Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Catalytic Asymmetric Allylation of Iminoesters and Iminophosphonates with a Variety of Allylsilanes Leading to Enantiomerically Enriched Allylglycine Derivatives

Hiroshi Kiyohara, Yoshitaka Nakamura, Ryosuke Matsubara, and Shū Kobayashi*

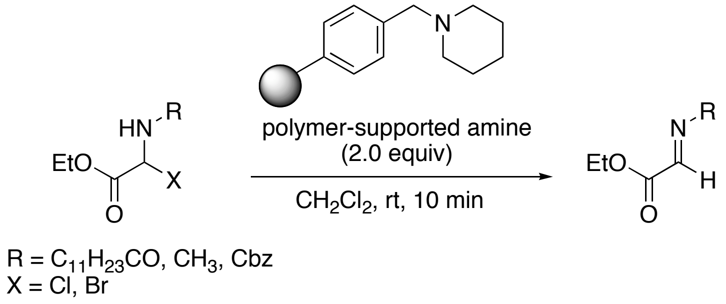
Graduate School of Pharmaceutical Sciences, The University of Tokyo, The HFRE Division, ERATO, Japan Science Technology Agency (JST), Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan

General. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA300, JNM-LA400, JNM-LA500, JNM-ECX-400, or JNM-ECX-600 spectrometer in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^{1}H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. IR spectra were measured on a JASCO FT/IR-610 spectrometer. Optical rotations were measured with a JASCO P-1010 polarimeter. High-performance liquid chromatography was carried out using following apparatus; SHIMADZU LC-10AT (liquid chromatograph), SHIMADZU SPD-10A (UV detector), and SHIMADZU C-R6A Chromatopac. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography was carried out using Wakogel B-5F. All reactions were carried out under argon atmosphere in dried glassware. All solvents were dried and distilled by standard procedures.

Materials

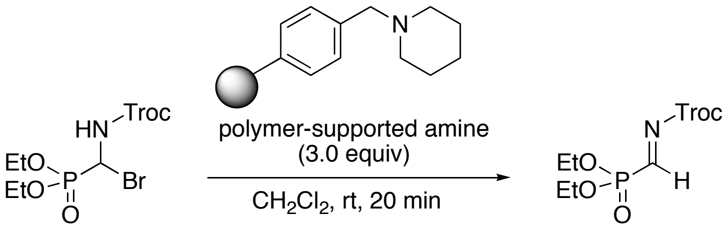
Allylsilanes were prepared following according to literature procedures.[1]

Preparation of α-iminoesters 1 [2]



To a solution of ethyl α-bromo-*N*-acylaminoacetate (0.30 mmol) in CH_2Cl_2 (3.0 mL) was added piperidinomethylpolystyrene (3.70 mmol/g, 243 mg, 0.90 mmol). The reaction mixture was stirred at rt for 10 min, followed by phase separation. The liquid phase was used immediately in the subsequent reactions.

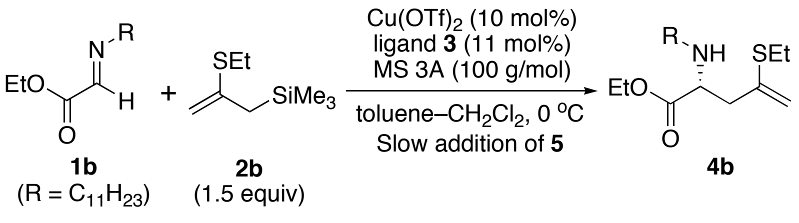
Preparation of α-iminophosphonate 5 [3]



To a solution of diethyl [bromo-(2,2,2-trichloro-ethoxycarbonylamino)-methyl]-phosphonate (0.30 mmol) in CH_2Cl_2 (3.0 mL) was added piperidinomethylpolystyrene (3.70 mmol/g, 243 mg, 0.90 mmol). The reaction mixture was stirred at rt for 20 min, followed by phase separation. The liquid phase was used immediately in the subsequent reactions.

Procedure I: For Catalytic Enantioselective Allylation

Experiments of entries 1-3 in Table 2 and those of entries 1 and 2 in Table 3 were conducted following this procedure.

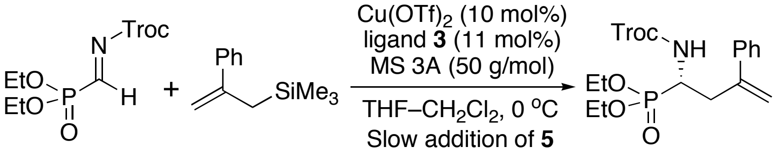


To a mixture of $Cu(OTf)_2$ (9.0 mg, 0.025 mmol) and ligand (*R*,*R*) **3** (13.5 mg, 0.028 mmol) was added toluene (1.5 mL) under an argon atmosphere. The mixture was stirred for 6 h, then molecular sieves 3A (indicated amount) were added, and then the mixture was cooled to 0 °C. An allylsilane **2b** toluene solution (0.17 mM, 0.2 mL) was added. Then, an *N*-acyl-α-iminoester dichloromethane solution (0.125 M, 2.0 mL, 0.25 mmol) and the allylsilane solution (toluene, 0.17 M, 2.0 mL) were slowly added over 0.5 h, and the reaction mixture was stirred for an additional 15 min. Saturated $NaHCO_3$ aq was added, and the mixture was vigorously stirred until the organic phase turned to blue. The aqueous layer was extracted with CH_2Cl_2 (3 times), and then the combined organic phases were washed with brine. The organic phase was dried over anhydrous sodium sulfate. After removal of solvents in vacuo, the crude mixture was purified by chromatography on alumina.[a]

[a] Use of silica gel brought about decomposition of the desired product due to its acidity.

