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An Asymmetric Nitroolefination of α-Alkyl-γ- and δ-Lactones with Modified Nitroenamines[1]

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Abstract --- New chiral nitroenamines **4a,b** having (*S*)-2-*t*-butyldimethylsiloxymethylpyrrolidine as an auxiliary were found to be very effective for asymmetric nitroolefination of α-alkyl-γ- and δ-lactones. The enantiomeric excess of the product increased remarkably in the reaction with γ-lactones compared with previous nitroenamines **1a,b**. A possible chelation model for the transition state of the asymmetric nitroolefination is discussed.

INTRODUCTION

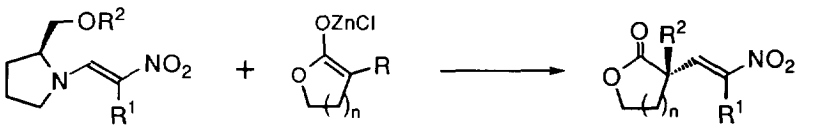
The development of a new method for the construction of an asymmetric quaternary carbon remains to be explored in organic synthesis. Among many methods[2] reported so far, the asymmetric alkylation[3] reaction of chiral enolates is one of the representative methods to give the products with high enantiomeric excesses (ee). Compared to several asymmetric alkylation reactions using chiral nucleophiles (*i.e.* enolates), asymmetric reactions using a chiral electrophile were limited.[4] Addition-elimination reactions using nitroolefins with a chiral leaving group seem to be promising,[5] because a nucleophile is proximal to a chiral leaving group in the transition state. A nitroalkene is a useful synthetic unit, because it can react as a dienophile with dienes (Diels-Alder reaction),[6] a 4π-component with alkenes ([4 + 2] cycloaddition),[7] and a Michael acceptor with nucleophiles,[8] to form carbon-carbon bonds stereoselectively, and also it has a versatile ability for functional group manipulation.[9] Therefore, the development of a method for the preparation of a chiral nitroalkene utilizing an addition-elimination reaction is one of the attractive works.

Recently we have published an asymmetric nitroolefination of α-alkyl lactones through an addition-elimination process using readily available chiral nitroenamines (*e.g.* **1a** and **1b**).[10] In this nitroolefination, (*S*)- or (*R*)-2-methoxymethylpyrrolidine (SMP or RMP) was an excellent auxiliary for the nitroolefination of *δ-lactones*. We applied this methodology to the expeditious asymmetric syntheses of natural products such as *Aspidosperma* and *Hunteria* types indole alkaloids,[11] Calabar bean alkaloids,[12] and diterpenoids.[13] A major drawback of this asymmetric reaction was that the enantioselectivities as well as the yields with *γ-lactones* were low.[10c] Here we reported an improved method for asymmetric nitroolefination reaction with γ-lactones as well as δ-lactones using new chiral nitroenamines **4a,b** having *a bulky substituent* to give high enantioselectivity in excellent chemical yield.

Our major efforts were focused to elucidate the effect of i) bulkiness on OR^2 in the chiral auxiliary, ii) the equivalent of zinc enolate, and iii) the reaction temperature, because the coordination of the three oxygen atoms

included in the chiral nitroenamine **1a** to zinc enolate was postulated under the reaction conditions of the previous asymmetric nitroolefination of γ-lactones.[10c]

Scheme 1



1a R^1 = H, R^2 = Me
1b R^1 = Me, R^2 = Me
2a R^1 = H, R^2 = H
2b R^1 = Me, R^2 = H
3a R^1 = H, R^2 = Tr
3b R^1 = Me, R^2 = Tr
4a R^1 = H, R^2 = TBS
4b R^1 = Me, R^2 = TBS

5a R = Me, n = 1
5b R = Et, n = 1
5c R = allyl, n = 1
6 R = Me, n = 2

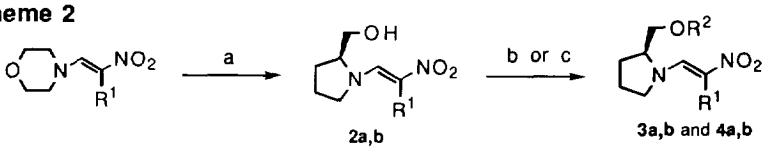
7a R^1 = H, R^2 = Me, n = 1
7b R^1 = H, R^2 = Et, n = 1
7c R^1 = H, R^2 = allyl, n = 1
7d R^1 = Me, R^2 = Me, n = 1
7e R^1 = Me, R^2 = Et, n = 1
7f R^1 = Me, R^2 = allyl, n = 1
8a R^1 = H, R^2 = Me, n = 2
8b R^1 = Me, R^2 = Me, n = 2

(Tr = Trityl, TBS = *t*-Butyldimethylsilyl)

RESULTS

The chiral nitroenamines **2** having hydroxy group were synthesized easily by the transamination reaction[14] from morphorino nitroenamine with (*S*)-prolinol.[15] The nitroenamines **2** were converted into trityl ethers **3** and *t*-butyldimethylsilyl ethers **4** in high yields by tritylation and silylation of the hydroxy group (Scheme 2). Although (*S*)-prolinol prepared from (*S*)-proline by the reduction with lithium aluminum hydride was not enantiomerically pure (> ca. 97 %ee), enantiomerically pure nitroenamines **2-4** could be obtained by recrystallization.

