*R*,*S*)-**4a** was obtained in a higher chemical yield (91%) with a reasonable diastereoselectivity (85% de). It has been known that the nature of counter anions of the electrophilic selenenylating agents affected profoundly the diastereoselectivity of selenocyclisation.[7a,c] Actually, when the cation was converted to triflate **2b**, tetrafluoroborate **2c** and hexafluorophosphate **2d** by the addition of the corresponding silver salt, the product yield increased considerably while keeping the selectivity quite high (Table 1). Thus, the optimal conditions were revealed to be the use of (*R*,*S*)-Fc*$SePF_6$ [(*R*,*S*)-**2d**] as an electrophilic reagent under stirring at −78 °C for 1 h and then at room temperature for 20 h in CH_2Cl_2. Typical results of cyclisation of a variey of alkenoic acids **3a**–**e** with (*R*,*S*)-Fc*$SePF_6$ under these conditions are summarised in Table 2. The use of the corresponding enantiomeric (*S*,*R*)-ferrocenylselenenyl bromide derived *in situ* from **1b** and bromine resulted in the formation of the expected (*S*,*R*)-**4a** in a high chemical isolated yield (77%) with an excellent diastereoselectivity (95% de). In the cases of **3a** and **3b** where the product was the five-membered ring lactone (*R*,*S*)-**4a** and the six-membered ring lactone (*R*,*S*)-**4b**, respectively, both chemical yields and the diastereoselectivities were high. However, in the case of **3c** where the product was the seven-membered ring product (*R*,*S*)-**4c**, the diastereoselectivity was lower. The intramolecular selenocyclisation of vinylacetic acid **3d** afforded the five-membered ring lactone (*R*,*S*)-**4d** with a low stereoselectivity (33% de). In contrast, *trans*-hex-3-enoic acid **3e** underwent selenocyclisation to give a similar five-membered ring lactone (*R*,*S*)-**4e** almost quantitatively with an excellent stereoselectivity (95% de). The exact reason for these discrepancies is not yet known.

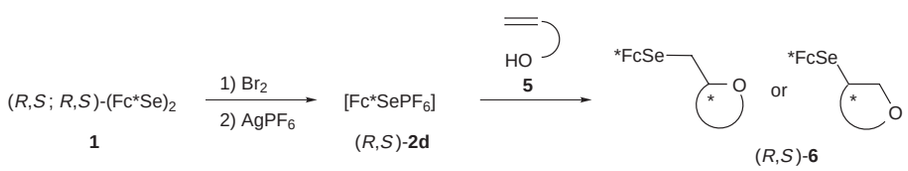
Intramolecular cyclic etherification of alkenols **5a**–**f** with (*R*,*S*)-Fc*$SePF_6$ [(*R*,*S*)-**2d**] proceeded smoothly to provide the corresponding cyclic products (*R*,*S*)-**6a**–**e** in good isolated yields (Scheme 2). In the case of various monosubstituted alkenols, the diastereoselectivity of the corresponding five-membered ring ether was higher than that of the six-membered ring product (Table 3; entries 2 and 3 *vs.* entry 1). Treatment of **5b** with (*S*,*R*)-**2d** also gave (*S*,*R*)-**6b** almost quantitatively with 98% de. The diastereoselectivity of cyclisation of *o*-allylphenol (**5d**) was low. The asymmetric intramolecular selenoetherification of disubstituted alkenol, *trans*-hex-3-enol (**5e**), showed a higher stereoselectivity (95% de), while in the case of *cis*-hex-3-enol (**5f**) the diastereoselectivity was lower (Table 3; entries 5 and 6).

