Supporting Information

Novel Radical Alkylation of Carboxylic Imides

Sunggak Kim^{*}, Chae Jo Lim, Changsik Song, and Won-jin Chung

*Center for Molecular Design & Synthesis and Department of Chemistry,
School of Molecular Science, Korea Advanced Institute of Science and Technology,
Taejeon 305-701, Korea*

General. ¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance-400 spectrometers. The chemical shifts in CDCl₃ or benzene-*d*₆ reported in δ (ppm) relative to CDCl₃ or Me₄Si as an internal reference. Splitting patterns are designated as follows: br s; broad singlet, s; singlet, d; doublet, t; triplet, m; multiplet, dt; double of triplet, td; triple of doublet, dd; double of doublet. IR spectra were measured on a BOMEM MB-100 Fourier Transform spectrometer. High resolution mass spectra were obtained on a VG AUTOSPEC Ultima GC/MS system using direct insertion probe (DIP) and electron impact (EI) (70 eV) method. Flash chromatography was carried out on Merck silica 60 (230-400 mesh ASTM). Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica gel 60 F₂₅₄ plates. All reagents were purchased from Aldrich Co. All dry solvents were freshly distilled under nitrogen from the appropriate drying agent before use. The photochemical reactor was RAYONET purchased from the southern new England ultraviolet company.

Preparation of *tert*-butyldiphenylsilyloxy-carbamic acid benzyl ester (5) To a solution of *N*-hydroxylamine hydrochloride (1.39 g, 20 mmol) and carbobenzyloxy chloride (Cbz-Cl, 3.14 mL, 22 mmol) in methylene chloride (40 mL) was added triethylamine (6.69 mL, 48 mmol) at 0°C. After being stirred for 3h at room temperature, *tert*-butyldiphenylsilyl chloride (TBDPS-Cl, 6.24 mL, 24 mmol) and triethylamine (3.35 mL, 24 mmol) were added and the reaction mixture was diluted with methylene chloride (100 mL), quenched with aqueous NH₄Cl solution and washed with water and brine. The organic layer was dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1 : 10) to give **5** (6.65 g, 16.4 mmol, 82%).

MW: C₂₄H₂₇NO₃Si = 405.56; **¹H NMR** (CDCl₃, 400 MHz) δ 1.11 (s, 9H), 5.08 (s, 2H), 6.89 (s, 1H), 7.24-7.72 (m, 15H); **¹³C NMR** (CDCl₃, 100 MHz) δ 19.1, 26.8, 67.6, 127.8, 128.3 (2C), 128.5, 130.2, 131.6, 135.6, 135.7, 157.8; **IR** (polymer) 3274, 2933, 2860, 1751, 1701, 1473, 1428, 1342, 1240, 1114, 823, 741, 700, 614, 504 cm⁻¹; **HRMS** (M⁺) calcd for C₂₄H₂₇NO₃Si: 405.1760, found 405.1761.

Preparation of Acetyl-*tert*-butyldiphenylsilyloxy-carbamic acid benzyl ester (6) To a solution of **5** (4.06 g, 10 mmol) and acetyl chloride (853 μl, 12 mmol) in methylene chloride (20 mL) was added triethylamine (1.67 mL, 12 mmol) at 0°C. After being stirred for 30min at room temperature, the reaction mixture was diluted with methylene chloride (50 mL), quenched with aqueous NH₄Cl solution and washed with water and brine. The organic layer was dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1 : 10) to give **6** (4.25 g, 9.5 mmol, 95%).

MW: C₂₆H₂₉NO₄Si = 447.60; **¹H NMR** (CDCl₃, 400 MHz) δ 1.10 (s, 9H), 2.12 (s, 3H), 4.91 (s, 2H), 7.09-7.69 (m, 15H); **¹³C NMR** (CDCl₃, 100 MHz) δ 19.9, 25.1, 27.0, 68.7, 127.3, 128.5, 128.7, 129.2, 130.0, 131.3, 134.4, 136.2, 153.0, 168.2; **IR** (polymer) 1734, 1719, 1427, 1302, 1260, 1130, 1114, 1074, 822, 743, 700, 508 cm⁻¹; **HRMS** (M⁺) calcd for C₂₆H₂₉NO₄Si: 447.1866, found 447.1870.