Scheme 2



2a,b **3a,b and 4a,b**

a) (*S*)-prolinol, MeOH reflux b) TrCl, Et_3N, cat. DMAP, CH_2Cl_2 r. t. c) TBSCl, imidazole, CH_2Cl_2 r. t.

The results of asymmetric nitroolefination of α-alkyl-γ-butyrolactones were summarized in Table 1. The reactions were carried out at -78 °C with four equivalents of zinc enolates to a chiral nitroenamine. Tetrahydrofuran (THF) was used as a solvent instead of dimethoxyethane (DME) in case of low solubility of a zinc enolate in DME. The enantioselectivity with nitroenamine **2a** (entry 3) having (*S*)-prolinol as a chiral auxiliary was much improved, compared with the previous nitroenamine **1a** having SMP as a chiral auxiliary (entry 1).[10c] Nitroenamine **4a** (entry 5) gave the best result both in the yield and the ee among new chiral nitroenamines **2a**, **3a**, and **4a**. The alkyl substituents on γ-lactone had little effect on ee (entries 5-7 and 8-10). Introduction of methyl substituent at R^1 in nitroenamine increased ee in 5-13 % (entries 8-10), compared to that

of no alkyl substituent (entries 5-7). In the case of entry 9, the ee of the product ran up to 98 % in a quantitative yield.

Table 1. Asymmetric Nitroolefination of γ-Butyrolactone Enolates [a]

	Nitroenamines			Zinc Enolates				Products		
Entry		R^1	R^2		R	Solvent	Time (h)		Yield (%) [b]	ee (%)
1 [c]	**1a**	H	Me	**5a**	Me	DME	4.5	**7a**	82	56
2 [c]	**1a**	H	Me	**5b**	Et	DME	2.5	**7b**	72	63
3	**2a**	H	H	**5a**	Me	THF	1.0	**7a**	77	83 [d]
4	**3a**	H	Tr	**5a**	Me	THF	1.0	**7a**	75	83 [d]
5	**4a**	H	TBS	**5a**	Me	DME	3.0	**7a**	92	88 [d]
6	**4a**	H	TBS	**5b**	Et	DME	1.0	**7b**	99	85 [e]
7	**4a**	H	TBS	**5c**	Allyl	DME	1.0	**7c**	96	86 [e]
8	**4b**	Me	TBS	**5a**	Me	THF	1.0	**7d**	87	93 [f]
9	**4b**	Me	TBS	**5b**	Et	THF	1.0	**7e**	99	98 [d]
10	**4b**	Me	TBS	**5c**	Allyl	THF	1.0	**7f**	92	95 [g]

a) The reactions were carried out at - 78 °C. b) Isolated yields. c) Taken from ref. 10c. d) HPLC (DAICEL CHIRALPAK AS, *i*-PrOH) analysis. e) HPLC (DAICEL CHIRALCEL OJ, *i*-PrOH) analysis. f) Chiral shift analysis [270 MHz ^{1}H NMR, $CDCl_3$, Eu(hfc)$_3$]. g) HPLC (DAICEL CHIRALPAK AD, EtOH) analysis.

The relationship between chiral nitroenamines and CD spectra of the products in the asymmetric nitroolefination is shown in Table 2. The CD spectra of the products from the reaction of γ-lactones with (*S*)-nitroenamines exhibited the same type of Cotton effect (entries 3-8) as that of the product (-)-**8a** from δ-lactone (entry 2). It can therefore be presumed that the stereochemistry of the products from γ-lactones is *S* configuration.

Table 2. Relationship between Chiral Reagents and CD spectra of the Products

	Chiral Reagents		Products		
Entry	Nitroenamine	Config.		λ_{ext} nm ($\Delta\varepsilon$) [a]	Config.
1	(+)-**4a**	*R*	(+)-**8a**	278 (-0.11)	*R* [b]
2	(-)-**4a**	*S*	(-)-**8a**	283 (+0.12)	*S* [b]
3	(-)-**4a**	*S*	(-)-**7a**	288 (+0.11)	*S*
4	(-)-**4a**	*S*	(-)-**7b**	285 (+0.32)	*S*
5	(-)-**4a**	*S*	(-)-**7c**	290 (+0.25)	*S*
6	(+)-**4b**	*S*	(-)-**7d**	303 (+0.19)	*S*
7	(+)-**4b**	*S*	(-)-**7e**	297 (+0.24)	*S*
8	(+)-**4b**	*S*	(-)-**7f**	298 (+0.16)	*S*

a) Solvent : MeOH b) See ref. 10c.