The nature of the counter anion (X) of Fc*SeX had a remarkable effect on the success of the asymmetric intramolecular selenocyclisation of *N*-ethoxycarbonylpent-4-enylamine (**7a**) (Scheme 3). Thus, the reaction did not occur with

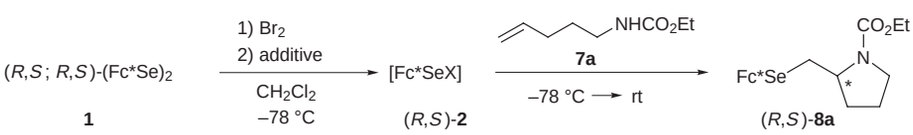
Table 3 Cyclisation of alkenols using (*R*,*S*)-Fc*SePF$_6$ [(*R*,*S*)-**2d**][a]

Entry	Substrate **5**	Product **6**	Yield (%)[b]	De (%)[c]
1	 **5a**	 (*R*,*S*)-**6a**	96	66
2	 **5b**	 (*R*,*S*)-**6b**	97	98
3	 **5c**	 (*R*,*S*)-**6c**	95	89
4	 **5d**	 (*R*,*S*)-**6d**	87	22
5	 **5e**	 (*R*,*S*)-**6e**	89	95
6	 **5f**	 (*R*,*S*)-**6e**	83[d]	34

[a] All reactions were performed in CH_2Cl_2 at −78 °C for 1 h and then at 25 °C for 4 h. [b] Isolated yield. [c] Measured by ^{1}H NMR integration. [d] The reaction was performed at −78 °C for 1 h and then at 25 °C for 20 h.



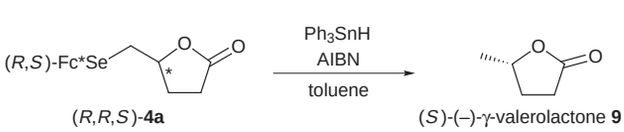
Scheme 2



Scheme 3

(*R*,*S*)-Fc*SeBr [(*R*,*S*)-**2a**], but it proceeded with (*R*,*S*)-Fc*SePF$_6$ [(*R*,*S*)-**2d**] to give a pyrrolidine derivative (*R*,*S*)-**8a** with moderate diastereoselectivity (68% de). Furthermore, the selectivity was revealed to be quite high (97% de) when (*R*,*S*)-Fc*SeBF$_4$ [(*R*,*S*)-**2c**] was used in place of **2d** (Table 4; entry 4 *vs.* entry 5). The results of the reactions of several other alkenyl urethanes to give pyrrolidine and piperidine derivatives are summarised in Table 5. The tendency of the diastereoselectivity in the intramolecular selenocyclisation of a variety of alkenyl urethanes was not very different from that of asymmetric selenoesterification (Table 2) and selenoetherification (Table 3).

Reductive cleavage of the chiral ferrocenylselenium moiety of (*R*,*S*)-**4a** with Ph_3SnH in toluene afforded the optically active lactone **9** which was revealed to have *S* configuration at the chiral γ-carbon by measurement of the optical rotation (Scheme 4).[19,20] This means that the absolute configuration of **4a** is (*R*,*R*,*S*) where the first *R* shows the absolute configuration



Scheme 4

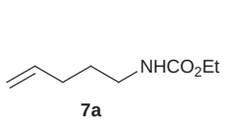
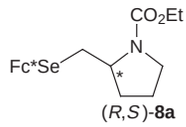
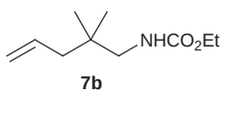
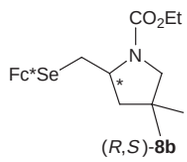
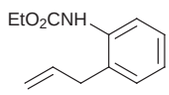
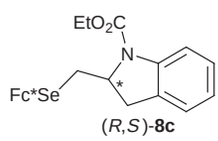
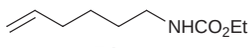
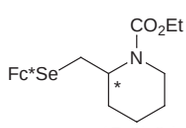
Table 4 Cyclisation of alkenyl urethane **7a** using various Fc*SeX [(*R*,*S*)-**2**]

Entry	Additive	X		*T*/°C (*t*/h)	Yield (%)[a]	De (%)[b]
1	none	Br	(*R*,*S*)-**2a**	−78 (1)→rt (20)	0	—
2	Et_3N	Br	(*R*,*S*)-**2a**	−78 (1)→rt (20)	trace	—
3	AgOTf	OTf	(*R*,*S*)-**2b**	−78 (1)→rt (20)	63	15
4	$AgBF_4$	BF_4	(*R*,*S*)-**2c**	−78 (1)→rt (20)	67	97
5	$AgPF_6$	PF_6	(*R*,*S*)-**2d**	−78 (1)→rt (20)	59	68

[a] Measured by ^{1}H NMR. [b] Measured by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group of the crude product.

