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Synthesis of Chiral Diferrocenyl Diselenides and Their Application to Asymmetric Reactions

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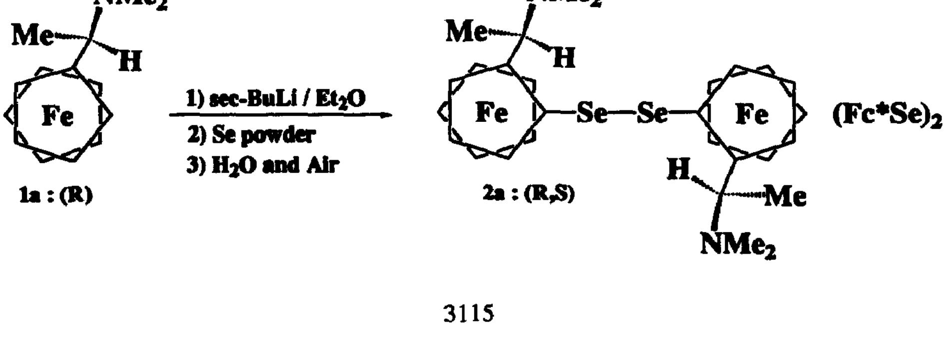
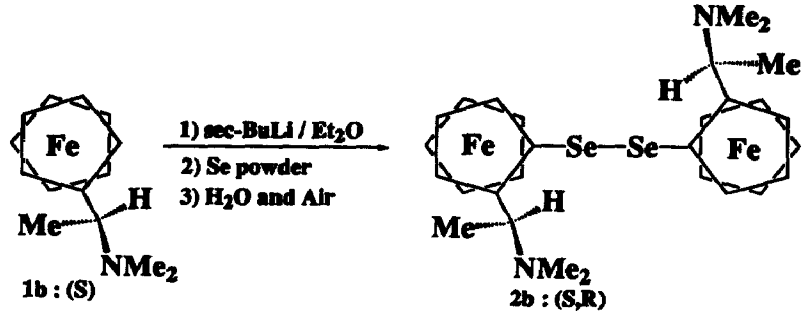
Abstract: Two optically active diferrocenyl diselenides, each of which possesses two chiral centers, were newly prepared from commercial 1-(dimethylamino)ethylferrocenes and applied to induce highly enantioselective selenoxide elimination producing axially chiral allenecarboxylic esters.

Chiral ferrocenyl phosphines are very important compounds in the field of catalytic asymmetric synthesis.[1] Herein, we report the first and facile synthesis of two optically active diferrocenyl diselenides(**2a**,**2b**), each of which possesses two chiral centers, from commercial chiral ferrocenes(**1a**,**1b**) and their application to a highly enantiomeric reaction.

The synthesis of the diselenides **2** was carried out by the following procedure. After lithiation of commercial chiral (R)-(+)-N,N-dimethyl-1-ferrocenylethylamine(**1a**) under N_2, selenium powder was added portionwise and the resulting mixture was stirred for 3 h at 0°C. The mixture was poured into water and then air was bubbled through the solution for 5 h at room temperature. A red solid of (R,S)-diferrocenyl diselenide(**2a**)(mp.98-100°C from hexane) was isolated in 77% yield by column chromatography on active alumina with ethyl acetate as eluent(Scheme I). Similarly, a red solid of (S,R)-diferrocenyl diselenide(**2b**)(mp 103°C from hexane) was prepared in 80% isolated yield from the (S)-(-)-N,N-dimethyl-1-ferrocenylethylamine(**1b**).[2-4]

Scheme I





Since asymmetric induction using organoselenium compounds is of current interest,[5-9] we decided to use these newly prepared diselenides for the enantioselective selenoxide elimination, hoping for a chirality transfer from the chiral ferrocenyl selenoxides to organic products.

When four novel chiral ferrocenyl vinyl selenides(4), prepared in 21-92% yield as yellow solids from 2 and ethyl propiolate derivatives (3), were oxidized with 1 mol equiv. of meta-chloroperbenzoic acid(MCPBA) under various conditions, axially chiral allenecarboxylic esters(5) were produced in moderate chemical yields with high enantioselectivities. The best enantioselectivity (up to 89% ee) was obtained by use of CH_2Cl_2 as solvent at low temperature in the presence of molecular sieves 4A (to remove a trace of water)(Scheme II, Table I).[10,11] With (R,S)- and (S,R)-isomers of 4, R- and S-isomers of 5 were produced, respectively. This is the first example of asymmetric selenoxide elimination leading to chiral allenecarboxylic derivatives which have so far been prepared normally by optical resolution of the corresponding racemic acids.[12]