Procedure II: For Catalytic Enantioselective Allylation

Experiments of entries 3- 5 in Table 3 were conducted following this procedure.

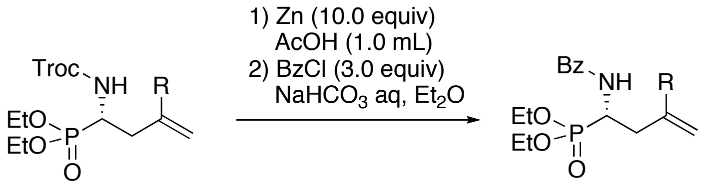


5 **2d** (1.5 equiv) **6c**

To a mixture of $Cu(OTf)_2$ (7.2 mg, 0.020 mmol) and ligand (*R*,*R*) **3** (10.8 mg, 0.022 mmol) was added freshly distilled THF* (2.0 mL) under argon atmosphere. The mixture was vigorously stirred until $Cu(OTf)_2$ had completely dissolved, by which point reaction mixture turned green. Molecular sieves 3A (indicated amount) were added, and the mixture was cooled to 0 °C. Allylsilane **2d** (0.30 mmol, 1.5 equiv to the iminophosphonate) in THF (1.0 mL) was added. Then, an *N*-acyl-α-iminoester dichloromethane solution (0.10 M, 2.0 mL, 0.20 mmol, 1.0 equiv) was slowly added over 4 h, and the reaction mixture was stirred for another 15 min. Saturated $NaHCO_3$ aq was added, and vigorously stirred until the organic phase turned blue. The aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic phases were washed with brine. The organic phase was dried over anhydrous sodium sulfate. After removal of solvents in vacuo, the crude mixture was purified by chromatography on silica gel.

In the experiment of entry 4 in Table 2, dichloromethane was used in place of THF, equivalents of allylsilane should be replaced as is indicated in Table 2, and simultaneous slow addition of allylsilane **2d** (1.0 equiv) is necessary. In the experiments of entries 5-7 in Table 2, dichloromethane was used in place of THF, and equivalents of allylsilane should also be replaced as is indicated in Table 2. In the experiments of entries 8 and 9 in Table 2, equivalents of allylsilane should also be replaced as is indicated in Table 2.

Transformation for determination of enantiomeric excess of the product 6d, 6e



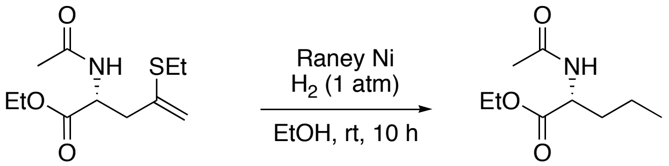
6d: R = CH_3
6e: R = H

7d: R = CH_3 (81%)
7e: R = H (78%)

To a solution of **6d** (39.6 mg, 0.1 mmol) in acetic acid (1.0 mL) was added zinc powder (65.0 mg, 1.0 mmol), the mixture was vigorously stirred for 3 h then filtered through celite. To the filtrate water (5 mL) was added and then washed with Et_2O (3 times). After that, Et_2O (3 mL) was added, the biphasic solution was vigorously stirred and solid $NaHCO_3$ was added little in portions until a basic aqueous phase was obtained (around pH 9). Benzoylchloride (35μL, 0.3 mmol) was added and the reaction mixture was stirred for 10 min. Saturated $NaHCO_3$ aq and Et_2O were added, the organics were extracted with Et_2O (5 times), the combined organic phases were washed with saturated NaCl aq. The organic phase was dried over Na_2SO_4, followed by removal of organic solvents in vacuo. The crude mixture was purified by chromatography on silica gel (hexane/acetone = 2/1).

Transformation for determination of absolute configuration of 4d

To determine the absolute configuration of the allylated product **4d**, it was converted to an amino acid ethyl ester derivative **8**.[4]



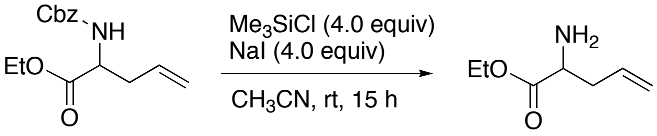
4b

8
(*N*-acetyl-norvaline ethyl ester)
34% yield

$[\alpha]_D^{27}$ +44.2 (c 0.43, H_2O)
ref. *S*-isomer: $[\alpha]_D^{25}$ -58.5
(c 4.0, H_2O, 100% ee)

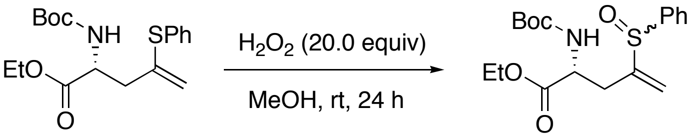
To a solution of **4d** (35.8 mg, 0.146 mmol) in ethanol (2.0 mL) was added Raney Ni (W2, ca 150 mg) under an argon atmosphere, argon was replaced by hydrogen (1 atm). The mixture was stirred vigorously for 10 h. The reaction mixture was then filtered through celite and washed with warm ethanol. After removal of organic solvents in vacuo, the crude products were purified by silica gel chromatography (hex/EtOAc = 2/3) to afford the desired product **8** (9.2 mg, 34% yield).

Several other deprotection and transformations proceeded smoothly as shown below.



