Lewis Acid-Promoted Nitroolefination of Enol Silyl Ethers *via* an Addition Elimination Process

Ji-Jun CHEN, Takeo KAWABATA, Hiroshi OHNISHI, Muhong SHANG, and Kaoru FUJI*

Institute for Chemical Research, Kyoto University, Uji, Kyoyo 611–0011, Japan.
Received October 21, 1998; accepted December 21, 1998

Lewis acid-promoted nitroolefination of enol silyl ethers has been developed. Enol ethers 1, 4, 5, and 6 derived from lactones and lactams furnished nitroolefines 2, 7, 8, and 9, respectively in 60—99% yields by the treatment with 3 in the presence of Lewis acids. Asymmetric nitroolefination of 5a and 6a with 12 gave 8a and 9a in 75% and 73% ee, respectively.

Key words nitroolefin; quaternary carbon; Lewis acid; nitroenamine; enol silyl ether; addition elimination

Asymmetric creation of quaternary carbon centers is a matter of infinite importance in organic synthesis.[1] Nearly ten years ago, we reported highly enantioselective asymmetric nitroolefination through an addition elimination process to construct a chiral quaternary carbon at the α-position of δ-lactones,[2] and the products were used as chiral building blocks for the total syntheses of optically active indole alkaloids[3,4] and diterpenoids.[5,6] Recently the strategy was successfully applied to enantioselective synthesis of (−)-pseudophyrynaminol,[7] (+)-esermethol,[8] and (−)-horsfiline.[9] In these studies we have employed zinc- and lithium enolates for asymmetric nitroolefination. Here, we describe nitroolefination of enol silyl ethers promoted by Lewis acids.

Nitroolefination of **1**[10] with achiral nitroenamine **3**[11] was examined in the presence of various Lewis acids (Table 1). Among Lewis acids (1.0 mol eq) screened (entries 1—6), $TiCl_4$ was found to be the most effective. Use of excess $TiCl_4$ resulted in a decrease in the yield of **2**[2b] due to the predominant decomposition of **1** (entry 7). The maximum yield was obtained when catalytic amount (0.1 mol eq) of $TiCl_4$ was used (entry 8).

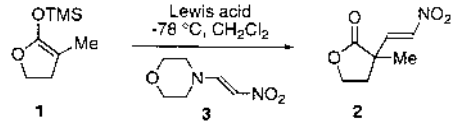
Lewis acid-promoted nitroolefination was further examined with enol silyl ethers **4**—**6** derived from a lactone and lactams. Results were shown in Table 2. Enol ether **4**[12] gave moderate yields of **7**[2b] under variety of conditions (entries 1—3), probably due to the lower reactivity of 6-membered enol ether than the 5-membered one. Enol silyl ethers **5a**—**d** were prepared from 1,3-dialkyl-2-pyrrolidinones by the treatment with lithium diisopropylamide (LDA) followed by chlorotrimethylsilane (TMSCl). They underwent nitroolefination within 0.3 h at −78 °C by the treatment with **3** in the presence of a catalytic amount (0.1 mole eq) of (iso-$PrO)_2TiBr_2$ or $Sm(OTf)_3$, affording **8a**—**d** in 70—99% yields (entries 4—11). For the former Lewis acid, CH_2Cl_2 was the solvent of choice, and tetrahydrofuran (THF) for the latter. Similarly, enol ethers **6** derived from 1,3-dialkyl-2-piperidinones gave nitroolefins **9** in moderate to good yields under similar conditions (entries 12—17), except the case of **6d** (entries 18, 19).

Asymmetric nitroolefination of **1** using chiral nitroenamines **10**—**12** in the presence of Lewis acid was next examined (Table 3). In contrast to the nitroolefination of **1** with **3**, stoichiometric amount of $TiCl_4$ was required for the transformation (entries 1, 2). Nitroolefination of **1** with **10**,[2] **11**,[7,8] or **12** in the presence of $TiCl_4$ gave **2** in moderate yield (57—61%) with low ee of 4—22% (entries 2, 3, 5). Use of Et_2AlCl improved the enantioselectivity up to 50% ee, but diminished the yield (entries 3 *vs*. 4, 5 *vs*. 6). Slow addition of **1** into a solution of **12** and Et_2AlCl in CH_2Cl_2 using a syringe pump improved the yield up to 73% without lowering the enantioselectivity (entry 7).