at the γ-carbon of the lactone ring and the following *R*,*S* is of the ferrocenylselenium moiety; thus, that of (*S*,*R*)-**4a** should be (*S*,*S*,*R*) where the first *S* shows the absolute configuration at the γ-carbon of the lactone ring. Therefore, this diastereoselective reaction seems to proceed as shown in Fig. 1: a chiral (*R*,*S*)-ferrocenylselenenyl hexafluorophosphate [(*R*,*S*)-**2d**] approaches the C=C moiety of **3a** from the less sterically-congested direction (main approach) to afford a chiral episelenonium ion (**10**) in which an intramolecular back side attack of the carboxylate

Table 5 Cyclisation of alkenyl urethanes **7** using (*R*,*S*)-Fc*SeBF$_4$ [(*R*,*S*)-**2c**][a]

Entry	Substrate **7**	Product **8**	Yield (%)[b]	De (%)[c]
1	 **7a**	 (*R*,*S*)-**8a**	67	97
2	 **7b**	 (*R*,*S*)-**8b**	72	56
3	 **7c**	 (*R*,*S*)-**8c**	66	31
4	 **7d**	 (*R*,*S*)-**8d**	70	85

[a] All reactions were performed in CH_2Cl_2 at −78 °C for 1 h and then at 25 °C for 20 h. [b] Measured by ^{1}H NMR. [c] Measured by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group of the crude product.

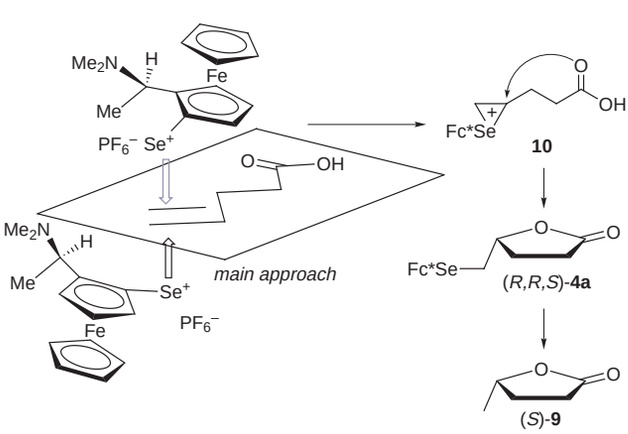


Fig. 1 Plausible scheme for the approach of chiral Se species.

anion occurs to afford the product (*R*,*R*,*S*)-**4a**. The method presented here might be useful for preparing optically active heterocyclic compounds such as lactones, cyclic ethers, piperidines and pyrrolidines.

Experimental

General

^{1}H and ^{13}C NMR spectra were measured on JEOL EX-400, JEOL AL-300 and JEOL JNM-GSX270 spectrometers for solutions in $CDCl_3$ with Me_4Si as an internal standard: the following abbreviations are used; s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. *J* values are measured in Hz. IR spectra were recorded with a Nicolet Impact 400D FT-IR spectrometer. Low-resolution mass spectra (LRMS) and high-resolution mass spectra (HRMS) were obtained with a JEOL JMS-SX102A spectrometer. Analytical thin layer chromatography (TLC) was performed with silica gel 60 Merck F-254 plates. Column chromatography on silica gel or alumina gel was performed with Wakogel C-300 or ICN Alumina N, Akt. I, respectively. Elemental analyses were performed at the Microanalytical Center of Kyoto University. Dichloromethane was distilled from CaH_2 just before use. (*R*)-(+)-*N*,*N*-Dimethyl-1-ferrocenylethylamine and (*S*)-(−)-*N*,*N*-dimethyl-1-ferrocenylethylamine were commercially available, but they were prepared by the reported method on a large scale.[21] Silver triflate, silver tetrafluoroborate, pent-4-enoic acid (**3a**), *cis*-hex-3-en-1-ol (**5f**) and *N*-allylaniline were purchased from Wako Pure Chemical Industries. Silver hexafluorophosphate, hex-5-enoic acid (**3b**), hex-3-enoic acid (**3e**), hex-5-en-1-ol (**5a**), pent-4-en-1-ol (**5b**) and 2-allylphenol (**5d**) were purchased from Tokyo Chemical Industry Co. Vinylacetic acid (**3d**) was purchased from Aldrich Chemical Co. Hept-6-enoic acid (**3c**) and *trans*-hex-3-en-1-ol (**5e**) were purchased from Nacalai tesque. Alkenol **5c** was prepared by the reduction of 2,2-dimethylpent-4-enal[22] with sodium borohydride. Alkenyl urethane **7a** was prepared by treatment of pent-4-enylamine[23] with ethyl chloroformate. Similarly, alkenyl urethanes **7b** and **7d** were also prepared from 2,2-dimethylpent-4-enylamine[23,24] and hex-5-enylamine,[23,24] respectively, which were synthesized from the corresponding commercial alkenol in an analogous manner to pent-4-enylamine. Alkenyl urethane **7c** was prepared from 2-allylaniline[23] by a similar method.

