**Cu(I)-catalyzed Enantioselective [2+2] Cycloaddition of
1-Methoxyallenylsilane with α -Imino Ester:
Chiral Synthesis of α,β -Unsaturated Acylsilanes**

Takahiko Akiyama,* Kazunori Daidouji, and Kohei Fuchibe

*Department of Chemistry, Faculty of Science,
Mejiro, Toshima-ku, Tokyo 171-8588, Japan
takahiko.akiyama@gakushuin.ac.jp*

Supporting Information

General. ^1H (400 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on a Varian Inova 400 spectrometer in CDCl_3 . Tetramethylsilane (TMS) ($\delta = 0$) or CHCl_3 ($\delta = 7.27$) served as internal standard for ^1H NMR, and CDCl_3 was used as an internal standard ($\delta = 77.0$) for ^{13}C NMR. was also used as an internal standard Internal standard IR spectra were recorded on a Shimadzu FT-IR 8600 spectrometer. Mass spectra were measured by GCMS-QP-5000 (Shimadzu) at an ionizing voltage of 70 eV. Purification of the products was performed by column chromatography on silica gel (Fuji sylisia D60L) or preparative TLC on silica gel (Wako gel B-5F). All solvents were purified according to the standard procedures. Elemental analysis (EA) was carried out on EA1110 instrument (Amco Inc.).

Preparation of azetidine 3 (R=SiMe₃) :General procedure

To a suspension of $[\text{Cu}(\text{MeCN})_4]\text{ClO}_4$ (6.5 mg, 0.02 mmol) and α -imino ester **2** (61.3 mg, 0.24 mmol) in THF (2.0 mL) was added 1-methoxyallenylsilane **1** (28.5 mg, 0.02 mmol) at room temperature. After being stirred at the temperature for 2 h, the reaction mixture was quenched by addition of 1N NaHCO_3 solution, extracted with ethyl acetate. The combined organic layers were washed with sat. NaHCO_3 solution, brine, dried over anhydrous Na_2SO_4 , and concentrated to dryness. The crude mixture was purified by TLC (SiO_2 , hexane : ethyl acetate : $\text{Et}_3\text{N} = 81:9:10$ v:v:v) to give α,β -amino ester **3** (R=SiMe₃) (58.9 mg) in 74% yield.

Preparation of acylsilane **4** (R=SiMe₃) from azetidine **3** (R=SiMe₃)

A solution of **3** (R=SiMe₃) (24.3 mg, 0.31 mmol) in THF (5 mL) was added 1N HCl (0.34 ml, 0.34 mmol) at 0 °C. After being stirred at the temperature for 12 h, the reaction mixture was quenched by addition of 1N NaHCO₃ solution, extracted with diethyl ether. The combined organic layers were washed with sat. NaHCO₃ solution, brine, dried over anhydrous Na₂SO₄, and concentrated to dryness. The crude mixture was purified by TLC (SiO₂, hexane : ethyl acetate : Et₃N = 81:9:10/ v:v:v) to give **4**, **4**unsaturated acylsilane **4** (R=SiMe₃) (26.9 mg) in 100% yield.

Asymmetric synthesis of azetidine **3**, General procedure (Table 3, Entry 1)

A suspension of powdered MS4A (100 mg), [Cu(MeCN)₄]RF₄ (6.3 mg, 0.02 mmol), (*R*)-Tol-BINAP (14.9 mg, 0.022 mmol) in THF (0.75 mL) was stirred at room temperature for 30 min. Then the reaction mixture was cooled to -78 °C, and a solution of α -imino ester **2** (51.1 mg, 0.20 mmol) in THF (0.75 mL) and 1-methoxyallenylsilane **1** (R=SiMe₃) (56.9 mg, 0.40 mmol) were added successively. After being stirred at the temperature for 24 h, the reaction mixture was quenched by addition of 1N NaHCO₃ solution, extracted with ethyl acetate. The combined organic layers were washed with sat. NaHCO₃ solution, brine, dried over anhydrous Na₂SO₄, and concentrated to dryness. The crude mixture was purified by TLC (SiO₂, hexane : ethyl acetate : Et₃N = 81:9:10/ v:v:v) to give **3**, α -amino ester **3** (R=SiMe₃) (71.5 mg) in 90% yield. The enantiomeric excess was determined by Daicel Chiralpak AD-H column to be 97% ee.