We also examined asymmetric nitroolefination of **5a** and **6a** (Table 4). Reaction of **5a** with chiral nitroenamine **10**, **11**, **12**, or **13**[8] in the presence of 0.1 mol eq of (iso-$PrO)_2TiBr_2$ gave **8a** in 65—93% yield with 38—60% ee (entries 1, 3, 5, 7). Higher asymmetric induction was achieved by using $Sm(OTf)_3$ as a promoter (entries 2, 4, 6, 8). The best result (66% yield, 75% ee) was obtained when **5a** was treated with **12** in the presence of $Sm(OTf)_3$ (entry 6). Similarly, asymmetric nitroolefination of **6a** in the presence of (iso-$PrO)_2TiBr_2$ proceeded in 51—73% ee (entries 9—12). Use of $Sm(OTf)_3$ has resulted in a decreased yield with similar enantioselectivity (entries 12 *vs*. 13).

In conclusion, we developed Lewis acid-promoted nitroolefination of enol silyl ethers. Catalytic amount of $Sm(OTf)_3$ or (iso-$PrO)_2TiBr_2$ was effective for asymmetric nitroolefination of **5a** and **6a** with **12** to furnish **8a** and **9a** in 75% and 73% ee, respectively.

Table 1. Nitroolefination of **1**[a]

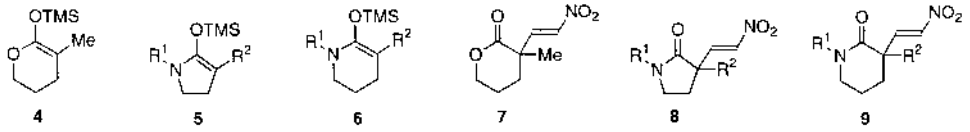


Entry	Lewis acid (mol eq)	Time (h)	Yield of **2** (%)[b]
1	(iso-$PrO)_2TiBr_2$ (1.0)	0.5	26
2	TMSOTf (1.0)	0.3	32
3	$Zn(OTf)_2$ (1.0)	3	47
4[c,d]	$Sm(OTf)_3$ (1.0)	24	42
5	$HfCl_4$ (1.0)	1.5	68
6	$TiCl_4$ (1.0)	0.3	71
7[e]	$TiCl_4$ (3.0)	0.5	46
8	$TiCl_4$ (0.1)	0.5	80
9	$TiCl_4$ (0.05)	1	23

a) Reactions were carried out in CH_2Cl_2 at −78 °C using 1.1—1.2 mol eq of **3** unless otherwise mentioned. *b*) Yield based on **1**. *c*) Run in THF. *d*) Run at −78 °C—r.t. *e*) 5.0 mol eq of **3** was used.

* To whom correspondence should be addressed.

Table 2. Nitroolefination of **4**, **5**, and **6** with **3**[a]



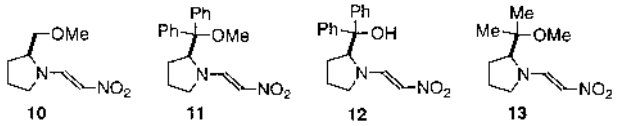
4 **5** **6** **7** **8** **9**

5a, 6a, 8a, 9a : $R^1 = R^2 = Me$ **5c, 6c, 8c, 9c** : $R^1 = Bn$, $R^2 = Me$
5b, 6b, 8b, 9b : $R^1 = Me$, $R^2 = Et$ **5d, 6d. 8d, 9d** : $R^1 = Me$, $R^2 = Bn$

Entry	Substrate	Ratio (substrate: **3**)	Lewis acid (mol eq)	Solvent	Time (h)	Product	Yield[b] (%)
1	**4**	3 : 1	$TiCl_4$ (1.0)	CH_2Cl_2	1.5	**7**	48
2	**4**	1 : 1	$TiCl_4$ (0.1)	CH_2Cl_2	0.5	**7**	39
3	**4**	3 : 1	$SnCl_4$ (0.1)	CH_2Cl_2	1.5	**7**	60
4	**5a**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**8a**	77
5	**5a**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**8a**	75
6	**5b**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**8b**	71
7	**5b**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**8b**	70
8	**5c**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**8c**	87
9	**5c**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**8c**	83
10	**5d**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**8d**	99
11	**5d**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**8d**	86
12	**6a**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**9a**	71
13	**6a**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**9a**	70
14	**6b**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**9b**	80
15	**6b**	1.5 : 1	$Sm(ORf)_3$ (0.1)	THF	0.3	**9b**	67
16	**6c**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**9c**	72
17	**6c**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.6	**9c**	68
18	**6d**	1.5 : 1	(iso-PrO)$_2$TiBr$_2$ (0.1)	CH_2Cl_2	0.3	**9d**	7
19	**6d**	1.5 : 1	$Sm(OTf)_3$ (0.1)	THF	0.3	**9d**	20