The results of asymmetric nitroolefination of α-methyl-δ-valerolactone **6** with new chiral nitroenamines were compiled in Table 3. Enantioselectivities of the reaction with **2a** and **2b** (entries 3 and 4) were lower than those with the previous chiral nitroenamines **1a** and **1b**, while **3a,b** and **4a,b** showed higher enantioselectivity (entries 5-8) than those with **1a** and **1b** (entries 1 and 2). The best choice of chiral auxiliary on the reaction of α-methyl-δ-valerolactone was (*S*)-2-*t*-butyldimethylsiloxymethylpyrrolidine to give both the excellent enantioselectivity and the high yield.

Table 3. Asymmetric Nitroolefination of δ-Valerolactone Enolate **6** [a]

	Nitroenamines			Enolate **6**			Products [b]		
Enrty [c]		R^1	R^2	equiv.	Time (h)	Solvent		Yield (%) [d]	ee (%) [e]
1	**1a**	H	Me	3.0	3.0	DME	**8a**	99	86
2	**1b**	Me	Me	3.0 (4.0) [f]	0.3 (1.0) [f]	DME	**8b**	69 (90) [f]	93 (96) [f]
3	**2a**	H	H	4.0	1.0	THF	**8a**	24	79
4	**2b**	Me	H	4.0	2.0	THF	**8b**	35	90
5	**3a**	H	Tr	4.0	1.0	THF	**8a**	66	89
6	**3b**	Me	Tr	4.0	1.0	THF	**8b**	76	97
7 [g]	**4a**	H	TBS	4.0	3.0	DME	**8a**	82	93 [h]
8	**4b**	Me	TBS	4.0	2.0	THF	**8b**	95	99
9 [i]	**1b**	Me	Me	2.0	0.5	THF	**8b**	87	93
10 [i]	**4b**	Me	TBS	2.0	0.5	THF	**8b**	99	95

a) The reaction was carried out at - 78 °C unless otherwise indicated. b) The configuration of the products **8a,b** was *S* (see ref. 10c). c) Entries 1 and 2 were cited from ref. 10c. d) Isolated yield. e) Chiral shift analysis [^{1}H-NMR (270 MHz, $CDCl_3$, $Eu(hfc)_3$)] f) The data in parentheses were results from the reaction using THF as a solvent. g) The reaction mixture was stirred for 2 h at -78 °C and for 1 h at -60 °C. h) HPLC (DAICEL, CHIRALPAK AS, *i*-PrOH) analysis. i) The reaction was carried out with zinc enolate **6** (2 eq.) and the reaction mixture was warmed from -78 °C to -40 °C.

Although more than three equivalents of lactone enolate were essential for giving high chemical yield in this reaction at -78 °C,[10c] we have found that two equivalents were sufficient to obtain the comparable yields when the reaction temperature was raised to -40 °C in the reaction of zinc enolate **6** (entries 9 and 10).

DISCUSSION

From the improved asymmetric nitroolefination reaction we obtained two significant results, 1) two equivalents of zinc enolate were enough to give both high yield and high enantioselectivity, when the temperature was raised to -40 °C, while three equivalents were necessary at -78 °C, and 2) higher enantioselectivities than those with the previous nitroenamines **1a,b** were observed with the new chiral nitroenamines **3a,b** and **4a,b** having a bulkier substituent than the methyl, namely, the steric effect of side chain in the chiral auxiliary was crucial.[16]

A possible equilibrium between activated nitroenamines (I) and (II) involving a complex through zinc is shown in Scheme 3, which may explain the temperature dependence on total amount of zinc enolate. Two equivalents of zinc enolate are consumed by the coordination with the nitroenamine to form the activated

nitroenamine (I) at -78 °C, which is more stable than the activated nitroenamine (II). The third molecule of zinc enolate is required to attack the complex (I) due to the bias of the equilibrium. On the elevated temperature, the rapid equilibrium releases the enolate which can attack the complexes (I) and (II). Thus, the reaction was completed with two equivalents of enolate.

Scheme 3

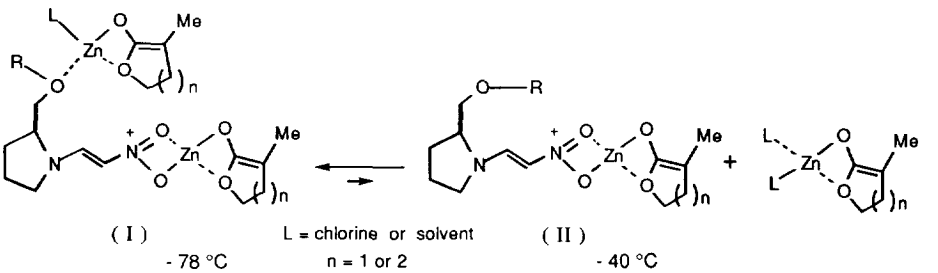
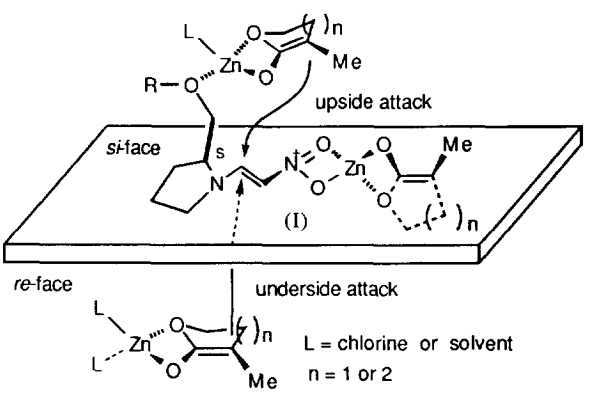


