Synthesis of 3-Alkoxycarbonyl-1 β -Methylcarbapenem Using Palladium-Catalyzed C-N Bond-Forming Reaction between Vinyl Halide and β -Lactam Nitrogen

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Supporting Informations

General. All reactions were performed under an argon atmosphere unless otherwise mentioned. All solvents and reagents were purified when necessary using standard procedures.

Column chromatography was performed with Merck Silica Gel 60 (70-230 or 230-400 mesh ATM) using the indicated solvent.

^1H NMR and ^{13}C NMR were recorded on JEOL EX-270 (270 MHz (^1H), 67.5 MHz (^{13}C)), JEOL EX-400 (400 MHz (^1H), 100 MHz (^{13}C)), or JEOL AL-400 (400 MHz (^1H), 100 MHz, (^{13}C)) instrument in CDCl_3 with tetramethylsilane as an internal standard.

Infrared spectra (IR) were recorded on a Perkin Elmer FTIR 1605 spectrometer.

Mass spectra were measured on JEOL DX303, JEOL JMS-700TZ, and JEOL JMS-FABmate mass spectrometers.

(3*S*,4*R*)-1-(*tert*-Butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-4-(prop-2-enyl)-2-azetidinone (2)

To a solution of **1** (2.00 g, 7.42 mmol) in DMF (20 ml) was added Et₃N (3.10 ml, 22.2 mmol), NaI (1.33 g, 8.87 mmol), and TBSCl (1.34g, 8.89 mmol) at 0 °C, and the mixture was stirred at room temperature for 10 hours. To the reaction mixture was added sat. aq. NaHCO₃, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford **2** (2.68 g, 6.98 mmol, 94%) as a colorless oil.

¹H NMR (270MHz, CDCl₃) δ 0.05 (s, 3 H), 0.07 (s, 3 H), 0.23 (s, 3 H), 0.24 (s, 3 H), 0.88 (s, 9 H), 0.96 (s, 9 H), 1.17 (d, *J* = 6.5 Hz, 3 H), 2.17-2.28 (m, 1 H), 2.52-2.62 (m, 1 H), 2.81 (dd, *J* = 5.4, 2.7 Hz, 1 H), 3.60 (ddd, *J* = 9.2, 3.2, 2.7 Hz, 1 H), 4.11 (qd, *J* = 6.5, 5.4 Hz, 1 H), 5.08-5.16 (m, 2 H), 5.69-5.84 (m, 1 H). IR (neat) 3078, 2956, 2930, 2885, 2858, 1746, 1641 cm⁻¹. LRMS (EI, *m/z*) 368 (M-Me)⁺, 326 (M-'Bu)⁺. HRMS (EI) calcd for C₁₆H₃₂NO₂Si₂ 326.1972 (M-'Bu)⁺, found 326.1978.

(3*S*,4*R*)-1-(*tert*-Butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-4-(2-oxoethyl)-2-azetidinone (3)

A solution of **2** (2.68 g, 6.98 mmol) in CH₂Cl₂ (30 ml) was cooled to -78 °C and treated with a stream of O₃/O₂ at -78 °C until the colorless solution had been

converted to a blue one. The reaction mixture was treated with a stream of O₂ at -78 °C to remove an excess amount of O₃. To the reaction mixture was added a solution of PPh₃ (4.58 g, 17.5 mmol) in CH₂Cl₂ (25 ml) at -78 °C, and the mixture was allowed to stir at room temperature for 12 hours. To the reaction mixture was added water, and the aqueous layer was extracted with CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford **3** (2.56 g, 6.63 mmol, 95%) as a colorless solid.

¹H NMR (270MHz, CDCl₃) δ 0.06 (s, 3 H), 0.09 (s, 3 H), 0.23 (s, 3 H), 0.23 (s, 3 H), 0.88 (s, 9 H), 0.96 (s, 9 H), 1.22 (d, *J* = 6.5 Hz, 3 H), 2.67 (ddd, *J* = 16.2, 8.6, 2.2 Hz, 1 H), 2.89 (ddd, *J* = 16.2, 4.6, 2.2 Hz, 1 H), 2.95 (dd, *J* = 5.7, 2.7 Hz, 1 H), 3.97 (ddd, *J* = 8.6, 4.6, 2.7 Hz, 1 H), 4.16 (qd, *J* = 6.5, 5.7 Hz, 1 H), 9.79 (dd, *J* = 2.2, 2.2 Hz, 1 H). IR (neat) 2954, 2928, 2884, 2855, 2733, 1727 cm⁻¹. LRMS (EI, *m/z*) 370 (M-Me)⁺, 328 (M-^tBu)⁺. HRMS (EI) calcd for C₁₅H₃₀NO₃Si₂ 328.1764 (M-^tBu)⁺, found 328.1749.

(3*S*,4*R*)-4-[(*Z*)-3-Bromo-3-methoxycarbonylprop-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (4**)**

To a solution of **3** (2.56 g, 6.63 mmol) in toluene (18 ml) and dichloroethane (9 ml) was added Ph₃P=C(Br)CO₂Me (3.68 ml, 8.61 mmol), and the mixture was stirred at 80 °C for 4 hours. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane / ether = 4 / 1) to afford **4** (2.69 g, 5.17 mmol, 78%) as a colorless solid along with *E*-isomer (449 mg, 0.862 mmol, 13%).

