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Diastereoselective Synthesis of *anti*-1,2-Aminoalcohol by Palladium(II) Catalyzed Aza-Claisen Rearrangement

Youn-Jung Yoon, Myung-Hee Chun, Jae-Eun Joo, Yong-Hyun Kim, Chang-Young Oh, Kee-Young Lee, Yiu-Suk Lee, and Won-Hun Ham

College of Pharmacy, SungKyunKwan University, Suwon 440-746, Korea

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In this study, a highly diastereoselective synthesis of *anti*-1,2-aminoalcohol was explored starting from L-amino acids as chiral sources. The higher yield and diastereoselectivity was shown when the aza-Claisen rearrangement was performed with allylic trichloroacetimidate **6a** in the presence of palldium(II) catalyst.

Key words: Aminoalcohol, Allylic trichloroacetimidate, aza-Claisen rearrangement, Palladium, Stereocontrol

INTRODUCTION

The Cope and Claisen [3,3]-rearrangements are among the important transformations in modern synthetic organic chemistry (Lutz, 1984). Although there has been increasing interest in the aza-Claisen rearrangements catalyzed by transition metal complexes, especially divalent palladium species, such reactions have so far been limited to allyl imidates or their related polyhetero compounds. (Overman, 1984; Schenck, T. G. *et al*, 1985; Metz *et al*, 1992; Gonda, J. *et al*, 1993; Anderson *et al*, 2003).

The rearrangement of allylic imidates and in particular of allylic trichloroacetimidates, which was reported for the first time by Overman (Overman, 1976), has been the subject of active investigations (Martin *et al*, 1999) these last few years since this transposition allows the synthesis of allylic amines that are useful synthons for the preparation of various nitrogen-containing compounds.

Based on the observation of high 1,2-stereoinduction (Oehrlein *et al*, 1989; Gonda *et al*, 1993) in [3,3]-sigmatropic rearrangements, we investigated the aza-Claisen rearrangement of allylic trichloracetimidates under Overmans catalytic conditions (Overman, 1980). As the result of this investigations indicate, we report a highly diastereoselective synthesis of *anti*-1,2-aminoalcohol starting from L-amino acids as chiral sources.

Correspondence to: Won-Hun Ham, College of Pharmacy, SungKyunKwan University, Suwon 440-746, Korea
Tel: 82-31-290-7706, Fax: 82-31-292-8800
E-mail: whham@speed.skku.ac.kr

MATERIALS AND METHODS

General procedure for hydroxylation of α-amino acid

To a stirred solution of L-amino acid **1a-c** (182 mmol) in 1 N H_2SO_4 (274 mL) at 0°C, a solution of 18.8 g (273 mmol) of $NaNO_2$ water (66 mL) were added over 2.5 h. The temperature was maintained below 5°C during the addition. The solution was saturated with $(NH_4)_2SO_4$ and extracted with ether (75 mL×3). The ether layers were washed with water and brine, dried with $MgSO_4$, filtered and concentrated. The residue was used for the next step without further purification.

The crude acid (48.1 mmol) was dissolved in methanol (80 mL). Dry HCl gas was passed until the reaction was completed and then, bubbled with N_2. The solvents were evaporated under reduced pressure. The reaction mixture was diluted with EtOAc (50 mL), washed with 0.5 N $NaHCO_3$ (20 mL×2) and brine, dried with $MgSO_4$, filtered and evaporated *in vacuo*. The residue was used without further purification, and the analytical sample was purified by flash chromatography.

(*S*)-Methyl 2-hydroxy-3-phenylpropanoate (2a)

Yield 68%; $[\alpha]_D^{25}$ 11.98 (*c* 1.0, CH_2Cl_2); mp 46.5~48.0°C; IR (neat) 3474, 1739, 1214 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.96 (dd, *J* = 6.8, 13.9 Hz, 1H), 3.13 (dd, *J* = 4.4, 13.9 Hz, 1H), 3.77 (s, 3H), 4.46 (dd, *J* = 4.4, 6.8 Hz, 1H), 7.20-7.32 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 40.56, 52.48, 71.27, 126.93, 128.93, 128.45, 129.47, 136.29, 174.58.