Ethyl 4-methoxy-3-methylene-4-trimethylsilyl-*N*-(*p*-toluenesulfonyl)-2-azetidinecarboxylate

R_f 0.7 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.20 (9H, s), 1.13 (3H, t, *J*=7.1 Hz), 2.35 (3H, s), 2.92 (3H, s), 4.09 (2H, q, *J*=7.1 Hz), 4.97 (1H, dd, *J*=2.7, 2.4 Hz), 5.06 (1H, dd, *J*=2.4, 1.6 Hz), 5.35 (1H, dd, *J*=1.6, 2.7 Hz), 7.22 (2H, d, *J*=8.2 Hz), 7.77 (2H, d, *J*=8.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ = -3.48, 14.06, 21.48, 50.02, 61.35, 63.35, 104.22, 110.70, 127.31, 129.05, 138.45, 138.75, 143.06,

166.96; IR(CHCl₃) 3028, 2966, 2939, 1732, 1687, 1598, 1463, 1371, 1365, 1336, 1290, 1249, 1232, 1199, 1089, 1041, 1021, 989, 948, 900 cm⁻¹.

Ethyl 3-methylene-4-trimethylsilyl-4-oxo-2-*N*-(*p*-toluenesulfonyl)amino-butanoate

Rf 0.5 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ 0.27 (9H, s), 1.09 (3H, t, *J*=7.1 Hz), 2.40 (3H, s), 3.99 (1H, dq, *J*=10.7, 7.1 Hz), 4.06 (1H, dq, *J*=10.7, 7.1 Hz), 4.59 (1H, d, *J*=7.7 Hz), 5.65 (1H, d, *J*=7.7 Hz), 6.13 (1H, s), 6.28 (1H, s), 7.27 (2H, d, *J*=8.1 Hz), 7.70 (2H, d, *J*=8.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ -1.73, 13.78, 21.45, 56.37, 62.05, 127.17, 129.44, 131.61, 137.17, 143.37, 148.11, 169.97, 235.26; IR(CHCl₃) 3683, 3026, 2977, 2399, 1737, 1600, 1521, 1423, 1333, 1228, 1205, 1163, 1045, 1029 cm⁻¹; Found: C, 53.72; H, 6.67; N, 3.60; S, 8.44%. Calcd for C₁₇H₂₅O₅NSSi: C, 53.24; H, 6.57; N, 3.65; S, 8.36%; $[\alpha]_D^{22}$ +98.5 (c 1.0, CHCl₃) (*S*, 86% ee).

Ethyl 4-methoxy-3-methylene-4-dimethylphenylsilyl-2-*N*-(*p*-toluenesulfonyl)-2-azetidinecarboxylate

Rf 0.7 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ 0.61 (3H, s), 0.65 (3H, s), 1.16 (3H, t, *J*=7.1 Hz), 2.42 (3H, s), 2.96 (3H, s), 4.13 (2H, q, *J*=7.14 Hz), 4.39 (1H, dd, *J*=2.5, 1.6 Hz), 4.92 (1H, dd, *J*=2.5, 2.0 Hz), 5.23 (1H, dd, *J*=1.6, 2.0 Hz), 7.28 (2H, d, *J*=8.1 Hz), 7.32-7.39 (3H, m), 7.63 (2H, d, *J*=7.9 Hz), 7.7 (2H, d, *J*=8.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ -6.88, -6.19, 14.12, 18.46, 27.35, 49.68, 61.36, 64.10, 111.17, 127.45, 128.94, 133.22, 133.81, 134.15, 136.76, 138.74, 139.18, 142.95, 167.08.