2,2-Dimethylpent-4-en-1-ol 5c. A colourless oil; 87% yield; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.89 (6 H, s, 2 × Me), 2.02 (2 H, d, *J* 7.7, CH_2), 3.33 (2 H, s, CH_2OH), 5.05 (2 H, dd, *J* 1.1 and 12.9, CH_2=CH) and 5.83 (1 H, ddd, *J* 1.1, 7.7 and 12.9, CH_2=C*H*).

***N*-Ethoxycarbonylpent-4-enylamine 7a.**[17c] A colourless oil; 77% yield; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.24 (3 H, t, *J* 7.3, CH_2CH_3), 1.40–1.56 (2 H, m, CH_2), 1.94–2.24 (2 H, m, CH_2), 3.19 (2 H, m, CH_2CH_3), 4.11 (2 H, q, *J* 7.3, CH_2CH_3), 4.67 (1 H, br, NH), 5.00–5.08 (2 H, m, CH_2=CH) and 5.73–5.88 (1 H, m, CH_2=C*H*).

***N*-Ethoxycarbonyl-2,2-dimethylpent-4-enylamine 7b.** A colourless oil; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.07 (6 H, s, CMe_2), 1.23 (3 H, t, *J* 7.3 Hz, CH_2CH_3), 1.41–1.56 (2 H, m, CH_2), 1.94–2.24 (2 H, m, CH_2), 3.19 (2 H, m, CH_2), 4.13 (2 H, q, *J* 7.3,

CH_2CH_3), 4.67 (1 H, br, NH), 5.01–5.08 (2 H, m, CH_2=CH) and 5.74–5.88 (1 H, m, CH_2=CH).

***N*-Ethoxycarbonyl-2-allylaniline 7c.** A white solid; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.27 (3 H, t, *J* 7.3, CH_2CH_3), 3.35 (2 H, d, *J* 5.9, CH_2=CH–CH_2), 4.20 (2 H, q, *J* 7.3, CH_2CH_3), 5.01–5.18 (2 H, m, CH_2=CH), 5.87–6.02 (1 H, m, CH_2=CH), 6.60 (1 H, br, NH), 7.02–7.28 (3 H, m, Ar) and 7.76–7.79 (1 H, m, Ar).

***N*-Ethoxycarbonylhex-5-enylamine 7d.** A colourless oil; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.24 (3 H, t, *J* 7.3, CH_2CH_3), 1.38–1.54 (4 H, m, 2 × CH_2), 2.06 (2 H, q, *J* 7.0, CH_2), 3.16 (2 H, m, CH_2), 4.11 (2 H, q, *J* 7.3, CH_2CH_3), 4.67 (1 H, br, NH), 4.96–5.05 (2 H, m, CH_2=CH) and 5.71–5.87 (1 H, m, CH_2=CH).