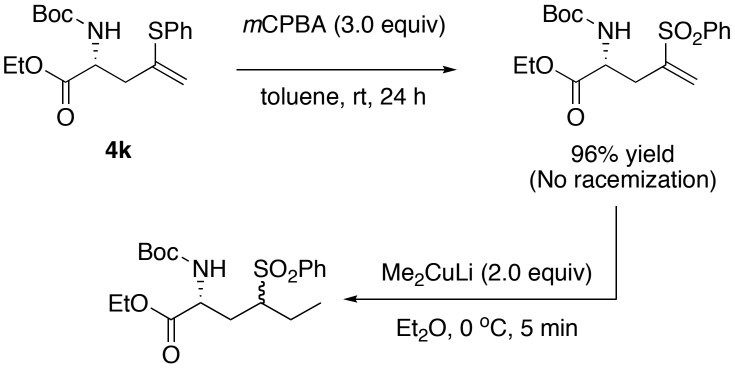
4i

65% yield



4k

71% yield

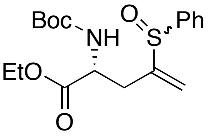


4k

96% yield
(No racemization)

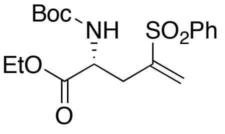
76% yield

Ethyl 2-(*tert*-butoxycarbonylamino)-4-phenylsulfenylpent-4-enoate:



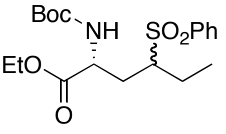
^{1}H NMR ($CDCl_3$) δ = 7.60-7.55 (2H), 7.50-7.40 (3H), 6.20-6.10 (1H), 5.80-5.70 (1H), 5.60-5.50 (1H), 4.40-4.15 (1H), 4.18-4.12 (2H), 2.60-2.40 (2H), 1.45-1.40 (9H), 1.25-1.20 (3H) ppm; ^{13}C NMR (C_6D_6) δ = 171.2, 171.1, 155.3, 150.2, 150.0, 141.9, 131.3, 129.3, 125.11, 125.08, 121.76, 120.4, 80.0, 79.9, 61.64, 61.58, 53.1, 52.1, 30.9, 29.8, 28.3, 14.15, 14.10 ppm; HRMS (FAB); Exact mass calcd for $C_{18}H_{26}NO_5S$ $[M+H]^+$, 368.1526. Found 368.1523.

Ethyl 2-(*tert*-butoxycarbonylamino)-4-phenylsulfonylpent-4-enoate:



$[\alpha]^{24}_D$ -5.24 (75% ee, c 1.90, $CDCl_3$); ^{1}H NMR (C_6D_6) δ = 7.90-7.85 (2H, m), 7.70-7.60 (1H, m), 7.60-7.50 (2H, m), 6.46 (1H, s), 5.91 (1H, s), 5.18 (1H, brd, *J* = 7.6 Hz), 4.42 (1H, q, *J* = 5.6 Hz), 4.25-4.10 (2H, m), 2.75-2.60 (2H, m), 1.42 (9H, s), 1.26 (3H, t, *J* = 6.8 Hz) ppm; ^{13}C NMR (C_6D_6) δ = 171.0, 145.9, 138.3, 133.7, 129.3, 128.4, 126.7, 80.1, 61.7, 52.3, 31.7, 28.2, 14.0 ppm; IR (neat): 3323, 2979, 2936, 2362, 1714, 1514, 1447, 1368, 1353, 1300, 1249, 1162 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{18}H_{26}NO_6S$ $[M+H]^+$, 384.1475. Found 384.1476.; Chiral HPLC: Daicel Chiralcel AD, hexane/^{i}PrOH = 9/1, flow rate = 1.0 mL/min t_R = 27.3 min for (*R*)-isomer, t_R = 35.0 min for (*S*)-isomer.

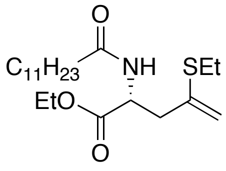
Ethyl 2-(*tert*-butoxycarbonylamino)-4-phenylsulfonylhexanoate:



^{1}H NMR ($CDCl_3$) δ = 8.0-7.85 (2H), 7.70-7.60 (2H), 5.35-5.25 (1H), 4.55-4.40 (1H), 4.25-4.0 (2H), 3.30-3.0 (1H), 2.45-2.15 (2H), 2.00-1.50 (2H), 1.43-1.40 (9 H), 1.35-1.20 (3H), 1.20-1.10 (3H) ppm; ^{13}C NMR ($CDCl_3$) δ = 171.7, 171.5, 137.6, 133.8, 129.22, 129.16, 129.0, 128.8, 77.2, 62.1, 61.8, 61.7, 51.5, 29.7, 28.2, 22..3, 21.7, 14.1, 10.9, 10.6 ppm; HRMS (FAB); Exact mass calcd for $C_{19}H_{30}NO_{6S}$ $[M+H]^+$, 400.1788. Found 400.1780.

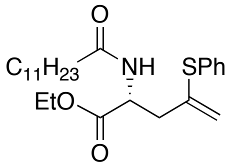
Physical data of allylated products are as follows.