Preparation of 1a To a mixture of **6** (895 mg, 2 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf, 919 μ l, 4 mmol) in THF (6 mL) at -78°C was slowly added a lithium *bis*(trimethylsilyl)amide (LHMDS, 1.0 M solution in THF, 3 mL, 3 mmol). After being stirred for 30min at -78°C, the reaction mixture was diluted with diethyl ether (10 mL), quenched with aqueous sodium bicarbonate and washed with water and brine. The organic layer was dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1 : 50) to give product **1a** (1.01 g, 1.8 mmol, 90%).

MW: C₃₂H₄₃NO₄Si₂ = 561.86; **¹H NMR** (CDCl₃, 400 MHz) δ 0.13 (s, 6H), 0.91 (s, 9H), 1.10 (s, 9H), 3.90 (d, *J* = 1.1 Hz, 1H), 4.00 (d, *J* = 1.1 Hz, 1H), 4.96 (s, 2H), 7.16-7.70 (m, 15H); **¹³C NMR** (CDCl₃, 100 MHz) δ -5.2, 18.1, 19.4, 25.4, 26.9, 67.7, 91.8, 127.2, 128.0, 128.1, 128.3, 129.8, 132.2, 135.7, 136.3, 149.4, 156.4; **IR** (polymer) 1719, 1654, 1474, 1428, 1261, 1114, 1020, 824, 742, 699 cm⁻¹; **HRMS** (M⁺) calcd for C₃₂H₄₃NO₄Si₂: 561.2731, found 561.2725.

Preparation of 1b To a mixture of **6** (895 mg, 2 mmol) and diethyl chlorophosphate (578 μ l, 4 mmol) in THF (6 mL) at -78°C was slowly added a lithium *bis*(trimethylsilyl)amide (LiHMDS, 1.0 M solution in THF, 3 mL, 3 mmol). After being stirred for 30min at -78°C, the reaction mixture was diluted with diethyl ether (10 mL), quenched with aqueous sodium bicarbonate and washed with water and brine. The organic layer was dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1:2) to give product **1b** (1.10 g, 1.9 mmol, 95%).

MW: C₃₀H₃₈NO₇PSi = 583.68; **¹H NMR** (benzene-*d*₆, 400 MHz) δ 1.08 (td, *J* = 7.1 Hz, 1.0 Hz, 6H), 1.14 (s, 9H), 4.07 (d, *J* = 1.9 Hz, 1H), 4.08-4.24 (m, 4H), 4.77 (d, *J* = 1.9 Hz, 1H), 5.15 (s, 2H), 7.11-7.93 (m, 15H); **¹³C NMR** (benzene-*d*₆, 100 MHz) δ 16.0, 16.1, 19.5, 26.4, 64.7, 64.8, 69.1, 96.1, 128.2, 128.5, 128.6, 128.7, 130.4, 131.5, 135.7, 135.9, 149.4 (2C), 156.6 (2C); **IR** (polymer) 1654, 1272, 1211, 1115, 1027, 821, 739, 701, 613 cm⁻¹; **HRMS** (M⁺) calcd for C₃₀H₃₈NO₇PSi: 583.2155, found 583.2152.

Typical procedure for radical alkylation. Method A A benzene solution (1 mL, 0.2M in iodide) of ethyl iodoacetate (43 mg, 0.2 mmol), **1a** (169 mg, 0.3 mmol) and 2,2'-azobis(isobutyronitrile) (AIBN, 3 mg, 0.02 mmol) was degassed with nitrogen for 10 min and then the solution was heated at 80°C under nitrogen for 6 h. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane= 1: 2) to give the product **8b** (36 mg, 0.13 mmol, 64%).

Method B A benzene solution (1 mL, 0.2M in iodide) of ethyl iodoacetate (43 mg, 0.2 mmol), **1a** (169 mg, 0.3 mmol) and hexamethylditin (66 mg, 0.2 mmol) was degassed for 10min and irradiated with a photoreactor (300nm) for 3h. The reaction mixture was concentrated under reduced pressure. Ethyl acetate, water and potassium fluoride were then added and the mixture was stirred at room temperature for 1h. Anhydrous magnesium sulfate was added and the mixture was filtered through silica gel. The residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane= 1: 2) to give the product **8b** (48 mg, 0.17 mmol, 86%).