General procedure for asymmetric intramolecular selenocyclisation

To a CH_2Cl_2 solution (2.0 mL) of (*R*,*S*)-**1a** (100.3 mg, 0.15 mmol) was added a 1.0 M CH_2Cl_2 solution of bromine (0.15 mL) dropwise at −78 °C under nitrogen to afford a ferrocenylselenenyl bromide. After 15 min stirring, a CH_2Cl_2 solution (1.0 mL) of silver hexafluorophosphate (75.5 mg, 0.30 mmol) was added. The resulting heterogeneous solution of ferrocenylselenenyl hexafluorophosphate was stirred at −78 °C for 15 min. Then a CH_2Cl_2 solution (1.0 mL) of pent-4-enoic acid (**3a**) (30.1 mg, 0.30 mmol) was added at −78 °C. The resulting mixture was stirred at −78 °C for 1 h and then at room temperature for 20 h. It was quenched with aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were dried over K_2CO_3 and evaporated under vacuum to give the crude product as a dark brown oil. The NMR spectrum of the crude product showed it to be a diastereomeric mixture and its ratio was determined by comparison of the respective methyl singlets of the NMe_2 group. Subsequent purification by silica gel column chromatography (hexane–AcOEt–Et_3N = 7:1:1 as eluent) gave the corresponding ferrocenylselenium-containing lactone **4a** as a brown oil. Repeated purification by alumina column chromatography (hexane–AcOEt–Et_3N = 7:1:1 as eluent) afforded pure **4a**, which was used for various analyses. The yield shown in Tables 1, 2, 4 and 5 was measured by ^1H NMR of the crude product after one short column chromatographic purification which contains a small amount of the starting diselenide **1**.

4-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}butan-4-olide 4a. A brown oil; 91% yield (Found: C, 52.01; H, 5.68; N, 3.26. $C_{19}H_{25}FeNO_2Se$ requires C, 52.56; H, 5.80; N, 3.23%); ν_{max}/cm^{-1} 2967, 2933, 1735, 1170, 1091, 1033 and 927; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.29 (3 H, d, *J* 6.6, Me), 1.79–1.87 (1 H, m, C*H*H), 1.98–2.11 (1 H, m, CH*H*), 2.11 (6 H, s, NMe_2), 2.46–2.53 (2 H, m, CH_2), 2.88 (1 H, dd, *J* 4.8 and 12.2, SeC*H*H), 3.10 (1 H, dd, *J* 8.3 and 12.2, SeCH*H*), 3.98 (1 H, q, *J* 6.6, CH), 4.09 (5 H, s, Fc), 4.20 (2 H, s, Fc), 4.35 (1 H, s, Fc) and 4.69 (1 H, m, OCH); *m*/*z* (FAB HRMS) 435.0385 (M^+, $C_{19}H_{25}FeNO_2Se$ requires 435.0402); *m*/*z* (FAB LRMS) 435 (M^+).

5-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}pentan-5-olide 4b. A brown oil; 77% yield; ν_{max}/cm^{-1} 2969, 2936, 1736 (C=O), 1242, 1170, 1092, 1030 and 927; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.30 (3 H, d, *J* 6.9, Me), 1.48–1.87 (2 H, m, CH_2), 2.04–2.15 (2 H, m, CH_2), 2.10 (6 H, s, NMe_2), 2.37–2.54 (2 H, m, CH_2), 2.90 (1 H, dd, *J* 5.4 and 12.5, SeC*H*H), 3.02 (1 H, dd, *J* 7.8 and 12.5, SeCH*H*), 3.98 (1 H, q, *J* 6.9, CH), 4.09 (5 H, s, Fc), 4.20 (2 H, s, Fc), 4.35 (1 H, s, Fc) and 4.43 (1 H, m, OCH); *m*/*z* (FAB HRMS) 449.0575 (M^+, $C_{20}H_{27}FeNO_2Se$ requires 449.0558); *m*/*z* (FAB LRMS) 449 (M^+).

6-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}hexan-6-olide 4c. A brown oil; 13% yield; ν_{max}/cm^{-1} 2963, 2931, 1736 (C=O), 1170, 1088 and 928; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.32 (3 H, d, *J* 6.9, Me), 1.49–1.66 (4 H, m, 2 × CH_2), 2.04–2.15 (2 H, m, CH_2), 2.10 (6 H, s, NMe_2), 2.26–2.33 (2 H, m, CH_2), 2.80 (1 H, dd, *J* 5.5 and 11.9, SeC*H*H), 2.93 (1H, dd, *J* 6.2 and 11.9, SeCH*H*), 3.99 (1 H, q, *J* 6.9, CH), 4.08 (5 H, s, Fc), 4.18 (3 H, br, Fc) and 4.30 (1 H, m, OCH); FAB LRMS (*m*/*z*) 463 (M^+); *m*/*z* (FAB HRMS) 463.0693 (M^+, $C_{21}H_{29}FeNO_2Se$ requires 463.0715); *m*/*z* (FAB LRMS) 463 (M^+).