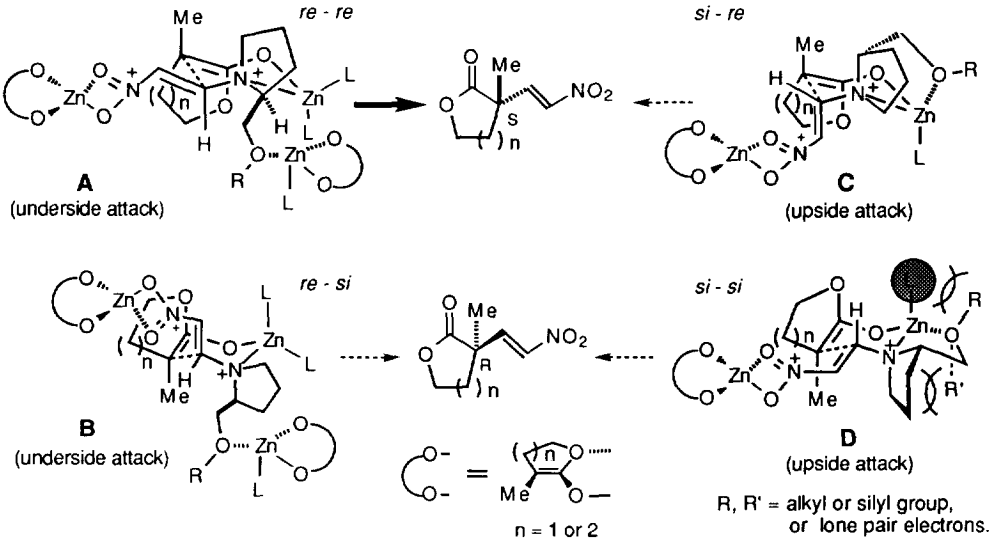
Figure 1 illustrates the approach of enolates to the nitroenamine leading to the four possible transition states **A**-**D** shown in Figure 2. The transition state **A** having an equatorial nitromethylene in chair conformation including zinc chelation is preferred over the transition state **B** having an axial nitromethylene. The transition state **D** is similarly preferred over the transition state **C**. On our previous studies on δ-lactone series using (*S*)-nitroenamine **1a**, the complex model **A** has been considered as transition state to the major product (*S*)-nitroolefin, without taking account of transition states **C** and **D** arising from the approach from the upper side.

Figure 1



Discrimination between transition states **A** and **B** cannot explain a remarkable increase in ee presently observed in the γ-lactone series, since the bulkiness of the side chain on the pyrrolidine cannot create large bias between them. Involvement of the transition state **D** may explain the present findings. It is beyond doubt that the transition state **A** is more stable than **D**. The contribution of transition state **D** might be reduced with increasing steric bulk of the substituent R. A consideration of above transition states is explicable of the high enantioselectivity in the nitroolefination with the nitroenamine **4** having a bulky substituent TBS.

Figure 2



CONCLUSION

We improved the enantioselectivity as well as the yield of *the nitroolefination of γ-lactones* with the new nitroenamines **4** having bulky (*S*)-2-*t*-butyldimethylsiloxymethylpyrrolidine as a chiral auxiliary. On the nitroolefination of δ-lactones, the reactions with the new nitroenamines **4** gave also better results than those with the previous nitroenamines **1**, even though the enantioselectivity and the yield in the previous studies were satisfied. The new nitroenamines **4** have an advantage of preparation in an enantiomerically pure form by recrystallization from inexpensive L-proline. The previous nitroenamines **1** are oily compounds so that we can not obtain them with a 100 % enantiomeric purity.

The participation of the transition state **D** as well as the transition state **A** is important for this asymmetric nitroolefination. The observed *bulky substituent effect* on the chiral auxiliary would be minimized *the upside attack* of zinc enolate coordinated to OR into the nitroenamine moiety in the transition state. Improvement in ee's and yields can expand the utility of asymmetric nitroolefination in enantioselective syntheses of natural products.