a) Reactions were run at −78 °C. *b*) Yield based on **3**.

Table 3. Nitroolefination of **1** with Chiral Nitroenamines **10**—**12**[a]



10 **11** **12** **13**

Entry	Nitroenamin	Lewis acid (mol eq)	Time (h)	Yield of **2** (%)[b]	Ee of **2** (%)[c]
1[d]	10	$TiCl_4$ (0.1)	4	0	—
2	10	$TiCl_4$ (1.0)	0.6	61	4
3	11	$TiCl_4$ (1.0)	0.6	61	20
4	11	Et_2AlCl (1.0)	0.5	35	22
5	12	$TiCl_4$ (1.0)	0.6	57	14
6[e]	12	Et_2AlCl (1.0)	1	34	50
7[e,f]	12	Et_2AlCl (1.0)	2	73	50

a) Reactions were carried out in CH_2Cl_2 at −78 °C using 1.0 mol eq of nitroenamine unless otherwise mentioned. *b*) Yield based on the nitroenamine employed. *c*) Ee was determined by HPLC analysis, see Experimental. *d*) Run at −78 °C—r.t. *e*) The ratio of **1** to **12** was 3 : 1. *f*) **1** was added slowly using a syringe pump during a period of 1 h.

Experimental

Melting points were measured using a Yanagimoto micro point apparatus and were uncorrected. NMR spectra were obtained with a Varian Gemini 200 (200 MHz) spectrometer, chemical shifts being given in ppm units (tetramethylsilane or chloroform as internal standards, indicating 0 or 7.24, respectively). IR spectra were recorded with a JACSO FT/IR-300 spectrometer. Specific rotations were measured with a Horiba SEPA-200 automatic digital polarimeter. MS spectra were recorded with a JEOL JMS-DX300 mass spectrometer. TLC analyses and preparative TLC were performed on commercial glass plates bearing a 0.25-mm layer and a 0.5-mm layer of Merck Kieselgel 60 F_{254}, respectively. Silica gel column chromatography was carried out with Wakogel C-200, Fuji Silysia BW-1277H, or Nacalai Tesque Silica gel 60 (150—325 mesh). THF, ether, and toluene were distilled over benzophenone ketyl before each use. Dichloromethane was distilled from calcium hydride. TMSCl was stirred over calcium chloride overnight and then distilled before use.

Determination of Enantiomeric Excess of 2[2b] HPLC conditions: Daicel Chiralpak AS, iso-PrOH, flow 0.1 ml/min, t_R=78, 87 min.

1,3-Dimethyl-2-(trimethylsilyloxy)pyrroline (5a), Typical Procedure for the Preparation of Enol Silyl Ether An LDA solution was prepared by adding a solution of *n*-BuLi in hexane (1.66 M, 39.5 ml, 66 mmol) to a solution of diisopropylamine (10.1 ml, 72 mmol) in dry THF (30 ml) at 0 °C under argon atmosphere followed by stirring for 30 min at 0 °C. A solution of 1,3-dimethyl-pyrrolidine-2-one (6.78 g, 60 mmol) in THF (18 ml) was added dropwise to the LDA solution at −78 °C. After being stirred for 60 min at −78 °C, the enolate solution was treated with TMSCl (10.0 ml, 90 mmol). The mixture was gradually warmed to ambient temperature during a period of 2 h. The resulting suspension was quickly filtered and the filtrate was concentrated, then *ca*. 20 ml of dry hexane was added and the mixture was filtered. The filtrate was concentrated *in vacuo* and the residue was distilled under reduced pressure to afford a mixture of **5a** and 1,3-dimethylpyrrolidine-2-one (ratio=3 : 1, 4.10 g, 37% yield) as a colorless oil: bp 70 °C (6.0 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.40 (s, 9H), 1.73 (s, 3H), 2.42 (br t, J=8.0 Hz, 2H), 2.54 (s, 3H), 3.08 (br t, J=8.0 Hz, 2H); MS *m/z* (rel. int. %) 186 (MH^+, 14), 163 (5), 113 (100), 112 (75), 98 (20), 84 (12), 56 (45); exact MS *m/z*: 186.1303 (Calcd for $C_9H_{20}NOSi$ MH^+: 186.1314).