Ethyl 3-methylene-4-dimethylphenylsilyl-4-oxo-2-*N*-(*p*-toluenesulfonyl)aminobutanoate

Rf 0.5 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.47 (3H, s), 0.48 (3H, s), 1.07 (3H, t, *J*=7.1 Hz), 2.41 (3H, s), 4.00 (2H, dq, *J*=0.9, 7.1 Hz), 4.57 (1H, d, *J*=7.7 Hz), 5.66 (1H, d, *J*=7.7 Hz), 5.98 (1H, s), 6.14 (1H, s), 7.26 (2H, d, *J*=8.5 Hz), 7.35-7.42 (3H, m), 7.47 (2H, d, *J*=7.7 Hz), 7.68 (2H, d, *J*=8.5); ¹³C NMR (100 MHz, CDCl₃) δ = -3.32, -3.29, 13.76, 21.48, 56.24, 62.08, 127.20, 128.25, 129.50, 129.99, 132.86, 133.77, 134.91, 137.16, 143.41, 148.10, 169.03, 233.56; IR(CHCl₃) 3030, 1739, 1601, 1429, 1406, 1369, 1338, 1253, 1161, 1111, 1094 cm⁻¹; Found: ¹C, 59.30; H, 6.15; N, 3.11; S, 7.25%. Calcd for C₂₂H₂₇O₅NSSi: C, 59.30; H, 6.11; N, 3.14; S, 7.20%; [α]_D²² +127.3 (c 1.0, CHCl₃) (*S*, 89% ee).

Ethyl 4-methoxy-3-methylene-4-*tert*-butyldimethylsilyl-2-*N*-(*p*-toluenesulfonyl)-2-azetidinecarboxylate

Rf 0.7 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.28 (s, 3H), 0.34 (s, 3H), 1.02 (s, 9H), 2.42 (s, 3H), 2.94 (s, 3H), 4.15 (q, 2H, *J*=7.1 Hz), 5.09 (dd, 1H, *J*=2.1, 2.5 Hz), 5.20 (dd, 1H, *J*=2.5, 1.0 Hz), 5.42 (dd, 1H, *J*=1.0, 2.1 Hz), 7.28 (d, 2H, *J*=6.6 Hz), 7.82 (d, 2H, *J*=6.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ = -6.88, -6.19, 14.12, 18.46, 21.53, 27.35, 28.17, 49.68, 61.36, 64.10, 111.17, 127.45, 128.94, 138.74, 139.18, 142.95, 167.08.

Ethyl 3-methylene-4-*tert*-butyldimethylsilyl-4-oxo-2-*N*-(*p*-toluenesulfonyl)aminobutanoate

Rf 0.5 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.19 (s, 3H), 0.20 (s, 3H), 0.87 (s, 9H), 1.09 (t, 3H, *J*=7.1 Hz), 2.40 (s, 3H), 4.03 (q, 2H, *J*=7.1 Hz), 4.56 (d, 1H, *J*=7.7 Hz), 5.66 (d, 1H, *J*=7.7 Hz), 6.17 (s, 1H), 6.29 (s, 1H), 7.27 (d,

2H, $J=7.7$ Hz), 7.68 (d, 2H, $J=7.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ = -5.24, -4.90, 13.79, 16.70, 21.46, 26.42, 29.66, 56.64, 62.09, 127.23, 129.51, 132.55, 143.38, 149.63, 169.11, 234.87; IR(CHCl_3) 3025, 1750, 1613, 1434, 1422, 1311, 1308, 1254, 1177, 1114, 1090 cm^{-1} ; Found: C, 56.15; H, 7.25; N, 3.11; S, 7.25%. Calcd for $\text{C}_{20}\text{H}_{31}\text{O}_5\text{NSSi}$: C, 56.44; H, 7.34; N, 3.29; S, 7.53%; $[\alpha]_{\text{D}}^{22} +99.3$ (c 1.0, CHCl_3) (*S*, 92% ee).

Ethyl 4-methoxy-3-methylene-4-triisopropylsilyl-2-*N*-(*p*-toluenesulfonyl)-2-azetidinecarboxylate

Rf 0.7 (toluene : ethyl acetate, 10 % Et_3N); ^1H NMR (400 MHz, CDCl_3) δ = 1.03-1.27 (m, 21H), 1.56-1.62 (m, 3H), 2.42 (s, 3H), 2.90 (s, 3H), 4.18 (q, 2H, $J=6.7$ Hz), 5.11-5.13 (m, 1H), 5.15-5.17 (m, 1H), 5.40-5.41 (m, 1H), 7.27 (d, 2H, $J=8.2$ Hz), 7.8 (d, 2H, $J=8.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ = 11.99, 14.17, 19.71, 20.03, 21.54, 48.91, 61.39, 64.59, 110.87, 127.53, 128.89, 138.96, 139.49, 142.89, 167.17.