3-{2-[1-(Dimethylamino)ethyl]ferrocenylseleno}butan-4-olide 4d. A brown oil; 7% yield; ν_{max}/cm^{-1} 2969, 2931, 1734 (C=O), 1171, 1088 and 931; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.35 (3 H, d, *J* 6.9, Me), 1.83–1.88 (2 H, m, CH_2), 2.13 (6 H, s, NMe_2), 2.62 (1 H, m, SeCH), 3.75 (2 H, m, OCH_2), 3.88 (1 H, q, *J* 6.9, CH), 4.09 (5 H, s, Fc), 4.20 (2 H, m, Fc) and 4.34 (1 H, m, Fc); *m*/*z* (FAB HRMS) 421.0237 (M^+, $C_{18}H_{23}FeNO_2Se$ requires 421.0243); *m*/*z* (FAB LRMS) 421 (M^+).

3-{2-[1-(Dimethylamino)ethyl]ferrocenylseleno}-4-ethylbutan-4-olide 4e. A brown oil; 9% yield; ν_{max}/cm^{-1} 2971, 2931, 2852, 2814, 2772, 1736 (C=O), 1106, 1092, 1055 and 928; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.94 (3 H, t, *J* 7.3, Me), 1.32 (3 H, d, *J* 6.9, Me), 2.04–2.15 (2 H, m, CH_2), 2.11 (6 H, s, NMe_2), 2.26–2.33 (2 H, m, CH_2), 2.59 (1 H, m, SeCH), 3.99 (1 H, q, *J* 6.9, CH), 4.08 (5 H, s, Fc), 4.20 (2 H, s, Fc), 4.33 (1 H, s, Fc) and 4.33–4.35 (1 H, m, OCH); *m*/*z* (FAB HRMS) 449.0550 (M^+, $C_{20}H_{27}FeNO_2Se$ requires 449.0556); *m*/*z* (FAB LRMS) 449 (M^+).

2-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}tetrahydropyran 6a. A brown oil; 96% yield (Found: C, 54.76; H, 6.68; N, 3.23. $C_{20}H_{29}FeNOSe$ requires C, 55.32; H, 6.73; N, 3.23%); ν_{max}/cm^{-1} 2968, 2933, 2873, 2855, 2816, 2773, 1092 and 927; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.27 (2 H, br, CH_2), 1.34 (3 H, d, *J* 6.8, Me), 1.45–1.54 (1 H, m, CH*H*), 1.49 (2 H, br, CH_2), 1.72–1.78 (1 H, m, C*H*H), 2.10 (6 H, s, NMe_2), 2.72–2.93 (2 H, m, *J* 6.6 and 17.3, $SeCH_2$), 3.41 (2 H, m, OCH_2), 3.91–3.99 (1 H, m, OCH), 3.95 (1 H, q, *J* 6.8, CH), 4.08 (5 H, s, Fc), 4.18 (2 H, s, Fc) and 4.35 (1 H, s, Fc); *m*/*z* (FAB HRMS) 435.0770 (M^+, $C_{20}H_{29}FeNOSe$ requires 435.0766); *m*/*z* (FAB LRMS) 435 (M^+).

2-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}tetrahydrofuran 6b. A brown oil; 97% yield (Found: C, 54.70; H, 6.52; N, 3.31. $C_{19}H_{27}FeNOSe$ requires C, 54.31; H, 6.48; N, 3.33%); ν_{max}/cm^{-1} 2969, 2933, 2856, 2816, 2772, 1106, 1092, 1058, 926 and 820; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.37 (3 H, d, *J* 6.8, Me), 1.47–1.67 (2 H, m, CH_2), 1.84–2.08 (2 H, m, CH_2), 2.13 (6 H, s, NMe_2), 2.72–2.99 (2 H, m, $SeCH_2$), 3.74 (1 H, dd, *J* 7.3 and 7.3, OC*H*H), 3.88 (1 H, dd, *J* 7.3 and 7.3, OCH*H*), 3.98 (1 H, q, *J* 6.8, CH), 4.04–4.09 (1 H, m, OCH), 4.09 (5 H, s, Fc), 4.20 (2 H, s, Fc) and 4.37 (1 H, s, Fc); *m*/*z* (FAB HRMS) 421.0607 (M^+, $C_{19}H_{27}FeNOSe$ requires 421.0609); *m*/*z* (FAB LRMS) 421 (M^+).