¹H NMR (270MHz, CDCl₃) δ 0.05 (s, 3 H), 0.07 (s, 3 H), 0.25 (s, 3 H), 0.26 (s, 3 H),

0.88 (s, 9 H), 0.98 (s, 9 H), 1.18 (d, $J = 5.9$ Hz, 3 H), 2.54 (ddd, $J = 15.4, 8.6, 7.3$ Hz, 1 H), 2.84 (dd, $J = 5.4, 2.7$ Hz, 1 H), 2.87 (ddd, $J = 15.4, 7.3, 3.2$ Hz, 1 H), 3.74 (ddd, $J = 8.6, 3.2, 2.7$ Hz, 1 H), 3.83 (s, 3 H), 4.12 (qd, $J = 5.9, 5.4$ Hz, 1 H), 7.30 (dd, $J = 7.3, 7.3$ Hz, 1 H). IR (neat) 3028, 2953, 2931, 2890, 2856, 2171, 1731, 1718, 1629 cm^{-1} . LRMS (EI, m/z) 504 (M-Me)⁺, 462 (M-^tBu)⁺. HRMS (EI) calcd for $\text{C}_{18}\text{H}_{33}\text{NO}_4\text{BrSi}_2$ 462.1131 (M-^tBu)⁺, found 462.1110.

(*E*-isomer) ¹H NMR (270MHz, CDCl_3) δ 0.06 (s, 3 H), 0.09 (s, 3 H), 0.24 (s, 6 H), 0.90 (s, 9 H), 0.96 (s, 9 H), 1.20 (d, $J = 5.9$ Hz, 3 H), 2.62 (ddd, $J = 15.9, 9.2, 7.6$ Hz, 1 H), 2.83 (dd, $J = 5.7, 2.4$ Hz, 1 H), 3.14 (ddd, $J = 15.9, 7.6, 3.8$ Hz, 1 H), 3.66 (ddd, $J = 9.2, 3.8, 2.4$ Hz, 1 H), 3.83 (s, 3 H), 4.12 (qd, $J = 5.9, 5.7$ Hz, 1 H), 6.67 (dd, $J = 7.6, 7.6$ Hz, 1 H).

(3*S*,4*R*)-4-[(*Z*)-3-Bromo-4-hydroxylbut-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (5)

To a solution of **4** (200 mg, 0.384 mmol) in CH_2Cl_2 (4 ml) was added DIBAL-H (0.95 mol / l in toluene, 1.05 ml, 1.00 mmol) at -78°C , and the mixture was stirred at -78°C for 30 minutes. To the reaction mixture was added methanol (0.2 ml) followed by the addition of sat. aq. Rochell salt (10 ml), and the mixture was allowed to stir at room temperature. The mixture was extracted with CH_2Cl_2 , and the organic layer was washed with sat. aq. NH_4Cl and brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 3 / 1) to afford **5** (88.9 mg, 0.181 mmol, 47%) as a pale yellow oil.

¹H NMR (270MHz, CDCl_3) δ 0.05 (s, 3 H), 0.08 (s, 3 H), 0.25 (s, 6 H), 0.88 (s, 9 H), 0.97 (s, 9 H), 1.18 (d, $J = 6.2$ Hz, 3 H), 1.90 (t, $J = 6.5$ Hz, 1 H), 2.39 (ddd, $J = 15.1,$

8.9, 7.0 Hz, 1 H), 2.76 (ddd, $J = 15.1, 7.0, 3.5$ Hz, 1 H), 2.83 (dd, $J = 5.4, 2.7$ Hz, 1 H), 3.67 (ddd, $J = 8.9, 3.5, 2.7$ Hz, 1 H), 4.12 (qd, $J = 6.2, 5.4$ Hz, 1 H), 4.26 (d, $J = 6.5$ Hz, 2 H), 6.06 (dd, $J = 7.0, 7.0$ Hz, 1 H). IR (neat) 3580-3150, 2955, 2929, 2858, 1746, 1722 cm^{-1} . LRMS (EI, m/z) 434 ($\text{M}^+ - \text{tBu}$). HRMS (EI) calcd for $\text{C}_{17}\text{H}_{33}\text{NO}_3\text{BrSi}_2$ 434.1182 ($\text{M}^+ - \text{tBu}$), found 434.1195.

(3*S*,4*R*)-4-[(*Z*)-3-Bromo-4-*tert*-butyldimethylsilyloxybut-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (6)

To a solution of **5** (88.9 mg, 0.181 mmol) in DMF (2 ml) was added imidazole (25.0 mg, 0.367 mmol) and TBSCl (33.0 mg, 0.219 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 hours. To the reaction mixture was added sat. aq. NaHCO_3 , and the aqueous layer was extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 10 / 1) to afford the crude product (100 mg).

To a solution of the above crude material in MeOH (2 ml) was added KF (32.0 mg, 0.551 mmol) at 0 °C, and the mixture was stirred at 0 °C for 5 minutes. To the reaction mixture was added sat. aq. NH_4Cl , and the aqueous layer was extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 5 / 1) to afford **6** (58.1 mg, 0.118 mmol, 65% (2 steps)) as a colorless oil.

^1H NMR (270MHz, CDCl_3) δ 0.07 (s, 6 H), 0.10 (s, 6 H), 0.88 (s, 9 H), 0.92 (s, 9 H), 1.20 (d, $J = 5.9$ Hz, 3 H), 2.58 (dd, $J = 8.1, 7.3$ Hz, 2 H), 2.84 (dd, $J = 4.6, 1.9$ Hz, 1

H), 3.80 (td, $J = 8.1, 1.9$ Hz, 1 H), 4.19 (qd, $J = 5.9, 4.6$ Hz, 1 H), 4.25 (d, $J = 1.4$ Hz, 2 H), 5.85 (bs, 1 H), 6.07 (tt, $J = 7.3, 1.4$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ - 5.26 (CH_3), -4.92 (CH_3), -4.18 (CH_3), 18.00 (C), 18.40 (C), 22.69 (CH_3), 25.79 (CH_3), 25.85 (CH_3), 35.65 (CH_2), 49.42 (CH), 63.75 (CH), 65.13 (CH), 67.84 (CH_2), 122.09 (CH), 128.98 (C), 168.18 (C). IR (neat) 3400-3060, 3125, 2956, 2930, 2857, 1758 cm^{-1} . LRMS (EI, m/z) 476 (M-Me) $^+$, 434 (M- t Bu) $^+$. HRMS (EI) calcd for $\text{C}_{20}\text{H}_{39}\text{NO}_3\text{BrSi}_2$ 476.1651 (M-Me) $^+$, found 476.1625.