ACKNOWLEDGMENT

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EXPERIMENTAL SECTION

General: Melting points are taken with a micro hot-stage apparatus (Yanagimoto) and are uncorrected. The infrared (IR) spectra are recorded with a Shimadzu IR-410 diffraction grating infrared spectrophotometer and ^{1}H-NMR spectra are obtained with a

JEOL JNM-EX-90, JEOL JNM-GX-270, Varian XL-300, or JEOL JNM-GX-400 NMR spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) are determined on a JEOL JMS-01SG or Hitachi M-80 mass spectrometer. The CD spectra were recorded in chloroform with a JASCO J-500C spectrophotometer. The HPLC analyses were performed with a Shimadzu LC-9A Liquid Chromatograph series using Daicel chiral columns (CHIRALCEL OJ, CHIRALPAK AS, or CHIRALPAK AD). Their data were recorded with a Shimadzu C-R6A Chromatopac. Wakogel C-200 (silica gel) (100-200 mesh, Wako) was used for column chromatography unless otherwise noted, and Kieselgel 60 F-254 plates (Merck) for thin layer chromatography (TLC) and preparative TLC (PTLC).

Material: Diisopropylamine was distilled from CaH_2 and THF was distilled from sodium benzophenone ketyl before use. *n*-BuLi (1.6 M hexane solution) was purchased from Wako Pure Chemical Industries, and titrated with *sec*-BuOH using *ortho*-phenanthroline as an indicator before use. Zinc chloride (1.0 M in diethyl ether) was purchased from Aldrich Chemical Company, Inc.

(*E*)-1-[(*S*)-2-Hydroxymethylpyrrolidin-1-yl]-2-nitroethylene (2a) A mixture of morphorino nitroenamine (3.00 g, 19.0 mmol) and L-prolinol (3.00g, 28.5 mmol) in MeOH (100 ml) was refluxed for 3 h under nitrogen atmosphere. After evaporation of the solvent, the residue was purified with silica gel column chromatography (elute: AcOEt) to give (-)-**2a** (3.16 g, 96.6 %). **2a** : yellow crystalline; mp 65-68 °C (AcOEt / hexane); $[\alpha]_D^{20}$ -78.5 (c 1.26, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.05 (m, 4H), 3.22 (m, 1H), 3.30 (m, 1H), 3.64 (m, 1H), 3.81 (m, 3H), 6.58, 8.43 (ABq, J = 10.6 Hz, 2H); IR ($CHCl_3$): 3425, 1617, 1314, 1248 cm^{-1}; MS m/z: 172 (M^+); Anal. Calcd for $C_7H_{12}N_2O_3$: C, 48.83; H, 7.03; N, 16.27. Found: C, 48.76; H, 7.12; N, 16.34.

(*E*)-1-[(*S*)-2-Hydroxymethylpyrrolidin-1-yl]-2-nitropropene (2b) A mixture of morphorino nitroenamine (1.72 g, 10 mmol) and L-prolinol (1.52 g, 15 mmol) in MeOH (25 ml) was stirred at 50 °C for 1 h under nitrogen atmosphere. After evaporation of the solvent, the residue was purified with silica gel column chromatography (elute: AcOEt) to give **2b** (1.57 g, 84 %). **2b** : yellow needles; mp 94 °C (AcOEt / hexane); $[\alpha]_D^{24}$ +255 (c 3.33, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 1.63-2.16 (m, 4H), 2.30 (s, 3H), 2.84-3.25 (m, 1H), 3.41-4.03 (m, 5H), 8.56 (s, 1H); IR ($CHCl_3$): 3372, 1611, 1375, 1247 cm^{-1}; MS m/z: 186 (M^+); Anal. Calcd for $C_8H_{14}N_2O_3$: C, 51.60; H, 7.58; N, 15.04. Found: C, 51.42; H, 7.41; N, 15.04.

(*E*)-1-[(*S*)-2-Triphenylmethyloxymethylpyrrolidin-1-yl]-2-nitroethylene (3a) To a dichloromethane (50 ml) solution of nitroenamine **2a** (1.99 g, 11.5 mmol), trityl chloride (3.53 g, 12.7 mmol), and 4-dimethylaminopyridine (DMAP) (0.14 g, 1.2 mmol) was added triethylamine (2.4 ml, 17.3 mmol) and the mixture was stirred for 3 h at room temperature under nitrogen atmosphere. The reaction mixture was poured into water and the aqueous layer was extracted with dichloromethane. The organic extracts were collected, washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give a residue. Purification with silica gel column chromatography (AcOEt / hexane) gave **3a** (3.9 g, 82 %). **3a** : colorless crystalline; mp 161-162 °C (AcOEt / hexane); $[\alpha]_D^{20}$ -101.8 (c 1.42, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 1.77 (m, 1H), 1.99 (m, 3H), 3.16-3.27 (m, 4H), 3.82 (m, 1H), 7.21-7.42 (m, 15H), 6.58, 8.44 (ABq, J = 10.6 Hz, 1H); IR ($CHCl_3$): 3017, 1619, 1310, 1252 cm^{-1}; MS m/z: 414 (M^+); Anal. Calcd for $C_{26}H_{26}N_2O_3$: C, 75.34; H, 6.32; N, 6.76. Found: C, 75.05; H, 6.62; N, 6.53.