Ethyl (1*R*)-2-(dodecanoylamino)-4-ethylsulfanylpent-4-enoate (4b):



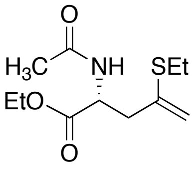
$[\alpha]^{24}_{D}$ –25.9 (93% ee, c 1.78, benzene); ^{1}H NMR (400 MHz, C_6D_6) δ = 5.95 (1H, brd, *J* = 7.6 Hz), 5.03 (1H, apparent q, *J* = 6.4 Hz), 4.99 (1H, s), 4.70 (1H, s), 4.0-3.9 (2H, m), 2.82 (1H, dd, *J* = 14.2, 5.2 Hz), 2.64 (1H, dd, *J* = 14.2, 6.3 Hz), 2.35 (2H, q, *J* = 7.4 Hz), 1.93 (2H, t, *J* = 7.5 Hz), 1.7-1.6(2H, m), 1.35-1.2 (16H, m), 0.99 (3H, t, *J* = 7.5 Hz), 0.92 (3H, t, *J* = 7.1 Hz), 0.91 (3H, t, *J* = 6.8 Hz)ppm; ^{13}C NMR (100 MHz, C_6D_6) δ = 171.8, 171.6, 141.1, 109.4, 61.2, 51.9, 39.8, 36.4, 32.3, 30.04, 29.95, 29.80, 29.77, 29.6, 25.9, 25.6, 23.1, 14.3, 14.0, 13.1ppm; IR (neat) 3331, 2921, 2848, 1735, 1643, 1529, 1468, 1379, 1289, 1218 cm^{-1}; LRMS (EI) m/z = 386 $[M]^+$; Anal. Calcd for $C_{21}H_{40}NO_3S$: C, 65.41; H, 10.19; N, 3.63. Found C, 65.34; H, 10.07; N, 3.69; Chiral HPLC: Daicel Chiralcel OD, hexane/^{i}PrOH = 40/1, flow rate = 1.0 mL/min t_R = 10.5 min for major isomer, t_R = 32.8 min for minor isomer.

Ethyl (1*R*)-2-(dodecanoylamino)-4-phenylsulfanylpent-4-enoate (4c):



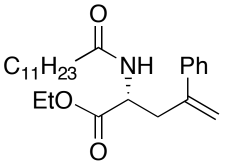
$[\alpha]^{24}_{D}$ –26.0 (92% ee, c 0.89, benzene); ^{1}H NMR (400 MHz, C_6D_6) δ = 7.45-7.4 (2H, m), 7.05-6.9 (2H, m), 6.14 (1H, brd, *J* = 7.8 Hz), 5.10 (1H, s), 5.1-5.0 (1H, m), 4.97 (1H, s), 3.91 (2H, q, *J* = 7.2 Hz), 2.86 (1H, dd, *J* = 14.4, 5.1 Hz), 2.64 (1H, dd, *J* = 14.4, 6.6 Hz), 1.96 (2H, dt, *J* = 7.4, 2.8 Hz), 1.7-1.6 (2H, m), 1.35-1.2 (16H, m), 0.90 (3H, t, *J* = 7.2 Hz), 0.88 (3H, t, *J* = 7.2 Hz)ppm; ^{13}C NMR (100 MHz, C_6D_6) δ = 172.0, 171.7, 141.6, 133.6, 133.1, 129.5, 128.2, 116.2, 61.3, 51.7, 39.8, 36.4, 32.3, 30.06, 30.04, 29.96, 29.81, 29.76, 29.6, 25.9, 23.1, 14.3, 14.0ppm; IR (neat) 3290, 2925, 2853, 1745, 1651, 1541, 1466, 1440, 1224, 1196, 1161 cm^{-1}; LRMS (EI) m/z = 433 $[M]^+$; Anal. Calcd for $C_{25}H_{39}NO_3S$: C, 69.24; H, 9.06; N, 3.23. Found C, 69.31; H, 9.02; N, 3.24; Chiral HPLC: Daicel Chiralcel AD, hexane/^{i}PrOH = 19/1, flow rate = 1.0 mL/min; t_R = 9.4 min for major isomer, t_R = 14.3 min for minor isomer.

Ethyl (1*R*)-2-(acetylamino)-4-ethylsulfanylpent-4-enoate (4d):



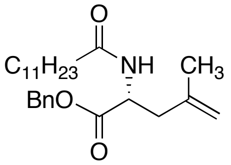
$[\alpha]^{24}_{D}$ –6.46 (82% ee, c 0.85, acetone); ^{1}H NMR (300 MHz, C_6D_6) δ = 6.02 (1H, brd, *J* = 7.1 Hz), 5.05-4.95 (1H, m), 4.98 (1H, s), 4.0-3.9 (2H, m), 2.79 (1H, dd, *J* = 14.4, 5.4 Hz), 2.61 (1H, dd, *J* = 14.4, 6.6 Hz), 2.34 (2H, q, *J* = 7.4 Hz), 1.59 (3H, s), 0.97 (3H, t, *J* = 7.4 Hz), 0.91 (3H, t, *J* = 7.1 Hz)ppm; ^{13}C NMR (75 MHz, C_6D_6) δ = 171.6, 168.8, 141.0, 109.4, 61.2, 52.1, 39.7, 25.6, 22.6, 14.0, 13.1ppm; IR (neat) 3289, 3071, 2981, 2929, 1746, 1660, 1544, 1442, 1374, 1194, 1161, 1025 cm^{-1}; MS (EI): m/z = 246 [M]$^+$; Anal. Calcd for $C_{14}H_{25}NO_4S$: C, 53.85; H, 7.81; N, 5.71. Found C, 53.62; H, 7.83; N, 5.67; Chiral HPLC: Daicel Chiralcel OD, hexane/^{i}PrOH = 40/1, flow rate = 1.0 mL/min t_R = 24.0 min for major isomer, t_R = 48.4 min for minor isomer.