(*S*)-Methyl 2-hydroxy-4-methylpentanoate (2b)
Yield 75%; $[\alpha]_D^{25}$ 1.82 (c 1.0, CH_2Cl_2); IR (neat) 3370, 1727, 1220 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.95 (m, 6H), 1.58 (m, 2H), 1.90 (m, 1H), 2.67 (br s, 1H), 3.79 (s, 3H), 4.22 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.78, 23.45, 43.72, 52.66, 69.32, 176.56.

General procedure for preparation of TBS-protected α-hydroxy ester
To a stirred solution of **2a-c** (43.3 mmol) in DMF (100 mL), imidazole (6.48 g, 5.22 mmol) and *tert*-butyldimethylsilyl chloride (TBDMS-Cl) (7.83 g, 51.9 mmol) were added, and stirring was allowed to continue for 5 h. The reaction mixture was quenched with H_2O (200 mL), extracted with ethyl acetate (50 mL×2), which was followed by washing with brine, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:15).

(*S*)-Methyl 2-(*tert*-butyldimethylsilanyloxy)-3-phenylpropanoate (3a)
Yield 98%; $[\alpha]_D^{25}$ 26.17 (*c* 1.0, CH_2Cl_2); IR (neat) 1758, 1255, 1130 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ -0.22 (s, 3H), -0.13 (s, 3H), 0.78 (s, 9H), 2.88 (dd, *J* = 9.0, 13.0 Hz, 1H), 3.07 (dd, *J* = 4.0, 13.0 Hz, 1H), 3.72 (s, 3H), 4.43 (dd, *J* = 4.0, 9.0 Hz, 1H), 7.19-7.29 (m, 5H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -4.89, 18.92, 26.27, 42.34, 52.57, 74.56, 127.32, 128.90, 130.50, 138.14, 174.32.

(*S*)-Methyl 2-(*tert*-butyldimethylsilanyloxy)-4-methylpentanoate (3b)
Yield 90%; $[\alpha]_D^{25}$ 28.68 (*c* 0.5, CH_2Cl_2); IR (neat) 1757, 1258, 1148 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.85 (s, 15H), 1.45 (m, 1H), 1.65(m, 1H), 1.78 (m, 1H), 3.68 (s, 3H), 4.18 (dd, *J* = 4.2, 4.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.13, 14.44, 18.50, 21.84, 24.26, 44.39, 51.88, 71.07, 174.55.

(*S*)-Methyl 2,3-(di-*tert*-butyldimethylsilanyloxy)-propanoate (3c)
Yield 87%; $[\alpha]_D^{25}$ 9.76 (*c* 1.0, CH_2Cl_2); IR (neat) 1760, 1257, 1125 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.07 (m, 12H), 0.88 (m, 18H), 3.71 (s, 3H), 3.73 (dd, *J* = 6.2, 10.0 Hz , 1H), 3.81 (dd, *J* = 4.8, 10.0 Hz, 1H), 4.27 (dd, *J* = 4.8, 6.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.14, 18.60, 52.01, 66.21, 74.26, 172.74.

Procedure for preparation of Methyl-protected α-hydroxy ester; (*S*)-Methyl 2-methoxy-3-phenylpropanoate (9a)
To a solution of **2a** (2.00 g, 11.1 mmol) and sodium hydride (399 mg, 13.3 mmol, 80% in mineral oil) in anhydrous THF (30 mL) at 50°C, methyl iodide (1.04 mL, 16.7 mmol) was added dropwise with stirring. The reaction was stirred for 3 h and then was quenched by dropwise addition of water. The mixture was diluted with EtOAc (100 mL), washed with water and brine, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:6) to give a 74 % yield of **9a**.
IR (neat) 1758, 1240, 1110 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.02 (m, 2H), 3.35 (s, 3H), 3.72 (s, 3H), 3.98 (dd, *J* = 5.1, 7.8 Hz, 1H), 7.21-7.31 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 39.18, 51.92, 58.36, 81.73, 126.72, 128.36, 129.29, 139.91, 172.58.

