Highly Selective Asymmetric Intramolecular Selenocyclisation

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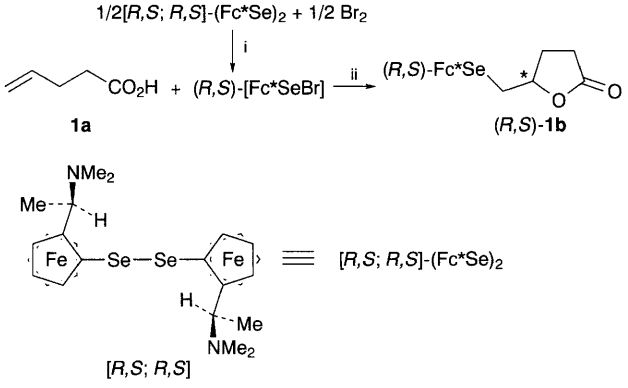
Asymmetric intramolecular selenocyclisation of alkenoic acids, alkenols and olefinic urethanes using chiral ferrocenylselenenyl cations proceeds smoothly to give the corresponding lactones, cyclic ethers and nitrogen-heterocyclic compounds, respectively, in moderate yields with very high diastereoselectivities.

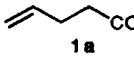
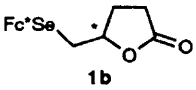
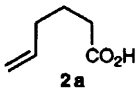
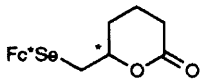
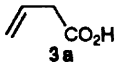
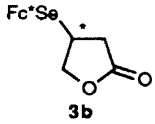
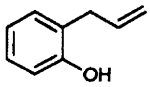
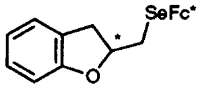
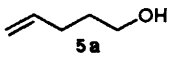
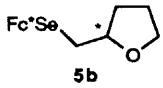
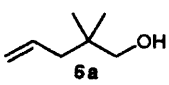
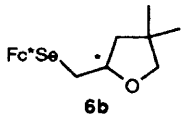
A substantial amount of work concerning asymmetric cyclisations has recently been published in which diastereoselective halocyclisations are especially useful for the synthesis of chiral heterocyclic compounds and for double bond functionalisation.[1,2] However, until very recently, there are no reports‡ on asymmetric intramolecular selenocyclisation, though selenocyclisation itself has been widely used for preparing heterocyclic compounds such as lactones, cyclic ethers, lactams and nitrogen-heterocycles in high yields.[3] Some of us recently succeeded in highly diastereoselective methoxyselenenylation of alkenes using chiral ferrocenylselenenyl bromide[4] prepared *in situ* from chiral diferrocenyl diselenide[5] and bromine. Here we present the preliminary results of asymmetric intramolecular selenocyclisation of alkenoic acids, alkenols and olefinic urethanes by the use of chiral ferrocenylselenenyl cations to afford the corresponding chiral lactones, cyclic ethers and nitrogen-heterocyclic compounds, respectively.[6]



Scheme 1 *Reagents and conditions*: i, CH_2Cl_2, −78 °C; ii, THF

The typical reaction procedure (Scheme 1) is as follows. The chiral [*R*,*S*; *R*,*S*]-diferrocenyl diselenide was converted *in situ* into the chiral (*R*,*S*)-ferrocenylselenenyl bromide by treatment with bromine in CH_2Cl_2 at −78 °C, and the bromide was reacted with pent-4-enoic acid **1a** in the presence of an excess of triethylamine in THF at −78 °C for 1 h and then at room temperature for 20 h with stirring. The product (*R*,*S*)-**1b** was isolated in a high yield with an excellent diastereoselectivity after purification on the alumina preparative TLC. The diastereoisomeric excess of (*R*,*S*)-**1b** was determined by ^{1}H NMR integration of the singlet methyl resonance of the NMe_2 group of the crude product. The reaction did not proceed

Table 1 Asymmetric intramolecular oxyselenenylation[a]

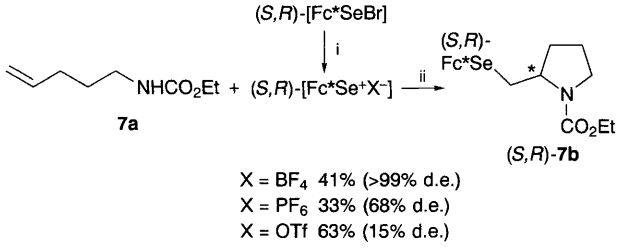
Substrate	$(Fc^*Se)_2$	Additive	*T*/°C (*t*/h)	Product	Yield (%)[b]	de (%)[c]
 **1a**	(*R*,*S*)	—	−78 (1) → room temp. (20)	 **1b**	0	—
	(*R*,*S*)	Et_3N	0 (1) → room temp. (20)		18	0
	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)		70	>95
	(*S*,*R*)	Et_3N	−78 (1) → room temp. (20)		84[d]	>95
 **2a**	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)	 **2b**	46	87
 **3a**	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)	 **3b**	56	34
 **4a**	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)	 **4b**	20	>95
 **5a**	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)	 **5b**	29	76
 **6a**	(*R*,*S*)	Et_3N	−78 (1) → room temp. (20)	 **6b**	55	75

[a] All the reactions were carried out on a 0.15 mmol scale. [b] Isolated yield. [c] The products' de values were determined by ^{1}H NMR. [d] Crude yield.