Ethyl (1*R*)-2-(dodecanoylamino)-4-phenylpent-4-enoate (4e):



$[\alpha]^{25}_D$ –3.08 (91% ee, c 1.52, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ = 7.40-7.27 (5H, m), 5.84 (1H, brd, *J* = 7.3 Hz), 5.31 (1H, s), 5.09 (1H, m), 4.67 (1H, q, *J* = 6.7 Hz), 4.09-3.91 (2H, m), 2.86 (1H, dd, *J* = 14.4, 5.1 Hz), 3.07 (1H, dd, *J* = 14.2, 5.9 Hz), 2.98 (1H, dd, *J* = 14.2, 5.9 Hz), 2.08-2.00 (2H, m), 1.60-1.48 (2H, m), 1.3-1.00 (19H, m), 0.88 (3H, t, *J* = 6.4 Hz)ppm; ^{13}C NMR (100 MHz, C_6D_6) δ =172.5, 171.7, 144.0, 140.4, 128.4, 127.8, 126.3, 116.4, 61.3, 51.5, 37.7, 36.4, 31.9, 29.6, 29.4, 29.3, 29.2, 25.3, 22.6, 14.1, 14.0ppm; IR (neat) 3300, 2924, 2853, 1744, 1648, 1538, 1455, 1378, 1200 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{25}H_{40}NO_3$ [M+H]$^+$, 402.3003. Found 402.3019; Chiral HPLC: Daicel Chiralcel AD, hexane/^{i}PrOH = 19/1, flow rate = 1.0 mL/min; t_R = 9.1 min for major isomer, t_R = 18.7 min for minor isomer.

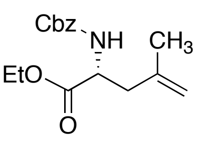
Benzyl (1*R*)-2-(dodecanoylamino)-4-methylpent-4-enoate (4f):



$[\alpha]^{24}_D$ +6.86 (90% ee, c 1.04, benzene); ^{1}H NMR (300 MHz, C_6D_6) δ = 7.4-7.3 (5H, m), 5.85 (1H, brd, *J* = 7.5 Hz), 5.18 (1H, d, *J* = 12.3 Hz), 5.13 (1H, d, *J* = 12.3 Hz), 4.81 (1H, s), 4.76 (1H, apparent dt, *J* = 8.0 5.5 Hz), 4.71 (1H, s), 2.58 (1H, dd, *J* = 13.9, 5.5 Hz), 2.39 (1H, dd, *J* = 13.9, 8.4 Hz), 2.20 (2H, t, *J* = 7.6 Hz), 1.70 (3H, s), 1.7-1.55 (2H, m), 1.35-1.2 (16H, m), 0.88 (3H, t, *J* = 6.7 Hz)ppm; ^{13}C NMR (75 MHz, C_6D_6) δ = 172.8, 172.3, 140.5, 135.2, 128.6, 128.4, 128.3, 114.6, 67.1, 50.3, 40.5, 36.5, 31.9, 29.6, 29.4, 29.3, 29.2, 25.6, 22.7, 21.8, 14.1ppm; IR (KBr) 3311, 2924, 2851, 1711, 1638, 1547, 1468, 1456, 1441, 1377, 1347, 1295, 1266, 1241, 1223, 1188, 749 cm^{-1}; MS (EI): m/z = 402 [M+H]$^+$; Anal. Calcd for $C_{25}H_{39}NO_3$: C, 74.77; H, 9.79; N, 3.49. Found C, 74.77; H, 9.82; N, 3.44;

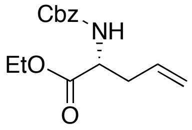
Chiral HPLC: Daicel Chiralcel OD, hexane/^{i}PrOH = 19/1, flow rate = 1.0 mL/min, detection 215 nm, t_R = 9.0 min for major isomer, t_R = 17.4 min for minor isomer.

Ethyl 2-N-Benzyloxycarbonylamino-4-methyl-4-pentenoate (4h):



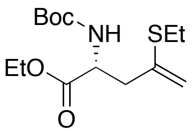
$[\alpha]^{24}_{D}$–5.74 (63% ee, c, 2.18, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 7.37-7.29 (5H, m), 5.24 (1H, brd, *J* = 7.6 Hz), 5.10 (2H, s), 4.84 (1H, s), 4.75 (1H, s), 4.47 (1H, d, *J* = 8.2 Hz), 4.45 (1H, d, *J* = 8.2 Hz), 4.19 (2H, m), 2.55 (1H, dd, *J* = 13.7, 5.5 Hz), 2.39 (1H, dd, *J* = 14.1, 8.6 Hz), 1.27 (3H, t, *J* = 7.2 Hz)ppm; ^{13}C NMR ($CDCl_3$) δ = 172.2, 155.7, 140.3, 136.2, 128.4, 128.1, 128.0, 114.7, 66.9, 61.4, 52.2, 40.7, 21.8, 14.1ppm; IR (neat) 3345, 2977, 1720, 1523, 1209, 1037, 898, 744 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{16}H_{21}NO_4$ $[M+H]^+$, 292.1549. Found 292.1554; Chiral HPLC: Daicel Chiralcel OD, hexane/^{i}PrOH = 9/1, flow rate = 0.5 mL/min, λ = 212 nm; t_R = 12.0 min (*R*), t_R = 22.4 min (*S*)

Ethyl 2-N-Benzyloxycarbonylamino-4-pentenoate (4i):