Procedure for preparation of MOM-protected α-hydroxy ester; (*S*)-methyl 2-(methoxymethoxy)-3-phenylpropanoate (9b)
To a solution of **2a** (3.00 g, 16.7 mmol) and diisopropylethylamine (4.70 mL, 33.3 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0°C, chloromethyl methyl ether (6.32 mL, 83.3 mmol) was added dropwise with stirring. After 30 min, the ice bath was removed, and the reaction was stirred for 15 h. The reaction mixture was diluted with EtOAc (200 mL) and was washed successively with 1 N HCl (30 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine. The mixture was then dried with $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:10) to give a 78 % yield of **9b**.
IR (neat) 1755, 1217, 1105 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.98 (dd, *J* = 9.0 , 13.9 Hz, 1H), 3.07 (s, 3H), 3.10 (dd, *J* = 4.4, 13.9 Hz,1 H), 3.73 (s, 3H), 4.43 (dd, *J* = 4.4, 9.0 Hz, 1H), 4.51 (d, *J* = 7.0 Hz, 1H), 4.63 (d, *J* = 7.0 Hz, 1H), 7.22-7.31 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 39.18, 52.01, 55.70 96.01, 126.73, 128.35, 129.45, 136.98, 172.54.

Procedure for preparation of BOM-protected α-hydroxy ester; (*S*)-Methyl 2-(benzyloxymethoxy)-3-phenyl propanoate (9c)
This compound was obtained by the above procedure (**9b**) using benzyl chloromethylether, and the residue was purified by flash chromatography (ethyl acetate:hexane = 1:6) to give a 76 % yield of **9c**.
IR (neat) 1760, 1230, 1190 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.99 (dd, *J* = 4.0, 13.0 Hz, 1H), 3.11 (dd, *J* = 9.0, 13.0 Hz, 1H), 3.69 (s, 3H), 4.17 (d, *J* = 11.5 Hz, 1H), 4.29 (d, *J* = 11.5 Hz, 1H), 4.42 (dd, *J* = 4.0, 9.0 Hz, 1H), 4.66 (d, *J* = 7.0 Hz, 1H), 4.75 (d, *J* = 7.0 Hz, 1H), 7.14-7.31 (m, 10H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 39.90, 51.72, 70.34, 94.60, 127.51, 128.39, 128.62, 129.02, 129.12, 130.24, 137.78, 138.10, 173.24.

General procedure for preparation of α,β-unsaturated methyl ester
To a stirred solution of **3a-c** (34.0 mmol) in diethyl ether

(60 mL) at -78°C, diisobutylaluminum hydride (DIBAL-H) (1.0 M solution in hexane, 37.4 mL, 37.4 mmol) was added, and the resultant mixture was stirred for 1 h before it was quenched by the addition of MeOH (11.2 mL). The reaction mixture was allowed to warm to r.t. and was poured into a 30% sodium potassium tartrate solution (50 mL). After being stirred for 0.5 h, the product was extracted with diethyl ether. The combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated *in vacuo*. The crude aldehyde was immediately used for the next step without further purification.

To a stirred solution of LiCl (1.73 g, 40.8 mmol) in CH_3CN (50 mL), trimethylphosphonoacetate (5.92 mL, 34.0 mmol) and diisopropylethylamine (6.61 mL, 40.8 mmol) were added, and stirring was allowed to continue for 1 h. The crude aldehyde in CH_3CN (10 mL) was added to the reaction mixture, and the mixture was stirred for 2 h. Then, the reaction mixture was quenched with H_2O (50 mL), diluted with EtOAc (100 mL), washed with 0.5 N HCl and brine, and dried with $MgSO_4$. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:10).

(*S*)-Methyl 4-(*tert*-butyldimethylsilanyloxy)-5-phenyl-2-pentenoate (4a)

Yield 75%; $[\alpha]_D^{25}$ +2.37 (*c* 1.0, CH_2Cl_2); IR (neat) 1726, 1660, 1275 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ -0.18 (s, 3H), -0.02 (s, 3H), 0.93 (s, 9H), 2.80 (dd, *J* = 7.5, 13.2 Hz, 1H), 2.89 (dd, *J* = 5.4, 13.2 Hz, 1H), 3.76 (s, 3H), 4.51 (m, 1H), 6.06 (dd, *J* = 1.8, 15.6 Hz, 1H), 7.05 (dd. *J* = 4.5, 15.6 Hz, 1H), 7.22-7.36 (m, 5H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.19, -4.65, 18.41, 26.09, 44.55, 51.78, 119.93, 126.79, 128.52, 130.15, 150.84, 167.26.