3-Ethyl-1-methyl-2-(trimethylsilyloxy)pyrroline (**5b**): Obtained as a mixture of **5b** and 3-ethyl-1-methylpyrrolidine-2-one (ratio=2 : 1): Colorless oil; bp 51 °C (3.0 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.19 (s, 9H), 0.92 (t, J=7.4 Hz, 3H), 1.95 (q, J=7.6 Hz, 2H), 2.22 (br t, J=8.4 Hz, 2H), 2.34 (s, 3H), 2.87 (br t, J=8.4 Hz, 2H); MS *m/z* (rel. int. %) 200 (MH^+, 28), 186 (3), 172 (2), 127 (21), 99 (100), 98 (62); exact MS *m/z*: 200.1447 (Calcd for $C_{10}H_{22}NOSi$ MH^+: 200.1471).

1-Benzyl-3-methyl-2-(trimethylsilyloxy)pyrroline (**5c**): Obtained as a mixture of **5c** and 1-benzyl-3-methylpyrrolidine-2-one (ratio=3 : 1): Colorless oil; bp 100 °C (0.9 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.20 (s, 9H), 1.52 (s, 3H), 2.17 (br t, J=9.0 Hz, 2H), 2.77 (br t, J=9.0 Hz, 2H), 3.78 (s, 2H), 7.12—7.30 (m, 5H); MS *m/z* (rel. int. %) 262 (MH^+, 20), 261 (M^+, 1), 244 (100), 189 (32), 156 (30), 144 (3), 129 (10), 98 (4), 91 (20), 73 (10); exact MS *m/z*: 262.1597 (Calcd for $C_{15}H_{24}NOSi$ MH^+: 262.1627). *m/z*: 261.1541 (Calcd for $C_{15}H_{23}NOSi$ M^+: 261.1549).

3-Benzyl-1-methyl-2-(trimethylsilyloxy)pyrroline (**5d**): Obtained as a mixture of **5d** and 3-benzyl-1-methylpyrrolidine-2-one (ratio=1 : 1): Colorless oil; bp 103 °C (1.2 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.20 (s, 9H), 2.10 (t, J=8.2 Hz, 2H), 2.37 (s, 3H), 2.87 (t, J=8.2 Hz, 2H), 3.27 (s, 2H), 7.05—7.30 (m, 5H); MS *m/z* (rel. int. %) 262 (MH^+, 22), 261 (M^+, 1), 244 (1), 189

Table 4. Nitroolefination of **5a** and **6a** with Chiral Nitroenamines **10**—**13**[a)]

Entry	Substrate	Nitroenamine	Lewis acid[b)]	Solvent	Product	Yield (%)[c)]	Ee (%)[d)]
1	**5a**	**10**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**8a**	89	60
2	**5a**	**10**	Sm(OTf)$_3$	THF	**8a**	73	66
3	**5a**	**11**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**8a**	65	38
4	**5a**	**11**	Sm(OTf)$_3$	THF	**8a**	62	51
5	**5a**	**12**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**8a**	85	56
6	**5a**	**12**	Sm(OTf)$_3$	THF	**8a**	66	75
7	**5a**	**13**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**8a**	93	56
8	**5a**	**13**	Sm(OTf)$_3$	THF	**8a**	88	69
9	**6a**	**10**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**9a**	58	51
10	**6a**	**11**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**9a**	32	56
11	**6a**	**12**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**9a**	60	73
12	**6a**	**13**	(iso-PrO)$_2$TiBr$_2$	CH_2Cl_2	**9a**	75	70
13	**6a**	**13**	Sm(OTf)$_3$	THF	**9a**	23	69

a) Reactions were run at −78 °C for 20 min. The ratio of substrate to nitroenamine was 1.5 : 1. *b*) 0.1 mol eq of Lewis acid was used. *c*) Yield based on the nitroenamine employed. *d*) Ee was determined by HPLC analysis, see **8a** and **9a** in Experimental.