$[\alpha]^{24}_{D}$–11.4 (87% ee, c, 2.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$): d = 7.37-7.30 (5H, m), 5.69 (1H, m), 5.34 (1H,, *J* = 7.6 Hz), 5.14 (4H, m), 4.44 (1H, dd, *J* = 6.4, 6.4 Hz), 4.20 (2H, m), 2.59 (1H, m), 2.51 (1H, m), 1.27 (3H, t, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$): d = 171.6, 155.7, 136.2, 132.0, 127.5, 128.12, 128.06, 119.3, 66.9, 61.4, 53.2, 36.7, 14.1; IR (neat): 3343, 2980, 1719, 1519, 1340, 1209, 1050, 698 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{16}H_{21}NO_4$ $[M+H]^+$, 278.1387. Found 278.1382.; Chiral HPLC: Daicel Chiralcel OD, hexane/^{i}PrOH = 9/1, flow rate = 1.0 mL/min, λ = 212 nm; t_R = 7.8 min (*R*), t_R = 11.3 min (*S*)

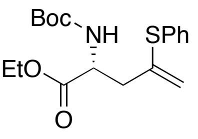
Ethyl 2-(*tert*-butoxycarbonylamino)-4-ethylsulfanylpent-4-enoate (4j):



$[\alpha]^{24}_{D}$ –21.6 (87% ee, c 1.05, benzene); ^{1}H NMR (C_6D_6): d = 5..31 (1H, brd, *J* = 8.1 Hz), 4.93 (1H, s), 4.72 (1H, apparent q, *J* = 6.8 Hz), 4.62 (1H, s), 4.0-3.85 (2H, m), 2.69 (1H, dd, *J* = 14.2, 5.1 Hz), 2.54 (1H, dd, *J* = 14.5, 7.3 Hz), 2.28 (2H, q, *J* = 7.4 Hz), 1.41(9H, s), 0.93 (3H, t, *J* = 7.4 Hz), 0.89 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (C_6D_6): d = 172.3, 156.0, 141.6, 110.0, 80.0, 61.7, 54.0, 40.5, 29.0, 26.2, 14.7, 13.7; IR (neat): 3374, 2976, 2932, 1717, 1504, 1366, 1169, 1030 cm-1; MS (EI): m/z = 304 [M]+; Anal. Calcd for C14H25NO4S: C, 55.42; H, 8.30; N, 4.62. Found C, 55.59; H, 8.23; N, 4.51; Chiral HPLC: Daicel

Chiralcel OD, hexane/^{i}PrOH = 200/1, flow rate = 1.0 mL/min t_R = 16.5 min for (R)-isomer, t_R = 18.9 min for (S)-isomer.

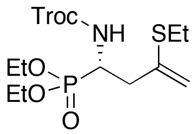
Ethyl 2-(*tert*-butoxycarbonylamino)-4-phenylsulfanylpent-4-enoate (4k):



$[\alpha]^{24}_D$ -23.2 (82% ee, c 1.27, EtOAc); ^{1}H NMR (C_6D_6) δ = 7.40-7.30 (2H, m), 7.05-6.85 (3H, m), 5.27 (1H, d, *J* = 8.4 Hz), 5.01 (1H, s), 4.91 (1H, s), 4.78 (1H, dd, *J* = 12.8, 7.6 Hz), 3.88 (2H, dd, *J* = 14.4, 7.6 Hz), 2.73 (1H, dd, *J* = 14.4, 4.8 Hz), 2.56 (1H, *J* = 14.4, 6.8 Hz), 1.42 (9H, s), 0.845 (3H, t, *J* = 7.6 Hz) ppm; ^{13}C NMR (C_6D_6): δ = 171.6, 155.3, 141.4, 133.7, 133.1, 129.4, 128.23, 128.15, 127.9, 127.9, 127.8, 116.3, 79.4, 61.1, 53.0, 39.0, 28.3, 14.0 ppm; IR (neat): 3379, 2975, 2358, 1714, 1609, 1503, 1366, 1278, 1238, 1166, 1026 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{18}H_{26}NO_4S$ $[M+H]^+$, 352.1577. Found 352.1580.

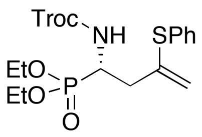
; Chiral HPLC: Daicel Chiralcel ADH, hexane/^{i}PrOH = 40/1, flow rate = 0.8 mL/min t_R = 36.7 min for (*R*)-isomer, t_R = 41.5 min for (*S*)-isomer.

Diethyl (1*S*)-3-ethylsulfanyl-1-(2,2,2-trichloroethoxycarbonylamino)-but-3-ene-1-phosphonate (6a):



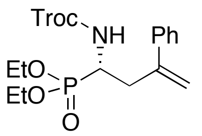
$[\alpha]^{23}_D$ +7.38 (82% ee, c 1.16, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ = 7.29 (1H, brd, *J* = 9.7 Hz), 5.27 (1H, s), 4.88 (1H, s), 4.81 (1H, d, *J* = 12.3 Hz), 4.81 (1H, d, *J* = 12.3 Hz) 4.75 (1H, d, *J* = 12.3 Hz), 4.4-4.25 (1H, m), 4.2-4.05 (4H, m), 2.72 (2H, dq, *J* = 7.3, 1.8 Hz), 2.72 (2H, apparent t, *J* = 5.0 Hz), 1.29 (3H, t, *J* = 6.9 Hz), 1.27 (3H, t, *J* = 6.9 Hz), 1.23 (3H, t, *J* = 7.3 Hz)ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ = 155.3 (d, *J* = 4.3 Hz), 141.3 (d, *J* = 17.3 Hz), 110.6, 96.9, 74.9 (d, *J* = 13.6 Hz), 63.3 (d, *J* = 6.8 Hz), 62.8, 62.8 (d, *J* = 6.8 Hz), 48.1 (d, *J* = 158.6 Hz), 37.6 (d, *J* = 5.0 Hz), 25.8, 16.8, 16.7, 13.8ppm; IR 3226, 3046, 2981, 2934, 1738, 1542, 1234, 1138, 1048, 969 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{13}H_{23}Cl_3NO_5PSNa$ $[M+Na]^+$, 464.0014, Found 464.0014; Chiral HPLC: Daicel Chiralpak AD, hexane/^{i}PrOH = 9/1, flow rate = 1.0 mL/min; t_R = 11.3 min for minor isomer, t_R = 16.2 min for major isomer.