(*S*)-Methyl 4-(*tert*-butyldimethylsilanyloxy)-6-methyl-2-heptenoate (4b)

Yield 87%; $[\alpha]_D^{25}$ -3.26 (*c* 1.0, CH_2Cl_2); IR (neat) 1729, 1660, 1260 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.94 (m, 15H), 1.37 (m, 1H), 1.51 (m, 3H), 1.75 (m, 1H), 3.78 (s, 3H), 4.36 (m, 3H), 6.01 (dd, *J* = 1.8, 15.3 Hz, 1H), 6.98 (dd, *J* = 4.8, 15.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -4.66, -4.18, 18.43, 22.88, 23.39, 24.46, 26.09, 47.03, 51.78, 70.44, 119.36, 151.93, 167.43.

(S)-Methyl 4,5-Bis-(*tert*-butyldimethylsilanyloxy)-2-pentenoate (4c)

Yield 90%; $[\alpha]_D^{25}$ +25.51 (*c* 1.0, CH_2Cl_2); IR (neat) 1730, 1661, 1260 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.04 (m, 12H), 0.86 (m, 18H), 3.46 (dd, *J* = 6.3, 9.9 Hz,1H), 3.56 (dd, *J* = 6.3, 9.9 Hz, 1H), 3.71 (s, 3H), 4.31 (m, 1H), 6.04 (dd, *J* = 3.9, 15.3 Hz, 1H), 7.01 (dd, *J* = 4.2, 15.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.20, -4.54, 18.47, 26.06, 51.70, 67.45, 120.63, 149.10, 167.18.

General procedure for preparation of allylic alcohol

To a stirred solution of **4a-c** (21.8 mmol) in diethyl ether (120 mL) at -78°C, diisobutylaluminum hydride (DIBAL-H) (1.0 M solution in hexane, 40.1 mL, 40.1 mmol) was added, and the resultant mixture was stirred for 1 h before it was quenched by the addition of MeOH (12 mL). The reaction mixture was allowed to warm to r.t. and was poured into a 30% sodium potassium tartrate solution (50 mL). After being stirred for 0.5 h, the product was extracted with diethyl ether. The combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:6).

(*S*)-4-(*tert*-Butyldimethylsilanyloxy)-5-phenyl-2-penten-ol (5a)

Yield 91%; $[\alpha]_D^{25}$ -2.44 (*c* 0.5, CH_2Cl_2); IR (neat) 3356, 1604, 1080 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ -0.23 (s, 3H), -0.10 (s, 3H), 0.83 (s, 9H), 1.42 (br s, 1H), 2.75 (m, 2H), 4.12 (m, 2H), 4.29 (m, 1H), 5.74 (m, 2H), 7.16-7.28 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.57, -3.99, 18.88, 26.55, 45.83, 63.86, 126.88, 128.75, 129.26, 130.62, 135.38, 139.26.

(*S*)-4-(*tert*-Butyldimethylsilanyloxy)-6-methyl-hept-2-en-1-ol (5b)

Yield 95%; $[\alpha]_D^{25}$ -2.30 (*c* 0.5, CH_2Cl_2); IR (neat) 3340, 1647, 1082 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.93 (m, 15H), 1.30 (m, 1H), 1.48 (m, 1H), 1.73 (m, 1H), 4.20 (m, 3H), 5.78 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -6.1, 22.83, 24.44, 26.17, 63.49, 71.47, 128.50, 135.97.

(*S*)-4,5-Bis-(*tert*-butyldimethylsilanyloxy)-pent-2-en-1-ol (5c)

Yield 94%; $[\alpha]_D^{25}$ +7.98 (*c* 0.5, CH_2Cl_2); IR (neat) 3357, 1730, 1660, 1097 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 12H), 0.90 (s, 18H), 1.59 (br s, 1H), 3.47(dd, *J* = 6.0, 9.6 Hz, 1H), 3.53 (dd, *J* = 6.6, 9.6 Hz, 1H), 4.15 (m, 3H), 5.75 (m, 1H), 5.85 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -4.96, -4.35, 18.57, 26.24, 26.17, 63.51, 68.25, 73.72, 129.90, 132.54.