(*E*)-1-[(*S*)-2-Triphenylmethyloxymethylpyrrolidin-1-yl]-2-nitropropene (3b) To a dichloromethane (5 ml) solution of nitroenamine **2b** (0.25 g, 1.34 mmol), trityl chloride (0.413 g, 1.48 mmol), and 4-dimethylaminopyridine (DMAP) (16 mg, 0.13 mmol) was added triethylamine (0.28 ml, 2.01 mmol) and the mixture was stirred for 15 h at room temperature under nitrogen atmosphere. The reaction mixture was poured into water and the aqueous layer was extracted with dichloromethane. The organic extracts were collected, washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give a residue. Purification with silica gel column chromatography (AcOEt / hexane = 1:1) gave **3b** (0.51 g, 89 %). **3b** : pale yellow needles; mp 48 °C (hexane); $[\alpha]_D^{25}$ +34.6 (c 1.01, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 1.69-2.19 (m, 4H), 2.31 (s, 3H), 3.18 (d, J = 5.6 Hz, 2H), 3.59 (t, J = 6.5 Hz, 2H), 3.69-3.97 (m, 1H), 7.16-7.47 (m, 15H), 8.50 (s, 1H); IR ($CHCl_3$): 1627, 1251 cm^{-1}; MS m/z: 428 (M^+); Anal. Calcd for $C_{27}H_{28}N_2O_3$: C, 75.67; H, 6.59; N, 6.54. Found: C, 75.88; H, 6.60; N, 6.52.

(*E*)-1-[(*S*)-2-*t*-Butyldimethylsiloxymethylpyrrolidin-1-yl]-2-nitroethylene (4a) To a dichloromethane (195 ml) solution of imidazole (8.37 g, 122.9 mmol) and *t*-butyldimethylsilyl chloride (9.27 g, 61.5 mmol), which had been stirred for 1 h at room temperature, was added a solution dichloromethane (150 ml) of nitroenamine **2a** (8.82 g, 51.2 mmol). After being stirred for 2 h the reaction mixture was washed with saturated sodium bicarbonate solution. The aqueous layer was extracted with dichloromethane. The combined dichloromethane solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. Purification of the residue with silica gel column chromatography (AcOEt / hexane) gave **4a** (14.29 g, 98 %). **4a**: pale yellow crystalline; mp 48-49 °C (hexane); $[\alpha]_D^{20}$ -112.2 (c 1.25, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.00 (s, 6H), 0.83 (s, 9H), 1.75 (m, 1H), 2.00 (m, 3H), 3.15 (m, 2H), 3.52 (dd, *J* = 6.9, 10.6 Hz, 1H), 3.64 (dd, *J* = 4.3, 10.6 Hz, 1H), 3.73 (m, 1H), 6.53 (d, *J* = 10.6 Hz, 1H), 8.36 (d, *J* = 10.9 Hz, 1H); IR ($CHCl_3$): 3019, 1617, 1310, 1252 cm^{-1}; MS m/z: 286 (M^+); Anal. Calcd for $C_{13}H_{26}N_2O_3Si$: C, 54.51; H, 9.15; N, 9.78. Found: C, 54.23; H, 9.15; N, 9.74.

(*E*)-1-[(*S*)-2-*t*-Butyldimethylsiloxymethylpyrrolidin-1-yl]-2-nitropropene (4b) To a dichloromethane (65 ml) solution of imidazole (1.25 g, 18.3 mmol) and *t*-butyldimethylsilyl chloride (1.84 g, 18.3 mmol), which had been stirred for 0.5 h at room temperature was added nitroenamine **2b** (1.14 g, 51.2 mmol). After being stirred for 2 h the reaction mixture was washed with saturated sodium bicarbonate solution. The aqueous layer was extracted with dichloromethane. The combined dichloromethane solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. Purification of the residue with silica gel column chromatography (AcOEt / hexane) gave **4b** (1.82 g, 99 %). **4b**: pale yellow needles; mp 62 °C (hexane); $[\alpha]_D^{25}$ +66.8 (c 3.30, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 0.03 (s, 6H), 0.89 (s, 9H), 1.70-2.21 (m, 4H), 2.34 (s, 3H), 3.44-4.02 (m, 5H), 8.52 (s, 1H); IR ($CHCl_3$): 1627, 1247 cm^{-1}; MS m/z: 300 (M^+); Anal. Calcd for $C_{14}H_{28}N_2O_3Si$: C, 55.96; H, 9.36; N, 9.32. Found: C, 55.82; H, 9.64; N, 9.31.