Diethyl (1*S*)-3-phenylsulfanyl-1-(2,2,2-trichloroethoxycarbonylamino)-but-3-ene-1-phosphonate (6b):



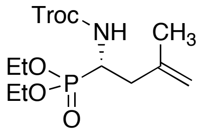
$[\alpha]^{23}_{D}$ –21.5 (79% ee, c 1.46, benzene); ^{1}H NMR (400 MHz, acetone-d_6) δ = 7.5-7.3 (5H, m),7.22 (1H, brs), 5.42 (1H, s), 5.04 (1H, s), 4.83 (1H, d, *J* = 12.3 Hz), 4.81 (1H, d, *J* = 12.3 Hz) 4.5-4.35 (1H, m), 4.1-4.00 (4H, m), 2.65 (2H, m), 1.23 (3H, t, *J* = 12.3 Hz), 1.21 (3H, t, *J* = 7.1 Hz)ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ = 155.4 (d, *J* = 4.9 Hz), 141.7 (d, *J* = 17.3 Hz), 133.6, 133.57, 130.2, 128.9, 118.1, 97.0, 74.9, 63.2, 62.8 (d, *J* = 6.6 Hz), 47.8 (d, *J* = 159.6 Hz), 37.6 (d, *J* = 5.7 Hz), 16.8, 16.7ppm; IR 3216, 3048, 2986, 2934, 1742, 1544, 1231, 1133, 1034, 968, 739 cm^{-1}; HRMS (FAB); Anal. Calcd for $C_{13}H_{23}Cl_{3}NO_{5}PS$: C,41.60; H, 4.72; N, 2.85. Found: C, 41.55; H, 5.00; N, 2.89; Chiral HPLC: Daicel Chiralpak AD-H, hexane/^{i}PrOH = 19/1, flow rate = 1.0 mL/min; t_R = 18.3 min for minor isomer, t_R = 22.5 min for major isomer.

Diethyl (1*S*)-3-phenyl-1-*N*-2,2,2-trichloroethoxycarbonylamino-but-3-ene-1-phosphonate (6c):



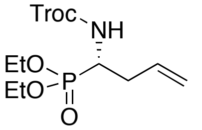
$[\alpha]^{25}_{D}$ –0.99 (85% ee, c 2.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38-7.26 (5H, m), 5.46 (1H, brd), 5.36 (1H, s), 5.19 (1H, s), 4.64 (2H, d, *J* = 11.9 Hz), 4.20-4.00 (5H, m), 3.23-3.18 (1H, m), 2.80-2.67 (1H, m), 1.35-1.30 (6H, m)ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.1 (d, *J* = 5.7 Hz), 143.4, 143.3, 139.8, 128.4, 127.8, 126.2, 115.9, 95.4, 74.6, 63.0 (d, *J* = 6.7 Hz), 62.6 (d, *J* = 7.6 Hz), 46.7 (d, *J* = 158.3 Hz), 35.7 (d, *J* = 3.8 Hz), 16.4, 16.3ppm; IR 3226, 3051, 2985, 1739, 1547, 1443, 1392, 1227, 1146, 1035, 973, 818, 725, cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{12}H_{21}Cl_{3}NO_{5}P$ $[M+H]^{+}$, 458.0452. Found 458.0456; Chiral HPLC: Daicel Chiralcel AD, hexane/^{i}PrOH = 9/1, flow rate = 0.8 mL/min; t_R = 13.7 min for minor isomer, t_R = 16.9 min (*S*) for major isomer.

Diethyl (1*S*)-3-methyl-1-*N*-2,2,2-trichloroethoxycarbonylamino-but-3-ene-1-phosphonate (6d):



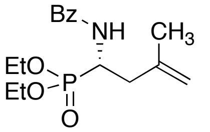
$[\alpha]^{25}_{D}$ -3.58 (89% ee, c 0.31, acetone); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.2-5.15 (1H, m), 4.84-4.67 (4H, m), 4.27-4.10 (5H, m), 2.58-2.54 (1H, m), 2.34-2.26 (4H, m), 1.73 (3H, s), 1.32-1.28 (6H, m)ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 154.3 (d, *J* = 5.8 Hz), 140.0, 114.5, 95.4, 74.6, 62.9 (d, *J* = 7.2 Hz), 62.6 (d, *J* = 7.2 Hz), 45.9 (d, *J* = 158.9 Hz), 38.01 (d, *J* = 2.9 Hz), 21.5, 16.5 (d, *J* = 4.3 Hz), 16.4 (d, *J* = 5.8 Hz)ppm; IR 3220, 2984, 1738, 1543, 1443, 1385, 1226, 1145, 1033, 967, 820, 730, 575 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{12}H_{21}Cl_3NO_5P$ [M+H]$^+$, 396.0301. Found 396.0301.