General procedure for palladium catalyzed aza-Claisen rearrangement

To a solution of **5a-c** (13.7 mmol) in CH_2Cl_2, trichloroacetonitrile (1.51 mL, 15.1 mmol) and 1,8-diazabicyclo [5.4.0]-undec-7-ene (DBU) (200 μL, 1.37 mmol) were added at 0°C, and the mixture was stirred at 0°C for 0.5 h. The reaction mixture was diluted with EtOAc (100 mL) and was washed with 0.5 N HCl. The organic extract was washed with brine, dried with $MgSO_4$, and evaporated *in vacuo*. Purification by silica gel chromatography (ethyl acetate:hexane=1:30) produced allylic trichloroacetimidate **6a-c**, and the compounds were used immediately.

To a solution of **6a-c** (4.58 mmol) in anhydrous THF (10 mL) under N_2, bis(acetonitrle)dichloropalladium(II) (119 mg, 0.458 mmol) was added, and the reaction mixture was stirred for 4-5 h at r.t. The crude reaction mixture was evaporated *in vacuo* and the residue was purified by flash chromatography (ethyl acetate:hexane = 1:30).

(3*R*,4*S*)-4-(*tert*-Butyldimethylsilanyloxy)-5-phenyl-3-(trichloroacetylamino)-1-pentene (7a)

Yield 61%; $[\alpha]_D^{25}$ +8.91 (*c* 1.0, CH_2Cl_2); IR (neat) 3425, 1720, 1498, 830 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ -0.16 (s, 3H), 0.00 (s, 3H), 0.80 (s, 9H), 2.70 (m, 2H), 4.04 (m, 1H), 4.17 (m, 1H), 5.25 (m, 2H), 5.84 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 7.05-7.20 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.68, -4.41, 18.81, 25.80, 40.32, 57.27, 74.50, 92.69, 120.07, 126.82, 128.69, 129.43, 131.67, 136.80, 160.83; HRMS *m/z* calcd for $C_{19}H_{29}Cl_3NO_2Si$ 437.8893, found 437.8901.

(3*R*,4*S*)-4-(*tert*-Butyldimethylsilanyloxy)-6-methyl-3-(trichloroacetylamino)-1-heptene (7b)

Yield 52%; $[\alpha]_D^{25}$ +5.55 (*c* 1.0, CH_2Cl_2); IR (neat) 3430, 1721, 1496, 832 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.10 (m, 6H), 0.83-0.96 (m, 15H), 1.29 (m, 1H), 1.45 (m, 1H), 1.64 (m, 1H), 3.92 (m, 1H), 4.40 (m, 1H), 5.33 (m, 2H), 5.85 (m, 1H), 7.26 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.33, -3.63, 18.25, 22.50, 23.70, 24.43, 26.08, 43.29, 57.72, 72.05, 93.80, 119.70, 132.04, 142.80; HRMS *m/z* calcd for $C_{16}H_{31}Cl_3NO_2Si$ 403.8721, found 403.8729.

(3*R*,4*S*)-4,5-Bis-(*tert*-butyldimethylsilanyloxy)-3-(trichloroacetylamino)-1-pentene (7c)

Yield 71%; $[\alpha]_D^{25}$ +23.06 (*c* 0.5, CH_2Cl_2); IR (neat) 3426, 1723, 1501, 835 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.01-0.20 (m, 12H), 0.82-0.97 (m, 18H), 3.55-3.64 (m, 1H), 3.72-3.83 (m, 2H), 4.60 (m, 1H), 5.31 (m, 2H), 5.79 (m, 1H), 7.65 (d, *J* = 7.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.14, -4.66, -4.14, 18.83, 26.97, 26.23, 57.63, 65.43, 72.85, 98.85, 118.50, 132.64, 161.62; HRMS *m/z* calcd for $C_{19}H_{39}Cl_3NO_3Si_2$ 492.0536, found 492.0546.

(3*R*,4*S*)-4-Methoxy-5-phenyl-3-trichloroacetylamino-1-pentene (11a)

Yield 63%; IR (neat) 3430, 2850, 1758, 1450 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.71 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.94 (dd, J = 14.0, 6.5 Hz, 1H), 3.26 (s, 3H), 3.63 (m, 1H), 4.40 (m, 1H), 5.36 (m, 2H), 5.91 (m, 1H), 7.17-7.33 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 40.55, 57.34, 70.18, 83.57, 95.60, 119.97, 127.00, 128.88, 129.21, 131.04, 136.89, 161.08.