Scheme II

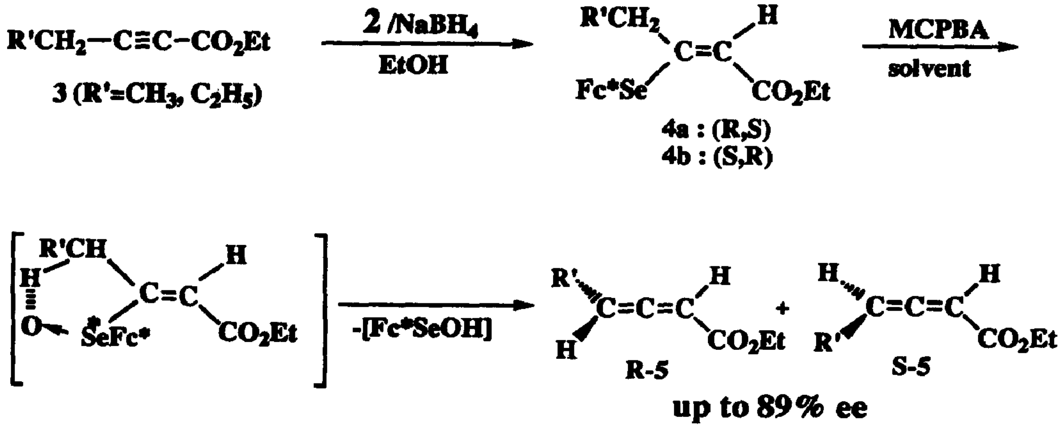


Table I Asymmetric Synthesis of Allenecarboxylic Ester (5) [a]

Run	Substrate	Conditions		Yield[b]	ee[c]	Config.
		solvent	time/h (temp/°C)	(%)	(%)	
1	4a(R'=CH$_3$)	CH$_2$Cl$_2$[d]	1(-78) → 70(-20)	47	83	R
2	4a(R'=C$_2$H$_5$)	CH$_2$Cl$_2$[d]	1(-78) → 70(-20)	38	75	R
3	4b(R'=CH$_3$)	MeOH	19(0)	35	30	S
4	4b(R'=CH$_3$)	CH$_2$Cl$_2$	24(0)	52	39	S
5	4b(R'=CH$_3$)	Et$_2$O	22(0)	21	16	S
6	4b(R'=CH$_3$)	CH$_2$Cl$_2$	1(-78) → 46(-20)	48	70	S
7	4b(R'=CH$_3$)	CH$_2$Cl$_2$[d]	1(-78) → 70(-20)	43	89	S
8	4b(R'=C2H$_5$)	CH$_2$Cl$_2$[d]	1(-78) → 70(-20)	59	82	S

[a] All the reactions were carried out in 0.20 mmol scale.
[b] Isolated yield. [c] Determined by HPLC.
[d] In the presence of molecular sieves 4A (powder).

Reich has reported diastereomeric oxidation (64% de) of (4-methylseleno)[2.2]paracyclophane.[6] When we carried out the MCPBA oxidation of methyl (R,S)-ferrocenyl selenide, prepared from 2a, NaBH$_4$, and MeI, in CD$_3$OD in an NMR tube at room temperature, the formation of the corresponding selenoxide of 72% de was observed.[13] This result together with high ee of the products even for longer reaction time gave a basis of the following speculation in the present asymmetric reactions. (1) The initial oxidation step proceeds highly diastereoselectively; (2) The intermediate chiral selenoxides may be stabilized by the steric, electronic and/or coordination effects of 1-(dimethylamino)ethyl moiety which diminish the racemization of the selenoxides; (3) In the intermediate selenoxides a highly diastereoselective hydrogen abstraction from methylene protons (asymmetric selenoxide elimination) occurs almost without loss of optical purity.

We are making efforts to apply these novel reagents to new types of asymmetric reactions, the results of which will be reported in due course.

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References and Notes

(1) For example : Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 867.

(2) Preliminary result of X-ray crystarography of **2b** comfirmed its (S,R)-configuration. Its full characterization will be reported in due course.

(3) It is known that lithiation of **1a** and **1b** with t-BuLi occurs highly diastereoselectively(>96%).[4] In fact, after seleniation we found the formation of an almost pure diselenide in either case (by ^{1}H-NMR). One recrystallization from hexane afforded a completely pure diselenide (**2a** and **2b**).

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(10) A typical experimental procedure is as follows. To a dry CH_2Cl_2 (1 ml) solution of **4b**(R'=CH_3)(0.20 mmol) containing a small amount of molecular sieves 4A(powder) was added dropwise a dry CH_2Cl_2(1 ml) solution of meta-chloroperbenzoic acid(70% purity; 0.22 mmol) at -78°C under N_2, and the resulting mixture was stirred for 1 h and then at -20°C for 70 h. The mixture was poured into a saturated aqueous NaCl solution(50 ml) and extracted with CH_2Cl_2(30 ml × 3). The extracts were dried over $MgSO_4$ and evaporated to leave a pale yellow semi-solid which was purified by TLC(SiO_2, hexane/EtOAc=9/1 as eluent) to afford (S)-ethyl 2,3-pentadienoate(**5**, R'=CH_3) of 89% ee in 43% chemical yield. The ee value and the configuration of the product were determined by HPLC on a Daicel Chiralcel OJ column and the optical rotation, respectively. The compound **5** obtained from **4a** and **4b** had levo- and dextro-rotation, meaning R and S configuration, respectively.[11]

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(13) In ^{1}H-NMR two signals of the selenoxide methyl groups(Fc*Se(O)$C\underline{H}_3$) appeared at δ 2.67(s) and 2.86(s) ppm in a ratio of 86 : 14 which shows 72% de in the oxidation. The methyl signal of the starting selenide (Fc*Se$C\underline{H}_3$) appeared at δ 2.08 ppm(in $CDCl_3$).

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