(3*S*,4*R*)-4-[(*Z*)-3-Bromo-3-methoxycarbonylprop-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (7)

To a solution of **4** (200 mg, 0.384 mmol) in MeOH (4 ml) was added KF (66.8 mg, 1.15 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 hour. To the reaction mixture was added sat. aq. NH_4Cl , and the aqueous layer was extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 2 / 1) to afford **7** (156 mg, 0.384 mmol, quant.) as a colorless solid.

^1H NMR (270MHz, CDCl_3) δ 0.07 (s, 3 H), 0.08 (s, 3 H), 0.88 (s, 9 H), 1.22 (d, $J = 5.9$ Hz, 3 H), 2.65-2.82 (m, 2 H), 2.88 (dd, $J = 4.6, 1.9$ Hz, 1 H), 3.80-3.91 (m, 4 H), 4.19 (qd, $J = 5.9, 4.6$ Hz, 1 H), 5.90 (bs, 1 H), 7.30 (dd, $J = 7.8, 7.8$ Hz, 1 H). IR (neat) 3450-3100, 2954, 2929, 2885, 2856, 1757, 1734, 1627 cm^{-1} . LRMS (FAB, m/z) 406 (M+H) $^+$, 390 (M-Me) $^+$, 348 (M- t Bu) $^+$. HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{28}\text{NO}_4\text{BrSiNa}$ 428.0869 (M+Na) $^+$, found 428.0887.

(5*R*,6*S*)-6-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-3-*tert*-butyldimethylsilyloxymethyl-carbapen-2-em (8)

(Table 1, Run 4)

To a suspension of Pd(OAc)₂ (2.5 mg, 0.0111 mmol), DPEphos (8.9 mg, 0.0165 mmol), and Cs₂CO₃ (71.7 mg, 0.220 mmol) in toluene (1 ml) was added a solution of **6** (54.1 mg, 0.110 mmol) in toluene (3 ml) at 0 °C followed by degassed, and the mixture was stirred at 80 °C for 6 hours. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane / ether = 4 / 1) to afford **8** (43.5 mg, 0.106 mmol, 96%) as a colorless oil.

¹H NMR (270MHz, CDCl₃) δ 0.07 (s, 6 H), 0.09 (s, 6 H), 0.88 (s, 9 H), 0.91 (s, 9 H), 1.22 (d, *J* = 6.2 Hz, 3 H), 2.52-2.81 (m, 2 H), 3.07 (dd, *J* = 5.1, 3.5 Hz, 1 H), 4.12-4.21 (m, 2 H), 4.23-4.33 (m, 1 H), 4.38-4.48 (m, 1 H), 5.23 (dd, *J* = 1.4, 1.4 Hz, 1 H). ¹³C NMR (100MHz, CDCl₃) δ -5.34 (CH₃), -4.89 (CH₃), -4.21 (CH₃), 18.03 (C), 18.41 (C), 22.46 (CH₃), 25.76 (CH₃), 25.91 (CH₃), 34.75 (CH₂), 53.54 (CH), 60.34 (CH₂), 65.63 (CH), 67.11 (CH), 111.81 (CH), 143.19 (C), 178.98 (C). IR (neat) 2955, 2929, 2857, 1778, 1654 cm⁻¹. LRMS (EI, *m/z*) 411 (M)⁺, 396 (M-Me)⁺, 354 (M-^tBu)⁺. HRMS (EI) calcd for C₂₁H₄₁NO₃Si₂ 411.2625 (M)⁺, found 411.2617.

(3*S*,4*R*)-4-[(*Z*,*S*)-3-Bromo-3-ethoxycarbonyl-1-methylprop-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (11a)

A solution of **9-β** (500 mg, 1.26 mmol), purified by silica gel column chromatography from diastereomixture **9**, in CH₂Cl₂ (8 ml) was cooled to -78 °C and treated with a stream of O₃/O₂ at -78 °C until the colorless solution had been converted to a blue one. The reaction mixture was treated with a stream of O₂ at -78 °C to remove an excess amount of O₃. To the reaction mixture was added a solution of PPh₃ (826 mg, 3.15 mmol) in CH₂Cl₂ (4 ml) at -78 °C, and the mixture

was allowed to stir at room temperature for 3 hours. To the reaction mixture was added water, and the aqueous layer was extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford crude product **10** (480 mg).

To a suspension of NaH (60%) (185 mg, 4.63 mmol) in THF (28 ml) was added $(\text{EtO})_2\text{POCH}_2\text{COOEt}$ (875 μl , 4.41 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 minutes. To the mixture was added Br_2 (240 μl , 4.66 mmol) in THF (3 ml) at 0 °C, and the mixture was stirred at room temperature for 2 hours. To the mixture was added NaH (60%) (185 mg, 4.63 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 minutes. To the mixture was added the crude material **10** (480 mg) in THF (12 ml) at 0 °C, and the mixture was stirred at room temperature for 2 hours. To the reaction mixture was added sat. aq. NaHCO_3 and aq. $\text{Na}_2\text{S}_2\text{O}_3$, and the aqueous layer was extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford **11a** (366 mg, 0.668 mmol, 53% (2 steps)) as a colorless oil along with *E*-isomer (124 mg, 0.227 mmol, 18% (2 steps)).