(3*R*,4*S*)-4-(Methoxymethoxy)-5-phenyl-3-trichloroacetylamino-1-pentene (11b)

Yield 58%; IR (neat) 3427, 2890, 1732, 1405 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.79 (dd, *J* = 14.0, 5.0 Hz, 1H), 2.90 (dd, *J* = 14.0, 8.5 Hz, 1H), 3.36 (s, 3H), 3.83 (m, 1H), 4.31 (d, 1H), 4.42 (m, 1H), 4.57 (m, 1H), 5.39 (m, 2H), 5.94 (m, 1H), 7.20-7.32 (m, 5H), 8.17 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 39.07, 56.47, 70.18, 83.57, 95.61, 119.65, 126.76, 127.76, 127.78, 128.52, 128.60, 128.77, 129.29, 129.55, 131.55, 136.80, 161.35.

(3*R*,4*S*)-4-(Benzyloxymethoxy)-5-phenyl-3-trichloroacetylamino-1-pentene (11c)

Yield 57%; IR (neat) 3430, 2910, 1733, 1420 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.78 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.91 (dd, *J* = 14.0, 8.5 Hz, 1H), 3.90 (m, 1H), 4.42 (m, 1H), 4.47 (m, 1H), 4.49 (m, 1H), 4.65 (d, *J* = 12 Hz, 1H), 4.75 (d, *J* = 6.5 Hz, 1H), 5.37 (t, 2H), 5.97 (m, 1H), 7.16-7.35 (m, 10H), 7.99 (d, *J* = 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 39.07, 56.47, 70.18, 83.57, 95.61, 119.65, 126.76, 127.76, 127.78, 128.52, 128.60, 128.77, 129.29, 129.55, 131.55, 136.80, 161.35.

Procedure for preparation of (4*S*,5*R*)-5-benzyl-4-vinyl-2-oxazolidinone (8a)

To a stirred solution of **7a** (3.00 g, 6.87 mmol) in THF (50 mL), tetrabutylammonium fluoride (TBAF) (5.96 mL, 20.6 mmol) was added, and stirring was allowed to continue for 3 h. The reaction mixture was extracted with ethyl acetate followed by washing with brine, drying with $MgSO_4$, and evaporating *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:3).

To a stirred suspension of sodium hydride (4.7 mg, 0.16 mmol, 80% dispersion) in THF (10 mL), crude alcohol (0.16 mmol) in THF (2 mL) was added, and stirring was continued for 10 min. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and was extracted with EtOAc (10 mL×2). The organic layers were washed with brine, dried with $MgSO_4$, filtered, and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate:hexane = 1:1) to give a 78 % yield of **8a**.

$[\alpha]_D^{25}$ -66.26 (*c* 1.0, CH_2Cl_2); mp 106.5~108.0°C; IR (neat) 3256, 1719, 1227 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) d 2.82 (dd, *J* = 4.6, 13.6 Hz, 1H), 3.00 (dd, *J* = 9.2, 13.6 Hz, 1H), 4.43 (t, *J* = 7.6 Hz, 1H), 4.89 (ddd, *J* = 4.6, 7.6, 9.2 Hz, 1H), 5.37 (m, 2H), 5.71 (br s, 1H), 5.90 (m, 1H), 7.22-7.49 (m, 5H); ^{13}C-NMR (75 MHz, $CDCl_3$) d 36.95, 58.46, 80.93, 119.95, 127.12, 128.85, 129.45, 133.20, 136.95, 159.79; HRMS *m/z* calcd for $C_{12}H_{14}Cl_3NO_3$ 204.2487, found 204.2494.

RESULTS AND DISCUSSION

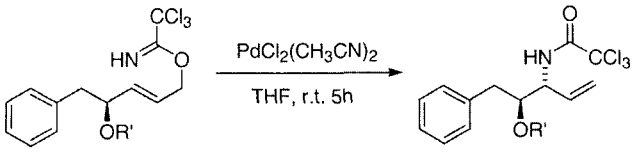
Allylic trichloroacetimidates were synthesized from L-amino acid **1a-c** as shown in Scheme 1. Compounds **1a-c** underwent diazotization reaction using HNO_2 to give α-

hydroxy acid (Mori *et al*, 1976), which was further treated with HCl (g) in methanol to give methyl esters **2a-c**. Further **2a-c** were protected by using *tert*-butyldimethylsilyl chloride to give methyl esters **3a-c**. The reduction of **3a-c** with diisobutylaluminum hydride (DIBAL-H) at -78°C was performed in order to give an aldehyde, which were subjected to Horner-Wardworth-Emmons reaction to afford the α,β-unsaturated methyl esters **4a-c**. **4a-c** were further treated with DIBAL-H at -78°C to afford the corresponding allylic alcohols **5a-c**, which was then followed by the treatment with trichloroacetonitrile and 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) at 0°C to give the key intermediate allylic trichloroacetimidates **6a-c** (Gonda *et al*, 1993).