General Procedure for 7a-f, 8a-b. To a dimethoxymethane (DME) (30 ml) solution of diisopropylamine (3.57 ml, 25.0 mmol) was added *n*-butyllithium (1.6M in hexane, 15.5 ml, 24.8 mmol) at -78 °C, then the mixture was stirred at 0 °C for 0.5 h. A DME (10 ml) solution of the lactone (24.6 mol) was added dropwise to the resulting lithium diisopropylamide (LDA) solution at -78 °C. After being stirred for 1 h , zinc chloride (1.0M in ether, 24.6 ml, 24.6 mmol) was added to the above lithium enolate of the lactone dropwise with vigorous stirring at -40 °C, then the mixture was stirred for 1 h at -40 to -30 °C. To a DME (30 ml) solution of nitroenamine (7 mmol) was added the above zinc enolate solution with a cannula at -78 °C, and then the mixture was stirred for 2 h, and additional for 1 h at -60 °C. The reaction mixture was quenched with 1 % HCl solution and extracted with ether. The ethereal extract was washed with saturated sodium bicarbonate solution, then with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified with silica gel column chromatography (AcOEt / hexane = 1 / 4) afforded a nitroolefin.

2-Methyl-2-[(*E*)-2-nitroethenyl]-4-butanolide (7a) pale yellow oil; $[\alpha]_D^{22}$ -34.9 (c 1.27, $CHCl_3$) [88 %ee, chiral HPLC analysis; DAICEL CHIRALPAK AS (25 x 0.46); eluent: isopropanol; flow rate: 0.2 ml/min.; Temp.: 20 °C; detector: 254 nm; (-)-**7a**; 42.5 min, (+)-**7a**; 38.8 min]; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 1.52 (s, 3H), 2.34 (dd of ABd, A part of AB, J_{AB} = 13.0 Hz, *J* = 7.0 and 5.9 Hz, 1H), 2.47 (t of ABd, B part of AB, J_{AB} = 13.0 Hz, *J* = 7.4 Hz, 1H), 4.37-4.42 (m, 2H), 7.14 (ABd, *J* = 13.7 Hz, 1H), 7.29 (ABd, *J* = 13.7 Hz, 1H); IR ($CHCl_3$): 2990, 1780, 1650, 1530, 1450, 1380, 1370, 1350, 1180, 1090, 1030, 960, 920 cm^{-1}; MS (FAB) m/z: 172 (M^++1); Anal. Calcd for $C_7H_9NO_4$: C, 49.12 H, 5.30 N, 8.18. Found: C, 48.95 H, 5.31 N, 8.18.

2-Ethyl-2-[(*E*)-2-nitroethenyl]-4-butanolide (7b) pale yellow oil; $[\alpha]_D^{23}$ -30.2 (c 2.99, $CHCl_3$); [85 %ee, chiral HPLC analysis; DAICEL CHIRALCEL OJ (25 x 0.46); eluent: isopropanol; flow rate: 0.2 ml/min.; Temp.: 2.5 °C; detector: 254 nm, (+)-**7b**: 107.9 min, (-)-**7b**: 125.3 min]. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 1.02 (t, *J* = 7.6 Hz, 3H), 1.79-1.97 (m, 2H), 2.40 (dd, 6.93, 7.59 Hz, 2H), 4.29-4.39 (m, 2H), 7.13, 7.29 (ABq, *J* = 13.9 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz): 176.31, 140.18, 140.43, 65.26, 47.53, 32.06, 29.58, 8.79; IR ($CHCl_3$): 1769, 1530, 1352, 1181 cm^{-1}; MS m/z: 186 (M^++1); Anal. Calcd for $C_8H_{11}NO_4$: C, 51.88 H, 5.99 N, 7.56. Found: C, 51.81 H, 6.12 N, 7.45.

2-Allyl-2-[(*E*)-2-nitroethenyl]-4-butanolide (7c) pale yellow oil; $[\alpha]_D^{23}$ -36.7 (c 3.34, $CHCl_3$); [86 %ee, chiral HPLC analysis; DAICEL CHIRALCEL OJ (25 x 0.46); eluent: isopropanol; flow rate: 0.2 ml/min.; Temp.: 1.0 °C; detector: 254 nm, (+)-**7c**: 147.1 min, (-)-**7c**: 170.0 min]. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.30-2.50 (m, 2H), 2.55 (δ, *J* = 7.3 Hz, 2H), 4.28-4.42 (m, 2H), 5.29 (d, *J* = 9.6 Hz, 2H), 5.64-5.79 (m, 1H), 7.11, 7.28 (ABq, *J* = 13.9 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz): 175.99, 140.75, 140.18, 130.37, 121.60, 65.35, 47.01, 40.50, 31.75; IR ($CHCl_3$): 1771, 1532, 1352, 1177 cm^{-1}; MS m/z: 198 (M^++1); Anal. Calcd. for $C_9H_{11}NO_4$: C, 54.82 H, 5.62 N, 7.10, Found: C,54.53 H, 5.73 N, 6.85.