(100), 188 (44), 186 (32), 160 (10), 131 (3), 112 (21), 98 (38), 91 (42), 73 (5); exact MS *m/z*: 262.1615 (Calcd for $C_{15}H_{24}NOSi$ MH^+: 262.1627). *m/z*: 261.1525 (Calcd for $C_{15}H_{23}NOSi$ M^+: 261.1549).

1,3-Dimethyl-2-(trimethylsilyloxy)-1,4,5,6-tetrahydropyridine (**6a**): Obtained as a mixture of **6a** and 1,3-dimethylpiperidine-2-one (ratio=3 : 1): Colorless oil; bp 51 °C (2.4 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.54 (s, 3H), 1.50—1.66 (m, 2H), 1.89 (br t, *J*=7.0 Hz, 2H); 2.44 (s, 3H), 2.81—2.92 (m, 2H); MS *m/z* (rel. int. %) 200 (MH^+, 42), 172 (4), 156 (4), 143 (20), 127 (100), 126 (90), 112 (88), 99 (30), 98 (35), 84 (18), 73 (21), 72 (32); exact MS *m/z*: 200.1447 (Calcd for $C_{10}H_{22}NOSi$ MH^+: 200.1471).

3-Ethyl-1-methyl-2-(trimethylsilyloxy)-1,4,5,6-tetrahydropyridine (**6b**): Obtained as a mixture of **6b** and 1,3-dimethylpiperidine-2-one (ratio=3 : 1): Colorless oil; bp 50 °C (1.5 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.14 (s, 9H), 0.89 (t, *J*=7.7 Hz, 3H), 1.49—1.62 (m, 2H), 1.89 (br t, *J*=6.2Hz, 2H), 1.97 (q, *J*=7.7 Hz, 2H), 2.42 (s, 3H), 2.82 (t, *J*=5.1 Hz, 2H); MS *m/z* (rel. int. %) 214 (MH^+, 10), 187 (1), 163 (3), 141 (22), 126 (15), 113 (100), 112 (41), 98 (15); exact MS *m/z*: 214.1611 (Calcd for $C_{11}H_{24}NOSi$ MH^+: 214.1627).

1-Benzyl-3-methyl-2-(trimethylsilyloxy)-1,4,5,6-tetrahydropyridine (**6c**): Obtained as a mixture of **6c** and 1,3-dimethylpiperidine-2-one (ratio=4 : 1): Colorless oil; bp 100 °C (0.9 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.32 (s, 9H), 1.50—1.65 (m, 2H), 1.73 (s, 3H), 2.03 (br t, *J*=6.3 Hz, 2H), 2.85—2.97 (m, 2H), 4.12 (s, 2H), 7.30—7.45 (m, 5H); MS *m/z* (rel. int. %) 276 (MH^+, 11), 275 (1), 248(1), 203 (100), 188 (18), 174 (4), 112 (46), 99 (10), 98 (3), 91 (92); exact MS *m/z*: 276.1764 (Calcd for $C_{16}H_{26}NOSi$ MH^+: 276.1784).

3-Benzyl-1-methyl-2-(trimethylsilyloxy)-1,4,5,6-tetrahydropyridine (**6d**): Obtained as a mixture of **6d** and 1,3-dimethylpiperidine-2-one (ratio=5 : 1): Colorless oil; bp 113 °C (0.9 mmHg); ^{1}H-NMR ($CDCl_3$) δ 0.22 (s, 9H), 1.50—1.65 (m, 2H), 1.82 (br t, *J*=6.2 Hz, 2H), 2.54 (s, 3H), 2.86—2.98 (m, 2H), 3.36 (s, 2H), 7.10—7.35 (m, 5H); MS *m/z* (rel. int. %) 276 (MH^+, 6), 275 (M^+, 18), 260 (10), 243 (5), 203 (100), 189 (38), 188 (22), 184 (22), 160 (10), 131 (15),126 (22), 112 (98), 98 (32), 91 (58), 73 (12), exact MS *m/z*: 276.1764 (Calcd for $C_{16}H_{26}NOSi$ MH^+: 276.1784). *m/z*: 275.1689 (Calcd for $C_{16}H_{25}NOSi$ M^+: 275.1705).