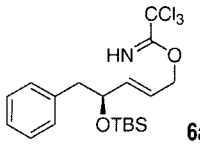
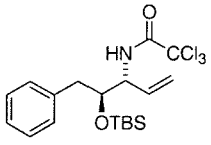
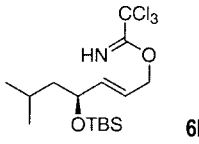
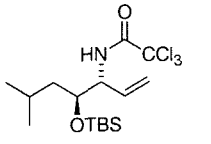
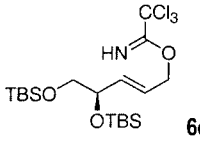
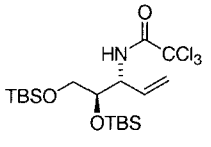
Without further purification, this relatively unstable allylic trichloroacetimidates **6a-c** underwent the aza-Claisen rearrangement in the presence of catalytic amount(10 mol %) of bis(acetonitrile)dichloropalladium(II) in THF at r.t. to afford *anti*-1,2-amino alcohols **7a-c** (Table I) (Doherty *et al*, 1993).

As shown in Table I, **6a** showed high diastereoselectivity (*anti*:*syn* = 10:1). The *anti*-orientation of the 1,2-aminoalcohol moieties of **7a** was confirmed by the preparation of oxazolidinone (**8a**) and the extensive NOE strudy between C_4-H and C_5-H (Scheme 2). But other compounds, such as **6b** and **6c**, failed to show significant diastereoselectivity. The observed stereoselectivity of the palladium-catalyzed aza-Claisen rearrangement can be explained based on the steric bulkiness of the substituents to the point of bond

Table I. Palladium(II) catalyzed aza-Claisen rearrangement of allylic trichloroacetimidates **6a-c**

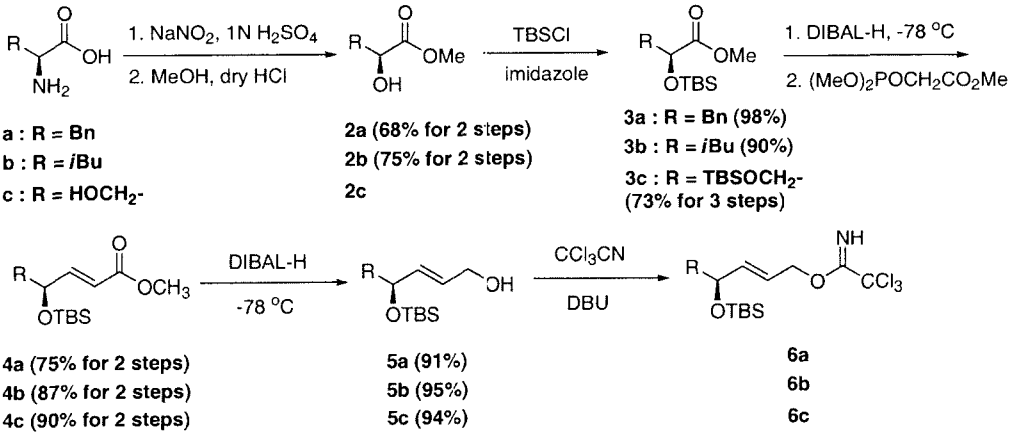


10a-c **11a-c**

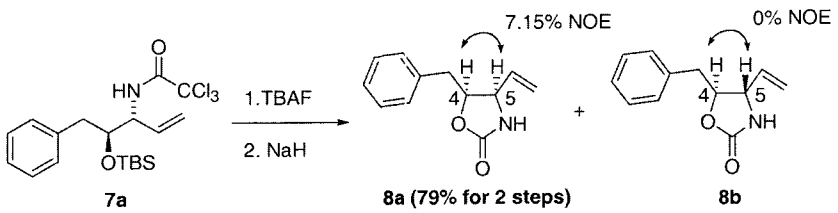
Entry	Substrate	Product	Yield[a], Ratio[b] (*anti*:*syn*)
1	 **6a**	 **7a**	61 % (10:1)
2	 **6b**	 **7b**	52 % (2.2:1)
3	 **6c**	 **7c**	71 % (3:1)

a. Yields for two steps from **5a-c**.