Method C A benzene solution (1 mL, 0.2M in iodide) of 4-phenoxybutyl iodide (55 mg, 0.2 mmol), **1a** (169 mg, 0.3 mmol) and hexamethylditin (20 mg, 0.06 mmol) was degassed for 10 min and irradiated with a photoreactor (300nm) for 12 h. The reaction mixture was concentrated under reduced pressure. Ethyl acetate, water and potassium fluoride were then added and the mixture was stirred at room temperature for 1h. Anhydrous magnesium sulfate was added and the mixture was filtered through silica gel. The residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane= 1: 3) to give the product **8a** (46 mg, 0.13 mmol, 67%).

(6-Phenoxy-hexanoyl)-carbamic acid benzyl ester (8a)

MW: C₂₀H₂₃NO₄ = 341.40; **¹H NMR** (CDCl₃, 400 MHz) δ 1.50-1.54 (m, 2H), 1.68-1.81 (m, 4H), 2.78 (t, *J* = 7.5 Hz, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 5.15 (s, 2H), 6.85-7.63 (m, 11H); **¹³C NMR** (CDCl₃, 100 MHz) δ 23.9, 25.6, 29.0, 35.9, 67.5, 67.9, 114.5, 120.5, 127.9, 128.4, 128.7, 129.4, 134.3, 134.9, 151.5, 159.0, 174.2; **IR** (polymer) 1774, 1622, 1654, 1521, 1242, 973, 752, 694 cm⁻¹; **HRMS** (M⁺) calcd for C₂₀H₂₃NO₄ = 341.1627, found 341.1624.

4-Benzyloxycarbonylamino-4-oxo-butyrac acid ethyl ester (8b)

MW: $C_{18}H_{21}NO_2 = 279.29$; 1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, $J = 7.1$ Hz, 3H), 2.63 (t, $J = 6.3$ Hz, 2H), 3.07 (t, $J = 6.3$ Hz, 2H), 4.10-4.15 (m, 2H), 5.16 (s, 2H), 7.33-7.37 (m, 5H), 7.50 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 28.3, 31.2, 60.7, 68.0, 128.5, 128.7, 128.8, 134.8, 151.5, 172.4, 172.9; **IR** (polymer) 1733, 1676, 1521, 1238, 763, 736, 698 cm^{-1} ; **HRMS** (M^+) calcd for $C_{14}H_{17}NO_5$: 279.1107, found 279.1107.

[Table]

(4-Oxo-4-phenyl-butryl)-carbamic acid benzyl ester

MW: $C_{18}H_{17}NO_4 = 311.33$; 1H NMR ($CDCl_3$, 400 MHz) δ 3.19 (d, $J = 7.7$ Hz, 1H), 3.20 (d, $J = 6.6$ Hz, 1H), 3.34 (d, $J = 6.7$ Hz, 1H), 3.35 (d, $J = 7.7$ Hz, 1H), 5.18 (s, 2H), 7.34-7.98 (m, 11H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.3, 32.6, 67.9, 128.1, 128.5, 128.6, 128.7, 133.2, 134.9, 136.5, 151.5, 173.2, 198.1; **IR** (polymer) 1758, 1682, 1637, 1527, 1210, 779, 733, 690 cm^{-1} ; **HRMS** (M^+) calcd for $C_{18}H_{17}NO_4$: 311.1158, found 311.1159.

(3-Methyl-4-oxo-4-phenyl-butryl)-carbamic acid benzyl ester

MW: $C_{19}H_{19}NO_4 = 325.36$; 1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (d, $J = 7.3$ Hz, 3H), 2.86 (dd, $J = 18.0$ Hz, 4.3 Hz, 1H), 3.46 (dd, $J = 18.0$ Hz, 9.5 Hz, 1H), 3.97-4.02 (m, 1H), 5.16 (s, 2H), 7.34-7.98 (m, 11H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.8, 36.5, 39.7, 67.9, 128.5 (2C), 128.6, 128.7, 133.0, 134.3, 134.9, 135.9, 151.5, 172.9, 202.9; **IR** (polymer) 1763, 1678, 1597, 1509, 1500, 1458, 1383, 1198, 978, 749, 701 cm^{-1} ; **HRMS** (M^+) calcd for $C_{19}H_{19}NO_4$: 325.1314, found 325.1321.