9- β ^1H NMR (270MHz, CDCl_3) δ 0.06 (s, 3 H), 0.08 (s, 3 H), 0.20 (s, 3 H), 0.28 (s, 3 H), 0.89 (s, 9 H), 0.97 (s, 9 H), 1.05 (d, J = 7.3 Hz, 3 H), 1.23 (d, J = 5.9 Hz, 3 H), 2.59-2.70 (m, 1 H), 2.79 (dd, J = 6.5, 2.7 Hz, 1 H), 3.53 (dd, J = 2.7, 2.7 Hz, 1 H), 4.04 (qd, J = 6.5, 5.9 Hz, 1 H), 5.10 (ddd, J = 17.0, 1.4, 1.4 Hz, 1 H), 5.16 (ddd, J = 10.8, 1.4, 1.4 Hz, 1 H), 5.97 (ddd, J = 17.0, 10.8, 5.7 Hz, 1 H). IR (neat) 3083, 2956,

2930, 2885, 2858, 1745, 1645 cm^{-1} . LRMS (EI, m/z) 382 (M-Me)⁺, 340 (M-^tBu)⁺. HRMS (EI) calcd for $\text{C}_{20}\text{H}_{40}\text{NO}_2\text{Si}_2$ 382.2597 (M-^tBu)⁺, found 382.2598.

11a ¹H NMR (270MHz, CDCl_3) δ 0.07 (s, 3 H), 0.10 (s, 3 H), 0.17 (s, 3 H), 0.21 (s, 3 H), 0.89 (s, 9 H), 0.94 (s, 9 H), 1.11 (d, $J = 7.3$ Hz, 3 H), 1.28 (d, $J = 6.8$ Hz, 3 H), 1.32 (t, $J = 6.5$ Hz, 3 H), 3.00 (dd, $J = 6.2, 2.4$ Hz, 1 H), 3.10-3.23 (m, 1 H), 3.64 (dd, $J = 4.1, 2.4$ Hz, 1 H), 4.11 (qd, $J = 6.8, 6.2$ Hz, 1 H), 4.22-4.34 (m, 2 H), 7.29 (d, $J = 9.2$ Hz, 1 H). ¹³C NMR (100MHz, CDCl_3) δ -5.36 (CH_3), -5.21 (CH_3), -4.50 (CH_3), -4.05 (CH_3), 14.24 (CH_3), 16.07 (CH_3), 18.04 (C), 18.55 (C), 23.17 (CH_3), 25.96 (CH_3), 26.38 (CH_3), 39.09 (CH), 56.09 (CH), 61.00 (CH), 62.65 (CH_2), 66.77 (CH), 118.52 (C), 144.49 (CH), 161.78(C), 172.74 (C). IR (neat) 2955, 2931, 2858, 1747, 1625 cm^{-1} . LRMS (EI, m/z) 532 (M-Me)⁺, 490 (M-^tBu)⁺. HRMS (EI) calcd for $\text{C}_{23}\text{H}_{43}\text{NO}_4\text{BrSi}_2$ 532.1914 (M-Me)⁺, found 532.1920.

(*E*-isomer) ¹H NMR (270MHz, CDCl_3) δ 0.06 (s, 3 H), 0.10 (s, 3 H), 0.13 (s, 3 H), 0.23 (s, 3 H), 0.89 (s, 9 H), 0.94 (s, 9 H), 1.12 (d, $J = 6.8$ Hz, 3 H), 1.27 (d, $J = 5.9$ Hz, 3 H), 1.34 (t, $J = 7.3$ Hz, 3 H), 2.96 (dd, $J = 6.5, 2.4$ Hz, 1 H), 3.53-3.69 (m, 2 H), 4.09 (qd, $J = 6.5, 5.9$ Hz, 1 H), 4.27 (q, $J = 7.3$ Hz, 2 H), 6.65 (d, $J = 9.7$ Hz, 1 H).

(3*S*,4*R*)-4-[(*Z,S*)-3-Bromo-4-hydroxyl-1-methylbut-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (12)

To a solution of **11a** (200 mg, 0.364 mmol) in CH_2Cl_2 (4 ml) was added DIBAL-H (0.95 mol / l in toluene, 1.00 ml, 0.95 mmol) at -78 °C, and the mixture was stirred at -78 °C for 30 minutes. To the reaction mixture was added methanol (0.2 ml) followed by the addition of sat. aq. Rochell salt (10 ml), and the mixture was allowed to stir at room temperature. The mixture was extracted with CH_2Cl_2 , and the

organic layer was washed with sat. aq. NH_4Cl and brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 4 / 1) to afford **12** (90.2 mg, 0.178 mmol, 49%) as a colorless oil.

^1H NMR (270MHz, CDCl_3) δ 0.06 (s, 3 H), 0.09 (s, 3 H), 0.19 (s, 3 H), 0.23 (s, 3 H), 0.89 (s, 9 H), 0.95 (s, 9 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.27 (d, J = 6.5 Hz, 3 H), 1.88-1.98 (m, 1 H), 2.93 (dd, J = 6.5, 2.7 Hz, 1 H), 3.00-3.12 (m, 1 H), 3.56 (dd, J = 3.8, 2.7 Hz, 1 H), 4.07 (qd, J = 6.5, 6.5 Hz, 1 H), 4.23 (d, J = 6.8 Hz, 2 H), 6.05 (d, J = 8.6 Hz, 1 H). IR (neat) 3600-3100, 2955, 2930, 2858, 1742, 1721, 1675 cm^{-1} . LRMS (EI, m/z) 490 (M-Me) $^+$, 448 (M- t Bu) $^+$. HRMS (EI) calcd for $\text{C}_{21}\text{H}_{41}\text{NO}_3\text{BrSi}_2$ 490.1808 (M-Me) $^+$, found 490.1778.

(3*S*,4*R*)-4-[(*Z,S*)-3-Bromo-4-*tert*-butyldimethylsilyloxy-1-methylbut-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (13a)

To a solution of **12** (90.2 mg, 0.178 mmol) in DMF (2 ml) was added imidazole (24.3 mg, 0.357 mmol) and TBSCl (32.2 mg, 0.214 mmol) at 0 $^\circ\text{C}$, and the mixture was stirred at room temperature for 3 hours. To the reaction mixture was added sat. aq. NaHCO_3 , and the aqueous layer was extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 10 / 1) to afford the crude product (100 mg).