1,3-Dimethyl-3-(2-nitrovinyl)pyrrolidin-2-one (8a); Typical Procedure for Nitroolefination of Enol Silyl Ether Dichloromethane (2 ml) was added to a mixture of (iso-PrO)$_2$TiBr$_2$ (6.5 mg, 0.02 mmol) and **3** (32 mg, 0.2 mmol) at −78 °C and the mixture was stirred for 10 min. To the suspension, a solution of **5a** (a mixture of **5a** and 1,3-dimethylpyrrolidine-2-one, ratio=3 : 1, 74 mg, 0.3 mmol of **5a**) in CH_2Cl_2 (1 ml) was added dropwise. After stirring for 20 min, the mixture was poured into 0.5 M HCl ice (10 ml), stirred for 5 min, and extracted with EtOAc (30 ml×3). The organic phase was washed with saturated aq. $NaHCO_3$ and brine, dried over Mg_2SO_4, and evaporated *in vacuo* to give a residue which was purified by preparative TLC (MeOH : EtOAc=2 : 9) to afford **8a** (28 mg, 77%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.39 (s, 3H), 2.01—2.30 (m, 2H), 2.90 (s, 3H), 3.40 (t, *J*=7.0 Hz, 2H), 7.10, 7.30 (ABq, *J*=13.6 Hz, 2H); IR ($CHCl_3$) 3310, 1690, 1531, 1352 cm^{-1}; MS *m/z* (rel. int. %) 184 (M^+, 100), 167 (8), 138 (30), 123 (32), 110 (45), 97 (40), 79 (42); exact MS *m/z*: 184.0854 (Calcd for $C_8H_{12}N_2O_3$ M^+: 184.0848).

$[\alpha]_D^{20}$ +14.1 (*c*=0.3, $CHCl_3$) (75% ee). HPLC conditions: Daicel Chiralpak AS, iso-PrOH only, flow 0.1 ml/min, t_R=78, 90 min.

3-Ethyl-1-methyl-3-(2-nitrovinyl)pyrrolidin-2-one (**8b**): Colorless crystals; mp 47—49 °C (ether); ^{1}H-NMR ($CDCl_3$) δ 0.94 (t, *J*= 7.5 Hz, 3H), 1.75 (qd, *J*=7.5, 2.5 Hz, 2H), 2.05—2.25 (m, 2H), 2.90 (s, 3H), 3.67 (t, *J*=6.9 Hz, 2H), 7.11, 7.31 (ABq, *J*=13.8 Hz, 2H); IR ($CHCl_3$) 1690, 1530, 1350 cm^{-1}; MS *m/z* (rel. int. %) 198 (M^+, 15), 184 (8), 170 (40), 152 (42), 123 (100), 98 (28), 79 (35); exact MS *m/z*: 198.1002 (Calcd for $C_9H_{14}N_2O_3$ M^+: 198.1004). *Anal*. Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.30; H, 7.19; N, 13.91.

1-Benzyl-3-methyl-3-(2-nitrovinyl)pyrrolidin-2-one (**8c**): Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.41 (s, 3H), 1.96—2.25 (m, 2H), 3.25 (t, *J*=7.0 Hz, 2H), 4.45, 4.52 (ABq, *J*=10.0 Hz, 2H), 7.11, 7.33 (ABq, *J*=13.6 Hz, 2H), 7.20—7.41 (m, 5H); IR ($CHCl_3$) 1690, 1530, 1355 , 1210, 700 cm^{-1}; MS *m/z* (rel. int. %) 260 (M^+, 23), 243 (5), 188 (2), 169 (3), 123 (21), 91 (100), 79 (3); exact MS *m/z*: 260.1154 (Calcd for $C_{14}H_{16}N_2O_3$ M^+: 260.1161). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.50; H, 6.19; N, 10.51