2-Methyl-2-[(*E*)-2-nitroprop-1-enyl]-4-butanolide (7d) pale yellow oil; $[\alpha]_D^{25}$ -55.7 (c 2.47, $CHCl_3$); [93 %ee, Eu(hfc)$_3$ chiral shift analysis]; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 1.53 (s, 3H) , 2.26 (d, *J* = 1.0 Hz, 3H), 2.42-2.48 (m, 2H), 4.35-4.41 (m, 2H), 7.35 (d, *J* = 1.0 Hz, 1H); IR ($CHCl_3$): 2990, 1780, 1530, 1390, 1330, 1190, 1110, 1030 cm^{-1}; MS (FAB) m/z: 186 (M^++1); Anal. Calcd. for $C_8H_{11}NO_4$: C, 51.88 H, 5.99 N, 7.56. Found: C,51.81 H, 6.06 N, 7.42.

2-Ethyl-2-[(*E*)-2-nitroprop-1-enyl]-4-butanolide (7e) pale yellow oil; $[\alpha]_D^{22}$ -32.8 (c 0.40, $CHCl_3$); [98 %ee, chiral HPLC analysis; DAICEL CHIRALPAK AS (25 x 0.46); eluent: isopropanol; flow rate: 0.2 ml/min.; Temp.: 15 °C; detector: 254 nm; (-)-**7e**; 38.1 min, (+)-**7e**; 43.2 min]; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 1.04 (t, *J* = 7.4 Hz, 3H), 1.82-2.01 (m, 2H), 2.25 (s, 3H), 2.41-2.56 (m, 2H), 4.30-4.44 (m, 2H), 7.33 (s, 1H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz): 117.32, 150.01, 135.25, 65.39, 47.12, 34.20, 29.79, 13.80, 9.06; IR ($CHCl_3$): 1771, 1528, 1333, 1192 cm^{-1}; MS m/z: 199 (M^+); Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26 H, 6.58 N, 7.03. Found: C, 54.00 H, 6.71 N, 6.88.

2-Allyl-2-[(*E*)-2-nitroprop-1-enyl]-4-butanolide (7f) pale yellow oil; $[\alpha]_D^{22}$ -50.6 (c 0.82, $CHCl_3$); [95 %ee, chiral HPLC analysis; DAICEL CHIRALPAK AD (25 x 0.46); eluent: ethanol; flow rate: 0.3 ml/min.; Temp.: 1 °C; detector: 254 nm; (-)-**7f**; 19.0 min, (+)-**7f**; 24.0 min]; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.24 (s, 3H), 2.36-2.47 (m, 1H), 2.56 (d, *J* = 7.3 Hz, 3H), 4.32-4.40 (m, 2H), 5.24 (d, J = 5.0 Hz, 1H), 5.29 (s, 1H), 5.68-5.81 (m, 1H), 7.32 (s, 1H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz): 177.19, 150.04, 134.91, 130.80, 121.33, 65.48, 46.72, 40.57, 33.58, 13.91; IR ($CHCl_3$): 1771, 1528, 1331, 1186 cm^{-1}; MS m/z: 212 (M^++1); Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.86 H, 6.20 N, 6.63. Found: C, 56.70 H, 6.36 N, 6.52.

(2*S*)-2-Methyl-2-[(*E*)-2-nitroethenyl]-5-pentanolide (8a) pale yellow oil; $[\alpha]_D^{25}$ -10.1 (c 4.48, $CHCl_3$); [93 %ee, chiral HPLC analysis; DAICEL CHIRALPAK AS (25 x 0.46); eluent: isopropanol; flow rate: 0.2 ml/min.; Temp.: 15 °C; detector: 254 nm, (+)-**8a**: 42.6 min, (-)-**8a**: 46.4 min]. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 1.54 (s, 3H), 1.93-2.15 (m, 4H), 4.43 (t, *J* = 5.3 Hz, 2H), 7.06 and 7.33 (ABq, *J* = 13.9 Hz, 2H); IR ($CHCl_3$): 1733, 1535, 1355, 1161 cm^{-1}; MS m/z: 186 (M^++1); HRMS calcd for $C_8H_{12}NO_4$: 186.0766, found: 186.0785.

(2*S*)-2-Methyl-2-[(*E*)-2-nitroethenyl]-5-pentanolide (8b) colorless needles, mp 62.0 °C (AcOEt / hexane); $[\alpha]_D^{25}$ -48.8 (c 4.65, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 1.50 (s, 3H), 1.81-2.13 (m, 4H), 2.18 (d, *J* = 1.0 Hz, 3H), 4.28-4.47 (m, 2H), 7.12 (d, *J* = 1.0 Hz, 1H); IR ($CHCl_3$): 1735, 1527, 1335, 1145 cm^{-1}; MS m/z: 200 (M^++1); Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26 H, 6.58 N, 7.03. Found: C, 54.21 H, 6.65 N, 7.06.

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16. The hydroxy group on nitroenamines **2a,b** might be changed to the bulky substituent because of its binding to the zinc enolate.

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