To a solution of the above crude material in MeOH (2 ml) was added KF (31.0 mg, 0.534 mmol) at 0 $^\circ\text{C}$, and the mixture was stirred at 0 $^\circ\text{C}$ for 5 minutes. To the reaction mixture was added sat. aq. NH_4Cl , and the aqueous layer was extracted with

CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 8 / 1) to afford **13a** (82.6 mg, 0.163 mmol, 92% (2 steps)) as a colorless solid.

¹H NMR (270MHz, CDCl₃) δ 0.07 (s, 6 H), 0.08 (s, 6 H), 0.88 (s, 9 H), 0.91 (s, 9 H), 1.07 (d, *J* = 6.5 Hz, 3 H), 1.14 (d, *J* = 5.9 Hz, 3 H), 2.82-2.98 (m, 2 H), 3.61 (dd, *J* = 7.0, 1.4 Hz, 1 H), 4.14-4.26 (m, 3 H), 5.77 (bs, 1 H), 5.86 (d, *J* = 10.0 Hz, 1 H). ¹³C NMR (100MHz, CDCl₃) δ -5.30 (CH₃), -5.26 (CH₃), -4.88 (CH₃), -4.27 (CH₃), 16.76 (CH₃), 18.02 (C), 18.37 (C), 22.83 (CH₃), 25.81 (CH₃), 39.51 (CH), 54.20 (CH), 61.92 (CH), 64.63 (CH), 67.74 (CH₂), 127.13 (C), 127.89 (CH), 168.76 (C). IR (neat) 3250-3000, 2953, 2926, 2856, 1758, 1713, 1672 cm⁻¹. LRMS (EI, *m/z*) 490 (M-Me)⁺, 448 (M-^tBu)⁺. HRMS (EI) calcd for C₂₁H₄₁NO₃BrSi₂ 490.1808 (M-Me)⁺, found 490.1819.

(3*S*,4*R*)-4-[(*Z,S*)-3-Bromo-3-ethoxycarbonyl-1-methylprop-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (14a)

To a solution of **11a** (200 mg, 0.364 mmol) in EtOH (4 ml) was added KF (63.9 mg, 1.10 mmol) at 0 °C, and the mixture was stirred at 0 °C for 2 hours. To the reaction mixture was added sat. aq. NH₄Cl, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 2 / 1) to afford **14a** (145 mg, 0.334 mmol, 92%) as a colorless solid.

¹H NMR (270MHz, CDCl₃) δ 0.07 (s, 6 H), 0.88 (s, 9 H), 1.14 (d, *J* = 5.9 Hz, 3 H), 1.15 (d, *J* = 6.8 Hz, 3 H), 1.33 (t, *J* = 7.3 Hz, 3 H), 2.90 (dd, *J* = 3.2, 2.4 Hz, 1 H),

2.95-3.08 (m, 1 H), 3.69 (dd, $J = 7.6, 2.4$ Hz, 1 H), 4.19 (qd, $J = 5.9, 3.2$ Hz, 1 H), 4.28 (q, $J = 7.3$ Hz, 2 H), 5.87 (bs, 1 H), 7.07 (d, $J = 10.0$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ -4.83 (CH_3), -4.28 (CH_3), 14.19 (CH_3), 15.95 (CH_3), 18.02 (C), 22.80 (CH_3), 25.82 (CH_3), 41.19 (CH), 53.75 (CH), 62.28 (CH), 62.69 (CH_2), 64.82 (CH), 117.36 (C), 145.17 (CH), 161.95 (C), 168.31 (C). IR (neat) 3350-3000, 2967, 2927, 2855, 1761, 1732, 1715, 1630 cm^{-1} . LRMS (EI, m/z) 418 (M-Me) $^+$, 376 (M-Bu) $^+$. HRMS (EI) calcd for $\text{C}_{17}\text{H}_{29}\text{NO}_4\text{BrSi}$ 418.1049 (M-Me) $^+$, found 418.1037.

(3*S*,4*R*)-4-[(*Z,S*)-3-Iodo-3-ethoxycarbonyl-1-methylprop-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (11b)

A solution of **9- β** (500 mg, 1.26 mmol), purified by silica gel column chromatography from diastereomixture **9**, in CH_2Cl_2 (8 ml) was cooled to -78°C and treated with a stream of O_3/O_2 at -78°C until the colorless solution had been converted to a blue one. The reaction mixture was treated with a stream of O_2 at -78°C to remove an excess amount of O_3 . To the reaction mixture was added a solution of PPh_3 (826 mg, 3.15 mmol) in CH_2Cl_2 (4 ml) at -78°C , and the mixture was allowed to stir at room temperature for 3 hours. To the reaction mixture was added water, and the aqueous layer was extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford crude product **10** (480 mg).

To a suspension of NaH (60%) (185 mg, 4.63 mmol) in THF (28 ml) was added $(\text{EtO})_2\text{POCH}_2\text{COOEt}$ (875 μl , 4.41 mmol) at 0°C , and the mixture was stirred at room temperature for 30 minutes. To the mixture was added I_2 (1.18 g, 4.65 mmol)

in THF (10 ml) at 0 °C, and the mixture was stirred at room temperature for 2 hours. To the mixture was added NaH (60%) (185 mg, 4.63 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 minutes. To the mixture was added the crude material **10** (480 mg) in THF (12 ml) at 0 °C, and the mixture was stirred at room temperature for 2 hours. To the reaction mixture was added sat. aq. NaHCO₃ and aq. Na₂S₂O₃, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford **11b** (173 mg, 0.290 mmol, 23% (2 steps)) as a colorless oil along with *E*-isomer (143 mg, 0.239 mmol, 19% (2 steps)).