Diethyl (1*S*)-1-(2,2,2-trichloroethoxycarbonylamino)-but-3-ene-1-phosphonate (6e):



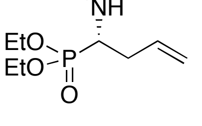
[α]$^{28}_{D}$ +0.99 (89% ee, c 1.22, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.8-5.74 (1H, m), 5.45-5.40 (1H, d, *J* = 10.2 Hz), 5.12-5.08 (1H, m), 4.74-4.69 (1H, m), 4.3-4.0 (4H, m), 2.64-2.58 (1H, m), 2.41-2.36 (1H, m), 1.31-1.28 (6H, m)ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 154.3 (d, *J* = 6.8 Hz), 132.7 (d, *J* = 13.0 Hz), 118.9, 95.4, 74.6 (d, *J* = 10.2 Hz), 63.2 (d, *J* = 7.2 Hz), 62.8 (d, *J* = 7.1 Hz), 62.6 (d, *J* = 5.6 Hz), 47.3 (d, *J* = 157.5 Hz), 34.3 (d, *J* = 4.4 Hz), 16.4 (d, *J* = 4.4 Hz), 16.37 (d, *J* = 10.2 Hz)ppm; IR 3220, 3053, 2986, 1740, 1541, 1440, 1227, 1155, 1035, 967, 811, 730, 559 cm^{-1} ; HRMS (FAB). Exact mass calcd for $C_{11}H_{19}Cl_3NO_5P$ [M+H]$^+$, 382.0145. Found 382.0140.

Diethyl (1*S*)-3-methyl-1-benzoylamino-but-3-ene-1-phosphonate (7d):



[α]$^{24}_{D}$ +3.25 (89% ee, c 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.8-7.75 (2H, m), 7.50-7.45 (1H, m), 7.45-7.40 (2H, m), 6.55-6.50 (1H, brd, *J* = 7.2 Hz), 4.9-4.8 (3H, m), 4.2-4.0 (4H, m), 2.7-2.6 (1H, m), 2.55-2.50 (1H, m), 1.79 (3H, s) 1.34 (3H, t, *J* = 6.9 Hz), 1.26 (3H, t, *J* = 6.9 Hz)ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.02 (d, *J* = 4.3 Hz), 140.7, 140.6, 134.0, 131.6, 128.7, 128.5, 127.3, 127.1, 114.1, 62.9 (d, *J* = 7.2 Hz), 62.5 (d, *J* = 7.2 Hz), 44.3 (d, *J* = 157.5 Hz), 37.9 (d, *J* = 2.9 Hz), 21.6, 16.44 (d, *J* = 5.8 Hz), 16.39 (d, *J* = 7.2 Hz)ppm. IR 3277, 2980, 1658, 1536, 1492, 1315, 1222, 1023, 977, 891, 699, 575 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{16}H_{24}NO_4P$ [M+H]$^+$, 326.1521. Found 326.1519; Chiral HPLC: Daicel Chiralcel OJ-H, hexane/^{i}PrOH = 100/1, flow rate = 0.3 mL/min; t_R = 32.5 min for major isomer, t_R = 42.1 min for minor isomer.

Diethyl (1*S*)-1-*N*-benzoylamino-but-3-ene-1-phosphonate (7e):



[α]$^{24}_{D}$ +4.29 (80% ee, c 0.76, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.8-7.7 (2H, m), 7.54-7.50 (1H, m), 7.45-7.42 (2H, m), 6.51 (1H, brd, *J* = 8.94 Hz), 5.88-5.82 (1H, m), 5.17-5.08 (2H, m), 4.80-4.75 (1H, m), 4.3-4.0 (4H, m), 2.72-2.67 (1H, m) , 2.55-2.50 (1H, m), 1.34 (3H, t, *J* = 6.9

Hz), 1.28 (3H, t, $J = 6.9$ Hz)ppm; ^{13}C NMR (150 MHz, $CDCl_3$) $\delta = 167.0$ (d, $J = 5.8$ Hz), 133.9, 133.17, 133.08, 131.8, 128.6, 127.0, 118.7, 62.9 (d, $J = 7.2$ Hz), 62.6 (d, $J = 7.2$ Hz), 44.9 (d, $J = 157.5$ Hz), 34.4, 16.5 (d, $J = 5.8$ Hz), 16.4 (d, $J = 5.8$ Hz)ppm; IR 3269, 2972, 2377, 2320, 1657, 1532, 1229, 1028, 966, 753, 701, 542 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{15}H_{22}NO_4P$ $[M+H]^+$, 312.1365. Found 312.1367; Chiral HPLC: Daicel Chiralcel OJ-H, hexane/^{i}PrOH = 100/1, flow rate = 0.5 mL/min; t_R = 17.9 min for major isomer, t_R = 23.8 min for minor isomer.

References:

(1) For preparation of allylsilane **2b** and **2c**, see (a) Narasaka, K.; Hayashi, Y.; Shimizu, H.; Niihata, S. *J. Am. Chem. Soc.* **1992**, *114*, 8869. For preparation of allylsilane **2d**, see (b) Narayanan, B. A.; Bunnelle, W.H. *Tetrahedron Lett.* **1987**, *28*, 6261.

(2) (a) Kobayashi, S.; Matsubara, R.; Kitagawa, H. *Org. Lett.* **2002**, *4*, 143. (b) Kobayashi, S.; Matsubara, R.; Nakamura, Y.; Kitagawa, H.; Sugiura, M. *J. Am. Chem. Soc.* **2003**, *125*, 2507. (c) Nakamura, Y.; Matsubara, R.; Kiyohara, H.; Kobayashi, S. *Org. Lett.* **2003**, *5*, 2481.

(3) Kobayashi, S.; Kiyohara, H.; Nakamura, Y.; Matsubara, R. *J. Am. Chem. Soc.* **2004**, *126*, 6558.

(4) Nandi, P. K.; Robinson, D. R. *J. Am. Chem. Soc.* **1972**, *94*, 1308.