3-Benzyl-1-methyl-3-(2-nitrovinyl)pyrrolidin-2-one (**8d**): Colorless oil: ^{1}H-NMR ($CDCl_3$) δ 2.04 (ddd, *J*=16.0, 8.7, 6.3 Hz, 1H), 2.25 (ddd, *J*=16.0, 7.5, 3.8 Hz, 1H), 2.40—2.60 (m, 1H), 2.75 (s, 3H), 2.82, 3.18 (ABq, *J*=13.3 Hz, 2H), 3.02—3.15 (m, 1H), 7.13, 7.40 (ABq, *J*=13.7 Hz, 2H), 7.20—7.36 (m, 5H); IR ($CHCl_3$) 1690, 1530, 1350 , 1220, 780, 740, 670 cm^{-1}; MS *m/z* (rel. int. %) 260 (M^+, 8), 243 (14), 213 (45), 123 (64), 91 (100), 77 (3), 65 (9), 51 (2); exact MS *m/z*: 260.1147 (Calcd for $C_{14}H_{16}N_2O_3$ M^+: 260.1161). *Anal*. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.35; H, 6.30; N, 10.66.

1,3-Dimethyl-3-(2-nitrovinyl)piperidin-2-one (**9a**): Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.45 (s, 3H), 1.75—2.08 (m, 4H), 2.97 (s, 3H), 3.35 (br t, *J*=3.7 Hz, 2H), 7.05, 7.34 (ABq, *J*=13.6 Hz, 2H); IR ($CHCl_3$) 1710, 1638, 1530, 1352 cm^{-1}; MS *m/z* (rel. int. %) 198 (M^+, 33), 184 (30) 167 (5), 152 (100), 137 (15), 124 (18), 111 (35), 98 (70), 72 (42); exact MS *m/z* 198.1015 (Calcd for $C_9H_{14}N_2O_3$ M^+: 198.1004).

$[\alpha]_D^{20}$ +12.3 (*c*=0.4, $CHCl_3$) (73% ee). HPLC conditions: Daicel Chiralcel OJ, trifluoroacetic acid : iso-PrOH : hexane=2 : 10 : 90, flow 1.0 ml/min, t_R=20, 23 min.

3-Ethyl-1-methyl-3-(2-nitrovinyl)piperidin-2-one (**9b**): Colorless prisms; mp 83—85 °C (ether); ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, *J*=7.4 Hz, 3H), 1.70—2.05 (m, 6H), 2.97 (s, 3H), 3.21—3.46 (m, 2H), 7.04, 7.34 (ABq, *J*=13.8 Hz, 2H); IR ($CHCl_3$) 1710, 1638, 1530, 1350 cm^{-1}; MS *m/z* (rel. int. %) 212 (M^+, 15), 198 (10), 184 (8), 166 (25), 152 (48), 137 (100), 123 (50), 112 (34), 98 (35), 79 (37), 72(42); exact MS *m/z* 212.1161 (Calcd for $C_{10}H_{16}N_2O_3$ M^+: 212.1161). *Anal*. Calcd for $C_{10}H_{16}N_2O_3$: C, 56.59; H, 7.60; N, 13.20. Found: C, 56.75; H, 7.65; N, 12.95.

1-Benzyl-3-methyl-3-(2-nitrovinyl)piperidin-2-one (**9c**): Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.60—1.90 (m, 4H), 3.11 (t, *J*=5.5 Hz, 2H), 4.43 (s, 2H), 6.92, 7.23 (ABq, *J*=13.7 Hz, 2H), 7.03—7.25 (m, 5H); IR ($CHCl_3$) 1710, 1638, 1530, 1360, 1210 cm^{-1}; MS *m/z* (rel. int. %) 274 (M^+, 40), 257 (2), 238 (5), 202 (2), 183 (7), 91 (100), 77 (3), 65 (8); exact MS found *m/z* 274.1306 (Calcd for $C_{15}H_{18}N_2O_3$ M^+: 274.1317). *Anal*. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.89; H, 6.72; N, 9.96.

3-Benzyl-1-methyl-3-(2-nitrovinyl)piperidin-2-one (**9d**): Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.65—1.90 (m, 4H), 2.97 (s, 3H), 3.00, 3.31 (ABq, *J*=13.5 Hz, 2H), 3.22 (br t, *J*=5.3 Hz, 2H), 6.98, 7.32 (ABq, *J*=13.6 Hz, 2H), 7.08—7.35 (m, 5H); IR ($CHCl_3$) 1710, 1640, 1530, 1350, 740 cm^{-1}; MS *m/z*

(rel. int. %) 274 (M^+, 6), 260 (30), 257 (75) 243 (14), 228 (65), 213 (45), 202 (20), 128 (85), 91 (100), 77 (3), 65 (10); exact MS *m*/*z* 274.1307 (Calcd for $C_{15}H_{18}N_2O_3$ M^+: 274.1318).