¹H NMR (270MHz, CDCl₃) δ 0.07 (s, 3 H), 0.10 (s, 3 H), 0.18 (s, 3 H), 0.22 (s, 3 H), 0.89 (s, 9 H), 0.94 (s, 9 H), 1.10 (d, *J* = 7.3 Hz, 3 H), 1.28 (d, *J* = 5.9 Hz, 3 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 2.96-3.05 (m, 2 H), 3.65 (dd, *J* = 4.1, 2.4 Hz, 1 H), 4.11 (qd, *J* = 5.9, 5.9 Hz, 1 H), 4.23-4.33 (m, 2 H), 7.22 (d, *J* = 8.9 Hz, 1 H). IR (neat) 2956, 2930, 2858, 1747, 1726, 1614 cm⁻¹. LRMS (EI, *m/z*) 580 (M-Me)⁺, 538 (M-^tBu)⁺. HRMS (EI) calcd for C₂₃H₄₃NO₄Si₂ 580.1775 (M-Me)⁺, found 580.1779.

(*E*-isomer) ¹H NMR (270MHz, CDCl₃) δ 0.06 (s, 3 H), 0.09 (s, 3 H), 0.13 (s, 3 H), 0.23 (s, 3 H), 0.89 (s, 9 H), 0.95 (s, 9 H), 1.11 (d, *J* = 6.5 Hz, 3 H), 1.27 (d, *J* = 5.9 Hz, 3 H), 1.33 (t, *J* = 7.3 Hz, 3 H), 2.95 (dd, *J* = 5.9, 1.9 Hz, 1 H), 3.51-3.62 (m, 2 H), 4.09 (qd, *J* = 5.9, 5.9 Hz, 1 H), 4.25 (q, *J* = 7.3 Hz, 2 H), 6.86 (d, *J* = 9.2 Hz, 1 H).

(3*S*,4*R*)-4-[(*Z*,*S*)-3-Iodo-3-ethoxycarbonyl-1-methylprop-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (14b)

To a solution of **11b** (143 mg, 0.239 mmol) in EtOH (3 ml) was added KF (41.6 mg,

0.716 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 hour. To the reaction mixture was added sat. aq. NH₄Cl, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ethyl acetate = 4 / 1) to afford **14b** (107 mg, 0.222 mmol, 93%) as a colorless solid.

¹H NMR (270MHz, CDCl₃) δ 0.07 (s, 6 H), 0.88 (s, 9 H), 1.14 (d, *J* = 6.5 Hz, 3 H), 1.14 (d, *J* = 7.3 Hz, 3 H), 1.32 (t, *J* = 7.0 Hz, 3 H), 2.81-2.96 (m, 2 H), 3.73 (dd, *J* = 8.1, 1.9 Hz, 1 H), 4.20 (qd, *J* = 6.5, 3.8 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2 H), 6.03 (bs, 1 H), 6.96 (d, *J* = 10.0 Hz, 1 H). ¹³C NMR (100MHz, CDCl₃) δ -4.86 (CH₃), -4.32 (CH₃), 14.17 (CH₃), 15.81 (CH₃), 17.98 (C), 22.78 (CH₃), 25.80 (CH₃), 45.89 (CH), 53.54 (CH), 62.22 (CH), 62.88 (CH₂), 64.69 (CH), 96.14 (C), 152.05 (CH), 162.42 (C), 168.53 (C). IR (neat) 3350-3020, 2973, 2927, 2856, 1761, 1719, 1616 cm⁻¹. LRMS (EI, *m/z*) 466 (M-Me)⁺, 424 (M-^tBu)⁺. HRMS (EI) calcd for C₁₇H₂₉NO₄Si 466.0911 (M-Me)⁺, found 466.0918.

(1*S*,5*R*,6*S*)-6-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-3-*tert*-butyldimethylsilyloxymethyl-1-methyl-carbapen-2-em (15)

(Scheme 5)

To a suspension of Pd(OAc)₂ (2.5 mg, 0.0111 mmol), DPEphos (8.9 mg, 0.0165 mmol), and Cs₂CO₃ (71.7 mg, 0.220 mmol) in toluene (1 ml) was added a solution of **13a** (55.7 mg, 0.110 mmol) in toluene (3 ml) at 0 °C followed by degassed, and the mixture was stirred at 80 °C for 1.5 hours. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane / ether = 4 / 1) to afford **15** (45.4 mg, 0.107 mmol, 97%) as a colorless oil.

^1H NMR (270MHz, CDCl_3) δ 0.07 (s, 6 H), 0.09 (s, 6 H), 0.88 (s, 9 H), 0.91 (s, 9 H), 1.05 (d, $J = 7.3$ Hz, 3 H), 1.21 (d, $J = 5.9$ Hz, 3 H), 3.00-3.15 (m, 1 H), 3.23 (dd, $J = 4.1, 4.1$ Hz, 1 H), 4.14-4.26 (m, 2 H), 4.28 (d, $J = 15.4$ Hz, 1 H), 4.45 (d, $J = 15.4$ Hz, 1 H), 5.16 (s, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ -5.31 (CH_3), -4.91 (CH_3), -4.21 (CH_3), 17.65 (CH_3), 18.02 (C), 18.41 (C), 22.28 (CH_3), 25.75 (CH_3), 25.92 (CH_3), 37.39 (CH), 56.67 (CH), 59.71 (CH), 60.01 (CH_2), 65.64 (CH), 117.35 (CH), 142.21 (C), 177.17 (C). IR (neat) 2957, 2930, 2858, 1775, 1653 cm^{-1} . LRMS (EI, m/z) 425 (M) $^+$, 410 (M-Me) $^+$, 368 (M- $t\text{Bu}$) $^+$. HRMS (EI) calcd for $\text{C}_{22}\text{H}_{43}\text{NO}_3\text{Si}_2$ 425.2781 (M) $^+$, found 425.2781.