Ethyl 3-methylene-4-triisopropylsilyl-4-oxo-2-*N*-(*p*-toluenesulfonyl)aminobutanoate

Rf 0.5 (toluene : ethyl acetate, 10 % Et_3N); ^1H NMR (400 MHz, CDCl_3) δ = 1.00-1.13 (m, 21H), 1.26-1.34 (m, 3H), 2.40 (s, 3H), 4.01 (q, 2H, $J=7.1$ Hz), 4.58 (d, 1H, $J=7.7$ Hz), 5.68 (d, 1H, $J=7.7$ Hz), 6.11 (s, 1H), 6.29 (s, 1H), 7.26 (d, 2H, $J=8.2$ Hz), 7.71 (d, 2H, $J=8.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ = 12.13, 13.77, 18.51, 21.45, 56.47, 62.05, 127.17, 129.54, 131.55, 137.21, 143.38, 150.46, 169.28, 234.87; IR(CHCl_3) 3026, 3014, 2947, 2870, 1740, 1597, 1467, 1369, 1339, 1256, 1225, 1161, 1094, 1022 cm^{-1} ; Found: C, 59.02; H, 8.11; N, 3.08; S, 6.85%. Calcd for $\text{C}_{23}\text{H}_{37}\text{O}_5\text{NSSi}$: C, 59.07; H, 7.97; N, 2.99; S, 6.86%; $[\alpha]_{\text{D}}^{22} +62.2$ (c 1.0, CHCl_3) (*S*, 60% ee).

Ethyl 4-triethylgermyl-4-methoxy-3-methylene-*N*-(*p*-toluenesulfonyl)-2-azetidinecarboxylate

Rf 0.7 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.95-1.15 (15H, m), 1.20 (3H, t, *J*=7.1 Hz), 2.42 (3H, s), 2.95 (3H, s), 4.15 (2H, q, *J*=7.1 Hz), 5.04 (1H, dd, *J*=2.7, 2.1 Hz), 5.12 (1H, dd, *J*=1.6, 2.7 Hz), 5.37 (1H, dd, *J*=2.1, 1.6 Hz), 7.28 (2H, d, *J*=8.1 Hz), 7.84 (2H, d, *J*=8.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ =4.01, 5.39, 9.16, 14.08, 21.52, 49.55, 61.37, 63.04, 109.69, 127.30, 129.07, 138.48, 139.71, 143.06, 167.00.

Ethyl 4-triethylgermyl-3-methylene-4-oxo-2-*N*-(*p*-toluenesulfonyl)aminobutanoate

Rf 0.5 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.94-1.10 (18H, m), 2.40 (s, 3H), 4.02 (q, 2H, *J*=7.1 Hz), 4.60 (d, 1H, *J*=7.6 Hz), 5.66 (d, 1H, *J*=7.6 Hz), 6.06 (s, 1H), 6.33 (s, 1H), 7.26 (d, 2H, *J*=8.2 Hz), 7.69 (d, 2H, *J*=8.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ =5.38, 8.84, 13.74, 21.44, 55.96, 62.09, 127.17, 129.48, 132.69, 143.40, 149.15, 169.02, 235.27; IR(CHCl₃) 3672, 3025, 2988, 2344, 1740, 1610, 1522, 1422, 1317, 1233, 1211, 1162, 1055, 1019 cm⁻¹; Found: C, 51.10; H, 6.67; N, 3.11; S, 6.85%. Calcd for C₂₀H₃₁O₅NSGe: C, 51.09; H, 6.65; N, 2.98; S, 6.82%; $[\alpha]_D^{22}$ +94.3 (c 1.0, CHCl₃) (*S*, 75% ee).