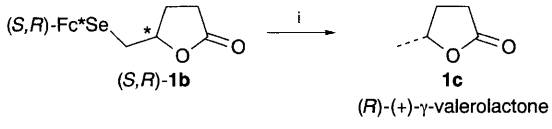
without triethylamine. At a higher reaction temperature (0 °C), (*R*,*S*)-**1b** was obtained in a low yield and as a racemate. The use of the chiral (*S*,*R*)-ferrocenylselenenyl bromide derived *in situ* from [*S*,*R*; *S*,*R*]-diferrocenyl diselenide and bromine resulted in the formation of the expected (*S*,*R*)-**1b** in a high yield with an excellent diastereoselectivity. Typical results are shown in Table 1. Next, we applied this optimum condition to other alkenoic acids **2a** and **3a**. In the case of **2a** affording the six membered-ring lactone (*R*,*S*)-**2b**, its yield was moderate, but the diastereoselectivity was high. However, in the case of **3a**, the diastereoselectivity of the product (*R*,*S*)-**3b** was low. On the other hand, in the case of intramolecular cyclic etherification of the alkenols **4a–6a**, the yields of the expected products (*R*,*S*)-[**4b–6b**] were rather low, but the selectivity was high.

On the other hand, ring cyclisation of olefinic urethanes **7a** did not proceed with (*S*,*R*)-ferrocenylselenenyl bromide. However, when we changed the counter anion from Br^- to BF_4^- using $AgBF_4$, the product **7b** was obtained in a moderate yield with an excellent diastereoselectivity. With PF_6^- and OTf^- (triflate) the selectivity became lower (Scheme 2). These results showed that the counter anion of chiral ferrocenylselenenyl moiety played an important role in the stereoselection of the produced nitrogen-heterocyclic compounds.

Reductive cleavage of the chiral ferrocenylselenium moiety of (*S*,*R*)-**1b** with Ph_3SnH in toluene[7] afforded the lactone **1c** which has *R*-configuration at the chiral centre§ (Scheme 3). Therefore, this diastereoselective reaction seems to proceed as follows: chiral (*S*,*R*)-ferrocenylselenenyl bromide approaches the C=C moiety of the Et_3N salt of **1a** from the less bulky direction to afford a chiral episelenonium ion in which an intramolecular rear attack of the carboxylate anion occurs to afford (*S*,*R*,*S*)-**1b**. This method might be very useful for preparing chiral heterocyclic compounds.



Scheme 2 *Reagents and conditions*: i, AgX, −78 °C, 1 h; ii, CH_2Cl_2, −78 °C for 1 h, then room temp. for 20 h



Scheme 3 *Reagents and conditions*: i, Ph_3SnH, AIBN, toluene

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Footnotes

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‡ Independently, Tomoda *et al.* have clarified a similar asymmetric intramolecular oxyselenenylation using some chiral arylselenium compounds: The 69th Annual Meeting of the Chemical Society of Japan, Kyoto, March 1995, Abstract 2HX37. Quite recently, after submission of our manuscript, Déziel *et al.* published intramolecular asymmetric selenocyclisations using their chiral C_2 symmetrical organoselenium reagent.[8]

§ The isolated yield of (*R*)-**1c** (γ-valerolactone) was low (*ca.* 20%), but its optical rotation observed {$[\alpha]_D$ +25.8 (*c* 0.5, $CHCl_3$)} clearly showed its *R*-configuration.[9]

References

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3 For examples, K. C. Nicolaou, N. A. Petasis and D. A. Claremon, in *Organoselenium Chemistry*, ed. D. Liotta, Wiley, New York, 1987, pp. 127 and references cited therein.

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5 Y. Nishibayashi, J. D. Singh, S. Fukuzawa and S. Uemura, *Tetrahedron Lett.*, 1994, **35**, 3115; Y. Nishibayashi, J. D. Singh, S. Fukuzawa and S. Uemura, *J. Org. Chem.*, 1995, **60**, 4114.

6 We have partly reported the results at the 69th Annual Meeting of the Chemical Society of Japan, Kyoto, March 1995, Abstract 2HX35.

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8 R. Déziel and E. Malenfant, *J. Org. Chem.*, 1995, **60**, 4660.

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