Ethyl (1*S*,5*R*,6*S*)-6-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-1-methyl-carbapen-2-em-3-carboxylate (17)

(Table 2, Run 4, Procedure using method B)

To a suspension of $\text{Pd}(\text{OAc})_2$ (2.5 mg, 0.0111 mmol) and DPEphos (8.9 mg, 0.0165 mmol) in toluene (0.5 ml) was added a solution of **14b** (53.0 mg, 0.110 mmol) in toluene (2.5 ml) at 0 °C followed by degassed, and the mixture was stirred at 100 °C for 2 minutes. To a suspension of K_2CO_3 (30.4 mg, 0.220 mmol) in toluene (1 ml) was added the mixture at 0 °C followed by degassed, and the mixture was stirred at 100 °C for 22 hours. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane / ether = 4 / 1) to afford **17** (35.0 mg, 0.0990 mmol, 90%) as a colorless oil.

^1H NMR (270MHz, CDCl_3) δ 0.08 (s, 6 H), 0.89 (s, 9 H), 1.11 (d, $J = 7.3$ Hz, 3 H), 1.25 (d, $J = 6.5$ Hz, 3 H), 1.32 (t, $J = 7.3$ Hz, 3 H), 3.19 (qdd, $J = 10.3, 7.3, 3.0$ Hz, 1 H), 3.25 (dd, $J = 6.5, 3.2$ Hz, 1 H), 4.21 (qd, $J = 6.5, 6.5$ Hz, 1 H), 4.24 (dd, $J = 10.3,$

3.2 Hz, 1 H), 4.28 (q, $J = 7.3$ Hz, 2 H), 6.33 (d, $J = 3.0$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ -4.87 (CH_3), -4.09 (CH_3), 14.20 (CH_3), 16.57 (CH_3), 18.02 (C), 22.45 (CH_3), 25.74 (CH_3), 38.46 (CH), 57.61 (CH), 60.15 (CH), 61.37 (CH_2), 66.36 (CH), 134.27 (C), 134.97 (CH), 160.73 (C), 175.09 (C). IR (neat) 3082, 2956, 2929, 2856, 1782, 1726, 1610 cm^{-1} . LRMS (EI, m/z) 338 (M-Me) $^+$, 296 (M- ^tBu) $^+$. HRMS (EI) calcd for $\text{C}_{17}\text{H}_{28}\text{NO}_4\text{Si}$ 338.1787 (M-Me) $^+$, found 338.1777.

(3*S*,4*R*)-4-[(*Z*,*R*)-3-Bromo-3-ethoxycarbonyl-1-methylprop-2-enyl]-1-(*tert*-butyldimethylsilyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (19)

A solution of **9- α** (500 mg, 1.26 mmol), purified by silica gel column chromatography from diastereomixture **9**, in CH_2Cl_2 (8 ml) was cooled to -78°C and treated with a stream of O_3/O_2 at -78°C until the colorless solution had been converted to a blue one. The reaction mixture was treated with a stream of O_2 at -78°C to remove an excess amount of O_3 . To the reaction mixture was added a solution of PPh_3 (826 mg, 3.15 mmol) in CH_2Cl_2 (4 ml) at -78°C , and the mixture was allowed to stir at room temperature for 3 hours. To the reaction mixture was added water, and the aqueous layer was extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford crude product **18** (480 mg).

To a suspension of NaH (60%) (185 mg, 4.63 mmol) in THF (28 ml) was added $(\text{EtO})_2\text{POCH}_2\text{COOEt}$ (875 μl , 4.41 mmol) at 0°C , and the mixture was stirred at room temperature for 30 minutes. To the mixture was added Br_2 (240 μl , 4.66 mmol) in THF (3 ml) at 0°C , and the mixture was stirred at room temperature for 2

hours. To the mixture was added NaH (60%) (185 mg, 4.63 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 minutes. To the mixture was added the crude material **18** (480 mg) in THF (12 ml) at 0 °C, and the mixture was stirred at room temperature for 2 hours. To the reaction mixture was added sat. aq. NaHCO₃ and aq. Na₂S₂O₃, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 6 / 1) to afford **19** (380 mg, 0.693 mmol, 55% (2 steps)) as a colorless oil along with *E*-isomer (256 mg, 0.467 mmol, 37% (2 steps)).

9- α ¹H NMR (270MHz, CDCl₃) δ 0.04 (s, 3 H), 0.07 (s, 3 H), 0.20 (s, 3 H), 0.27 (s, 3 H), 0.89 (s, 9 H), 0.97 (s, 9 H), 1.03 (d, *J* = 6.5 Hz, 3 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 2.52-2.65 (m, 1 H), 2.87 (dd, *J* = 5.9, 2.7 Hz, 1 H), 3.61 (dd, *J* = 2.7, 2.7 Hz, 1 H), 4.05 (qd, *J* = 6.5, 5.9 Hz, 1 H), 5.04 (ddd, *J* = 10.0, 1.4, 1.4 Hz, 1 H), 5.10 (ddd, *J* = 17.3, 1.4, 1.4 Hz, 1 H), 5.73 (ddd, *J* = 17.3, 10.0, 7.3 Hz, 1 H). IR (neat) 3079, 2956, 2930, 2884, 2858, 1745, 1640 cm⁻¹. LRMS (EI, *m/z*) 382 (M-Me)⁺, 340 (M-^tBu)⁺. HRMS (EI) calcd for C₂₀H₄₀NO₂Si₂ 382.2597 (M-^tBu)⁺, found 382.2594.