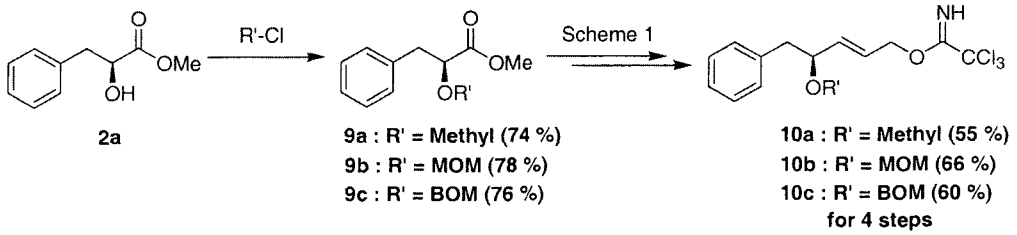
b. Ratio was determined by GC. Condition: Capillary column HP1. Gradient of temperature is 150-280°C. HP5890.



Scheme 1. Synthesis of allylic trichloroacetimidates **6a-c**



Scheme 2. Synthesis of oxazolidinone from **7a**



Scheme 3. Synthesis of allylic trichloroacetimidates **10a-c**

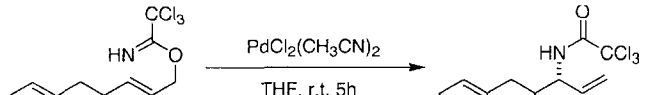
formation(OTBS *vs* R). It can be postulated that the Pd(II) catalyst may form a complex that coordinates to both the imine and olefine bonds in the less hindered side and nucleophilic attack might be expected to occur anti-periplanar to the OTBS group. But the increased bulkiness of R group shown in **6b** and **6c** gave rise to the low selectivity of *anti*-product.

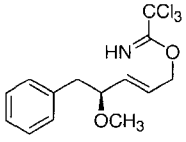
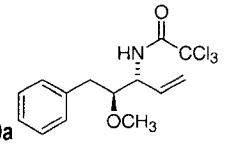
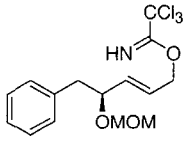
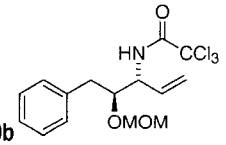
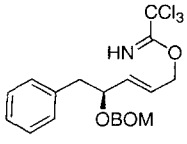
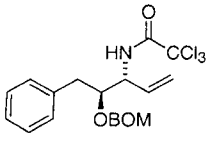
To investigate the influence of protecting groups on the oxygen atom and possibility of chelation between Pd and this oxygen moiety, differently protected esters **9a-c** were prepared from **2a**. Following the same procedure (Scheme 1), allylic trichloroacetimidates **10a-c** were easily synthesized (Scheme 3) and underwent palladium(II) catalyzed aza-Claisen rearrangement.

Contrary to our expectation, the reaction likely did not proceed by chelation mechanism. Because the selectivity was increased in proportion to the bulkiness of protecting group as shown in Table II. That means the diastereoselectivity was influenced only by steric competitiveness between the two substituents to the point of bond formation as shown in the previous examples **6a-c**.

In summary, higher yield and diastereoselectivity were shown when the aza-Claisen rearrangement was performed on allylic trichloroacetimidate **6a** in the presence of palldium(II) catalyst.

Table II. Palladium(II) catalyzed aza-Claisen rearrangement of allylic trichloroacet- imidates **10a-c**



Entry	Substrate	Product	Yield[a], Ratio[b] (*anti*:*syn*)
1	 **10a**	 **11a**	62.7 % (1.38:1)
2	 **10b**	 **11b**	58.4 % (6.2:1)
3	 **10c**	 **11c**	56.6 % (9.95:1)

a. Yields for two steps from corresponding allylic alcohols.
b. Ratio was determined by GC. Condition: Capillary column HP1. Gradient of temperature is 150-280°C. HP5890.

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