(*S*)-2-Diphenylhydroxymethyl-1-(2-nitrovinyl)pyrrolidine (**12**): A mixture of (*S*)-2-(diphenylhydroxymethyl)pyrrolidine[13,14] (730 g, 2.9 mmol) and **3** (460 mg, 2.9 mmol) in MeOH (10 ml) was heated under reflux for 10 h. Solvent was removed and the residue was purified by SiO_2 column chromatography (EtOAc : hexane = 3 : 7) to give **12** (660 mg, 80% yield) as yellow needles: mp 205—206 °C (ethanol); $[\alpha]_D^{20}$ −243 (*c* = 1.0, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.38—1.65 (m, 1H), 1.70—1.91 (m, 1H), 2.02—2.35 (m, 2H), 2.95—3.13 (m, 2H), 3.03 (br d, *J* = 8.1 Hz, 1H), 4.69 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.47 (d, *J* = 10.8 Hz, 1H), 7.20—7.45 (m, 10H), 7.84 (d, *J* = 10.8 Hz, 1H); IR (KBr) 3485, 2984, 1615, 1448, 1401, 1328, 1251 cm^{-1}; MS *m*/*z* (rel. int. %) 325 (MH^+, 12), 306 (12), 263 (13), 235 (15), 182 (63), 165 (36), 141 (58), 125 (52), 105 (100), 96 (95), 77 (60); exact MS *m*/*z* 325.1547 (Calcd for $C_{19}H_{20}N_2O_3$ MH^+: 325.1552). *Anal*. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.25; H, 6.23; N, 8.60.

References and Notes

1) *a*) Fuji K., *Chem. Rev.*, **93**, 2037—2066 (1993); *b*) Corey E. J., Guzman-Perez A., *Angew. Chem. Int. Ed. Engl.*, **37**, 388—401 (1998).
2) *a*) Fuji K., Node M., Nagasawa H., Naniwa Y., Terada S., *J. Am. Chem. Soc.*, **108**, 3855—3856 (1986); *b*) Fuji K., Node M., Nagasawa H., Naniwa Y., Taga T., Machida K., Snatzke G., *ibid*., **111**, 7921—7925 (1989).
3) *a*) Node M., Nagasawa H., Fuji K., *J. Am. Chem. Soc.*, **109**, 7901—7903 (1987); *b*) *Idem*, *J. Org. Chem.*, **55**, 517—521 (1990).
4) Node M., Hao X.-J., Fuji K., *Chem. Lett.*, **1991**, 57—60.
5) *a*) Node M., Hao X.-J., Nagasawa H., Fuji K., *Tetrahedron Lett.*, **30**, 4141—4144 (1989); *b*) Hao X.-J., Node M., Fuji K., *J. Chem. Soc., Perkin Trans 1*, **1992**, 1505—1509.
6) Fuji K., Zheng S.-Z., Node M., Hao X.-J., *Chem. Pharm. Bull.*, **39**, 202—203 (1991).
7) Fuji K., Kawabata T., Ohmori T., Node M., *Synlett*, **1995**, 367—368.
8) Fuji K., Kawabata T., Ohmori T., Shang M., Node M., *Heterocycles*, **47**, 951—964 (1998).
9) Lakshmaiah G., Kawabata T., Shang M., Fuji K., *J. Org. Chem.* in print.
10) Rubottom G. M., Gruber J. M., Marreno R., Juve H. D., Kim C. W., Jr., *J. Org. Chem.*, **48**, 4940—4944 (1983).
11) Faulques M., Rene L., Royer R., *Synthesis*, **1982**, 260—263.
12) Fouque E., Rousseau G., Seyden-Penne J., *J. Org. Chem.*, **55**, 4807—4817 (1990).
13) *a*) Corey E. J., Bakshi R. K., Shibata S., *J. Am. Chem. Soc.*, **109**, 5551—5553 (1987); *b*) Mathre D. J., Jones T. K., Xavier L. C., Blacklock T. J., Reamer R. A., Mohan J. J., Jones E. T. T., Hoogsteen K., Baum M. W., Grabowski E. J. J., *J. Org. Chem.*, **56**, 751—762 (1991).
14) This material has recently become commercially available from Aldrich.