19 ¹H NMR (400MHz, CDCl₃) δ 0.03 (s, 3 H), 0.07 (s, 3 H), 0.25 (s, 3 H), 0.30 (s, 3 H), 0.86 (s, 9 H), 0.98 (s, 9 H), 1.12 (d, *J* = 7.3 Hz, 3 H), 1.21 (d, *J* = 5.9 Hz, 3 H), 1.33 (t, *J* = 7.3 Hz, 3 H), 2.95 (dd, *J* = 5.9, 2.7 Hz, 1 H), 3.11-3.23 (m, 1 H), 3.65 (dd, *J* = 4.1, 2.7 Hz, 1 H), 4.10 (qd, *J* = 5.9, 5.9 Hz, 1 H), 4.27 (q, *J* = 7.3 Hz, 2 H), 7.06 (d, *J* = 9.2 Hz, 1 H). IR (neat) 2956, 2930, 2858, 1748, 1739, 1625 cm⁻¹. LRMS (EI, *m/z*) 532 (M-Me)⁺, 490 (M-^tBu)⁺. HRMS (EI) calcd for C₂₃H₄₃NO₄BrSi₂ 532.1913 (M-Me)⁺, found 532.1931.

(*E*-isomer) ^1H NMR (270MHz, CDCl_3) δ 0.06 (s, 3 H), 0.09 (s, 3 H), 0.22 (s, 3 H), 0.28 (s, 3 H), 0.90 (s, 9 H), 0.96 (s, 9 H), 1.07 (d, $J = 6.5$ Hz, 3 H), 1.25 (d, $J = 5.9$ Hz, 3 H), 1.34 (t, $J = 7.0$ Hz, 3 H), 2.91 (dd, $J = 7.3, 1.9$ Hz, 1 H), 3.55-3.70 (m, 2 H), 4.06 (qd, $J = 7.3, 5.9$ Hz, 1 H), 4.28 (q, $J = 7.0$ Hz, 2 H), 6.45 (d, $J = 10.0$ Hz, 1 H).

(3*S*,4*R*)-4-[(*Z*,*R*)-3-Bromo-3-ethoxycarbonyl-1-methylprop-2-enyl]-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (20)

To a solution of **19** (380 mg, 0.693 mmol) in EtOH (8 ml) was added KF (121 mg, 2.08 mmol) at 0 °C, and the mixture was stirred at 0 °C for 2 hours. To the reaction mixture was added sat. aq. NH_4Cl , and the aqueous layer was extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane / ether = 2 / 1) to afford **20** (277 mg, 0.638 mmol, 92%) as a colorless solid.

^1H NMR (400MHz, CDCl_3) δ 0.07 (s, 3 H), 0.08 (s, 3 H), 0.88 (s, 9 H), 1.14 (d, $J = 6.8$ Hz, 3 H), 1.24 (d, $J = 6.4$ Hz, 3 H), 1.35 (t, $J = 7.2$ Hz, 3 H), 2.82-2.88 (m, 1 H), 2.96-3.06 (m, 1 H), 3.65 (dd, $J = 7.2, 2.4$ Hz, 1 H), 4.19 (qd, $J = 6.4, 5.2$ Hz, 1 H), 4.29 (q, $J = 7.2$ Hz, 2 H), 6.08 (bs, 1 H), 7.12 (d, $J = 9.6$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ -4.80 (CH_3), -4.26 (CH_3), 14.16 (CH_3), 15.95 (CH_3), 17.96 (C), 22.84 (CH_3), 25.78 (CH_3), 41.07 (CH), 54.08 (CH), 62.72 (CH_2), 62.74 (CH), 65.24 (CH), 117.65 (C), 145.22 (CH), 161.98 (C), 168.04 (C). IR (neat) 3300-3000, 2922, 2852, 1762, 1715, 1631 cm^{-1} . LRMS (EI, m/z) 418 (M-Me^+), 376 ($\text{M-}^t\text{Bu}^+$). HRMS (EI) calcd for $\text{C}_{14}\text{H}_{23}\text{NO}_4\text{BrSi}$ 376.0579 ($\text{M-}^t\text{Bu}^+$), found 376.0564.

Ethyl (1*R*,5*R*,6*S*)-6-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-1-methyl-carbapen-2-em-3-carboxylate (21)

(Scheme 9, Procedure using method B)

To a suspension of Pd(OAc)₂ (2.5 mg, 0.0111 mmol) and DPEphos (8.9 mg, 0.0165 mmol) in toluene (0.5 ml) was added a solution of **20** (47.8 mg, 0.110 mmol) in toluene (2.5 ml) at 0 °C followed by degassed, and the mixture was stirred at 100 °C for 2 minutes. To a suspension of K₂CO₃ (30.4 mg, 0.220 mmol) in toluene (1 ml) was added the mixture at 0 °C followed by degassed, and the mixture was stirred at 100 °C for 36 hours. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane / ether = 4 / 1) to afford **21** (22.0 mg, 0.0662 mmol, 56%) as a colorless oil.

¹H NMR (400MHz, CDCl₃) δ 0.08 (s, 3 H), 0.09 (s, 3 H), 0.89 (s, 9 H), 1.26 (d, *J* = 6.0 Hz, 3 H), 1.26 (d, *J* = 7.2 Hz, 3 H), 1.31 (t, *J* = 7.2 Hz, 3 H), 3.13 (dd, *J* = 6.8, 2.8 Hz, 1 H), 3.15-3.24 (m, 1 H), 3.72 (dd, *J* = 7.6, 2.8 Hz, 1 H), 4.17 (qd, *J* = 6.8, 6.0 Hz, 1 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 6.34 (d, *J* = 2.4 Hz, 1 H). ¹³C NMR (100MHz, CDCl₃) δ -4.75 (CH₃), -4.13 (CH₃), 14.18 (CH₃), 17.95 (C), 19.19 (CH₃), 22.75 (CH₃), 25.76 (CH₃), 43.87 (CH), 61.35 (CH₂), 62.36 (CH), 66.57 (CH), 66.81 (CH), 134.65 (C), 136.64 (CH), 160.66 (C), 176.51 (C). IR (neat) 2958, 2930, 2857, 1785, 1726, 1610 cm⁻¹. LRMS (EI, *m/z*) 338 (M-Me)⁺, 309 (M-OEt)⁺, 296 (M-^tBu)⁺. HRMS (EI) calcd for C₁₇H₂₈NO₄Si 338.1787 (M-Me)⁺, found 338.1772.