2-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}-4,4-dimethyltetrahydropyran 6c. A brown oil; 95% yield (Found: C, 56.20; H, 6.96; N, 3.11. $C_{21}H_{31}FeNOSe$ requires C, 56.27; H, 6.97; N, 3.12%); ν_{max}/cm^{-1} 2959, 2931, 2867, 2816, 2772, 1106, 1091, 1050, 1001 and 819; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.06 (6 H, s, CMe_2), 1.34 (3 H, d, *J* 6.8, Me), 1.33 (1 H, dd, *J* 6.8 and 12.2, C*H*H), 1.80 (1 H, dd, *J* 6.8 and 12.2, CH*H*), 2.10 (6 H, s, NMe_2), 2.89 (2 H, dd, *J* 6.6 and 17.3, $SeCH_2$), 3.45 (1 H, d, *J* 8.1, OC*H*H), 3.53 (1 H, d, *J* 8.1, OCH*H*), 3.95 (1 H, q, *J* 6.8, CH), 4.08 (5 H, s, Fc), 4.08–4.22 (1 H, m, OCH), 4.18 (2 H, s, Fc) and 4.35 (1 H, s, Fc); *m*/*z* (FAB HRMS) 449.0929 (M^+, $C_{21}H_{31}FeNOSe$ requires 449.0992); *m*/*z* (FAB LRMS) 449 (M^+).

2-{2-[1-(Dimethylamino)ethyl]ferrocenylselenomethyl}tetrahydrobenzofuran 6d. A brown oil; 87% yield; ν_{max}/cm^{-1} 2969,

2931, 2816, 2772, 1597, 1480, 1462, 1229, 1092, 927, 820 and 749; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.32 (3 H, d, *J* 6.8, Me), 2.11 (6 H, s, NMe_2), 2.83–3.15 (2 H, m, CH_2), 3.20–3.39 (2 H, m, $SeCH_2$), 4.00 (1 H, q, *J* 6.8, CH), 4.09 (5 H, s, Fc), 4.31 (3 H, br s, Fc) and 4.90 (1 H, m, OCH), 6.71–6.83 (2 H, m, Ar) and 7.04–7.24 (2 H, m, Ar); *m*/*z* (FAB HRMS) 469.0602 (M^+, $C_{23}H_{27}FeNOSe$ requires 469.0609); *m*/*z* (FAB LRMS) 469 (M^+).

3-{2-[1-(Dimethylamino)ethyl]ferrocenylseleno}-2-ethyltetrahydrofuran 6e. A brown oil; 89% yield; ν_{max}/cm^{-1} 2968, 2933, 2872, 2854, 2815, 2773, 1092 and 927; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.83 (3 H, t, *J* 7.3, Me), 1.30 (3 H, d, *J* 6.8, Me), 1.43–1.52 (2 H, m, CH_2), 1.90–1.96 (1 H, m, C*H*H), 2.02–2.10 (1 H, m, CH*H*), 2.11 (6 H, s, NMe_2), 2.21–2.27 (1 H, m, SeCH), 3.76–3.86 (2 H, m, OCH_2), 3.76–3.86 (1 H, m, OCH), 3.99 (1 H, q, *J* 6.8, CH), 4.09 (5 H, s, Fc), 4.21 (2 H, s, Fc) and 4.34 (1 H, s, Fc); *m*/*z* (FAB HRMS) 435.0771 (M^+, $C_{20}H_{29}FeNOSe$ requires 435.0766); *m*/*z* (FAB LRMS) 435 (M^+).