Ethyl 4-oxo-2-*N*-(*p*-toluenesulfonyl)amino-4-trimethylsilylbutanoate

Rf 0.6 (toluene : ethyl acetate, 10 % Et₃N); ¹H NMR (400 MHz, CDCl₃) δ =0.18 (s, 9H) 1.07 (3H, t, *J*=7.1 Hz), 2.40 (s, 3H), 3.19 (1H, dd, *J*=14.3, 4.2 Hz), 3.25 (1H, dd, *J*=14.3, 4.2 Hz), 3.95-4.04 (3H, m), 5.56 (1H, d, *J*=7.7 Hz), 7.28 (2H, d, *J*=8.4 Hz), 7.72 (2H, d, *J*=8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ =-3.68, 13.73, 21.43, 50.59, 50.81, 61.77, 127.17, 129.32, 136.90, 143.45, 170.40, 244.71; IR(CHCl₃) 3030, 1734, 1645, 1342, 1253, 1217, 1207, 1161, 1093 cm⁻¹; Found: ¹C, 51.72; H, 6.78; N, 3.77; S,

8.63%. Calcd for $C_{16}H_{25}O_5NSSi$: C, 51.72; H, 6.78; N, 3.77; S, 8.63%.

Reference

1. Elemental analysis was carried out several times and the best result is shown.

daidouji
2-4-frel
Date: Jan 23 02
Solvent: CDCl3
Ambient temperature
User: vnmr1
UNITY_INOVA-400 "varian"
PULSE SEQUENCE
Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz
8 repetitions
OBSERVE H1 399.9552057 MHZ
DATA PROCESSING
FT size 65536
Total time 1 minute

daidouji
2-22-crude
Date: Feb 11 02
Solvent: CDCl3
Ambient temperature
User: Vnmr1
UNITY_INOVA-400 "varian"
PULSE SEQUENCE
Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz
8 repetitions
OBSERVE H1 399.9552039 MHz
DATA PROCESSING
F1 size 65536
Total time 1 minute

daidouji
2-93-fra1

Date: Jul 18 02

Solvent: CDCl₃

Ambient temperature

User: vnmr1

UNITY_INOVA-400 "varian"

PULSE SEQUENCE

Relax delay 1.496 sec

Pulse 45.0 degrees

Acq. time 3.504 sec

Width 5999.7 Hz

8 repetitions

OBSERVE H1

399.9551756 MHz

DATA PROCESSING

FI size 65536

Total time 1 minute

daidouji
4-7-fra1

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: vnmr1
INOVA-400 "u400"

Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz
8 repetitions
OBSERVE H1, 399.9551758 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 40 sec

daidouji
tbs

Pulse Sequence: s2pu1

Solvent: CDCl3

Ambient temperature

User: vnmr1

INOVA-400 "u400"

Relax. delay 1.496 sec

Pulse 45.0 degrees

Acq. time 3.504 sec

Width 5999.7 Hz

8 repetitions

OBSERVE H1, 399.9551758 MHz

DATA PROCESSING

FT size 65536

Total time 0 min, 40 sec

daidouji
4-31-fra1

Pulse Sequence: s2pul

Solvent: CDCl₃

Ambient temperature

User: Vnmr1

INOVA-400 "u400"

Relax. delay 1.496 sec

Pulse 45.0 degrees

Acq. time 3.504 sec

Width 5999.7 Hz

8 repetitions

OBSERVE H1, 399.9551762 MHz

DATA PROCESSING

FT size 65536

Total time 0 min, 40 sec

daidouji
4-35-crude

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: vnmr1
INOVA-400 "u400"

Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz

8 repetitions
OBSERVE H1, 399.9551758 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 40 sec

daidouji
3-109-fra1

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
USC: vnmr1
INOVA-400 "ud00"

Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz
8 repetitions
OBSERVE H1, 399.9551763 MHz
DATA PROCESSING
FT size 65336
Total time 0 min, 40 sec

daidouji
Et3Ge

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: vnmr1
INOVA-400 "u400"

Relax. delay 1.496 sec
Pulse 45.0 degrees
Acq. time 3.504 sec
Width 5999.7 Hz
8 repetitions
OBSERVED F1 399.9551754 MHz
DATA PROCESSING
F1 size 65536
Total time 0 min, 40 sec