***N*-Ethoxycarbonyl-2-{2-[1-(dimethylamino)ethyl]ferrocenylselenomethyl}pyrrolidine 8a.** A brown oil; 77% yield (Found: C, 54.20; H, 6.99; N, 4.96. $C_{22}H_{32}FeN_2O_2Se$ requires C, 54.67; H, 6.78; N, 5.54%); ν_{max}/cm^{-1} 2966, 1729 (C=O), 1167 and 1090; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.28 (3 H, t, *J* 7.3, Me), 1.23 (2 H, m, CH_2), 1.33 (3 H, d, *J* 6.9, Me), 1.73–1.84 (2 H, m, CH_2), 2.10 (6 H, s, NMe_2), 2.76–2.99 (2 H, m, $SeCH_2$), 3.99 (1 H, q, *J* 6.9, CH), 4.08 (5 H, s, Fc), 4.18 (3 H, br, Fc), 4.18 (2 H, q, *J* 7.3, CH_2 of Et group) and 4.30 (3 H, m); *m*/*z* (FAB HRMS) 492.0972 (M^+, $C_{22}H_{32}FeN_2O_2Se$ requires 492.0981); *m*/*z* (FAB LRMS) 492 (M^+).

***N*-Ethoxycarbonyl-2-{2-[1-(dimethylamino)ethyl]ferrocenylselenomethyl}-4,4-dimethylpyrrolidine 8b.** A brown oil; 3% yield; ν_{max}/cm^{-1} 2968, 1722 (C=O), 1090 and 933; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.05 (6 H, s, 2 × Me), 1.28 (3 H, t, *J* 7.3, Me), 1.32 (3 H, d, *J* 6.9, Me), 1.76–1.87 (2 H, m, CH_2), 2.12 (6 H, s, NMe_2), 2.75–3.03 (2 H, m, $SeCH_2$), 3.99 (1 H, q, *J* 6.9, CH), 4.08 (5 H, s, Fc), 4.18 (3 H, br, Fc), 4.20 (2 H, q, *J* 7.3, CH_2) and 4.20 (3 H containing CH_2 of Et group, m); *m*/*z* (FAB LRMS) 520 (M^+).

***N*-Ethoxycarbonyl-2,3-dihydro-2-{2-[1-(dimethylamino)ethyl]ferrocenylselenomethyl}indole 8c.** A brown oil; 3% yield; ν_{max}/cm^{-1} 2969, 1724 (C=O), 1090 and 932; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.06 (3 H, t, *J* 7.3, Me), 1.32 (3 H, d, *J* 6.8, Me), 2.13 (6 H, s, NMe_2), 2.56–3.11 (2 H, m, CH_2), 3.18–3.38 (2 H, m, $SeCH_2$), 4.00 (1 H, q, *J* 6.8, CH), 4.08 (5 H, s, Fc), 4.20 (3 H containing CH_2 of Et group, m), 4.31 (3 H, br s, Fc), 6.70–6.83 (2 H, m, Ar) and 7.04–7.27 (2 H, m, Ar); *m*/*z* (FAB HRMS) 504.0998 (M^+, $C_{26}H_{32}FeN_2O_2Se$ requires 504.0991); *m*/*z* (FAB LRMS) 504 (M^+).

***N*-Ethoxycarbonyl-2-{2-[1-(dimethylamino)ethyl]ferrocenylselenomethyl}piperidine 8d.** A brown oil; 53% yield (Found: C, 53.65; H, 6.68; N, 5.43. $C_{23}H_{34}FeN_2O_2Se$ requires C, 53.78; H, 6.56; N, 5.7%); ν_{max}/cm^{-1} 2968, 2931, 2872, 1721 (C=O), 1092 and 927; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.28 (3 H, t, *J* 7.3, Me), 1.23 (4 H, m, 2 × CH_2), 1.33 (3 H, d, *J* 6.9, Me), 1.73–1.84 (2 H, m, CH_2), 2.10 (6 H, s, NMe_2), 2.76–2.99 (2 H, m, $SeCH_2$), 3.99 (1 H, q, *J* 6.9, CH), 4.08 (5 H, s, Fc), 4.18 (3 H, br, Fc), 4.18 (2 H, q, *J* 7.3, CH_2 of Et group) and 4.30 (3 H, m); *m*/*z* (FAB LRMS) 506 (M^+).

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18 Here *R* of (*R*,*S*) shows the absolute configuration at the carbon of the 1-(dimethylamino)ethyl moiety, while *S* of (*R*,*S*) shows the configuration around the ferrocene axis.
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