4-Benzyloxycarbonylamino-4-oxo-butyrac acid *tert*-butyl ester

MW: C₁₆H₂₁NO₅ = 307.34; **¹H NMR** (CDCl₃, 400 MHz) δ 1.42 (s, 9H), 2.55 (t, J = 6.3 Hz, 2H), 2.99 (t, J = 6.3 Hz, 2H), 5.15 (s, 2H), 7.30-7.38 (m, 5H), 7.64 (br s, 1H); **¹³C NMR** (CDCl₃, 100 MHz) δ 28.0, 29.5, 31.3, 67.9, 80.8, 128.4, 128.7, 134.3, 134.9, 151.5, 171.7, 173.1; **IR** (polymer) 1763, 1707, 1655, 1509, 1498, 1367, 1203, 1151, 1128, 1072, 741, 699 cm⁻¹; **HRMS** (M⁺) calcd for C₁₆H₂₁NO₅ = 307.1420, found 307.1414.

(3-Benzenesulfonyl-propionyl)-carbamic acid benzyl ester

MW: C₁₇H₁₇NO₅S = 347.39; **¹H NMR** (CDCl₃, 400 MHz) δ 3.24 (t, J = 7.2 Hz, 2H), 3.46 (t, J = 7.0 Hz, 2H), 5.15 (s, 2H), 7.33-7.92 (m, 11H); **¹³C NMR** (CDCl₃, 100 MHz) δ 29.8, 50.8, 68.2, 128.1, 128.5, 128.7, 128.9, 129.4, 133.9, 134.6, 138.7, 151.3, 170.7; **IR** (polymer) 1774, 1654, 1637, 1509, 1318, 1224, 1211, 1157, 773, 737 cm⁻¹; **HRMS** (M⁺) calcd for C₁₇H₁₇NO₅S = 347.0827, found 347.0825.

(3-Cyano-propionyl)-carbamic acid benzyl ester

MW: C₁₂H₁₂N₂O₃ = 232.24; **¹H NMR** (CDCl₃, 400 MHz) δ 2.65 (t, J = 7.1 Hz, 2H), 3.19 (t, J = 7.1 Hz, 2H), 5.17 (s, 2H), 7.33-7.38 (m, 5H), 7.65 (br s, 1H); **¹³C NMR** (CDCl₃, 100 MHz) δ 12.1, 32.1, 68.3, 118.6, 128.5, 128.8, 128.9, 134.5, 151.6, 171.0; **IR** (polymer) 1762, 1685, 1509, 1500, 1402, 1238, 1219, 1096, 740 cm⁻¹; **HRMS** (M⁺) calcd for C₁₂H₁₂N₂O₃: 232.0848, found 232.0850.

2-(2-Benzyloxycarbonylamino-2-oxo-ethyl)-malonic acid diethyl ester

MW: C₁₇H₂₁NO₇ = 351.35; **¹H NMR** (CDCl₃, 400 MHz) δ 1.24 (t, J = 7.2 Hz, 3H), 3.38 (d, J = 7.3 Hz, 2H), 3.88 (t, J = 7.3 Hz, 1H), 4.15-4.22 (m, 4H), 5.16 (s, 2H), 7.33-7.36 (m, 5H), 7.64 (br s, 1H); **¹³C NMR** (CDCl₃, 100 MHz) δ 14.0, 35.4, 47.2,

61.8, 68.1, 128.5, 128.7, 128.8, 134.7, 151.4, 168.5, 171.6; **IR** (polymer) 1702, 1655, 1509, 1499, 1372, 1213, 1178, 1027, 774, 743, 700 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_7$: 351.1318, found 351.1309.

6-Benzyloxycarbonylamino-6-oxo-hexanoic acid ethyl ester

MW: $\text{C}_{16}\text{H}_{21}\text{NO}_5 = 307.34$; **^1H NMR** (CDCl_3 , 400 MHz) δ 1.23 (t, $J = 7.1$ Hz, 3H), 1.65-1.69 (m, 4H), 2.31 (t, $J = 7.1$ Hz, 2H), 2.76 (t, $J = 7.0$ Hz, 2H), 4.07-4.13 (m, 2H), 5.16 (s, 2H), 7.33-7.39 (m, 5H), 7.50 (br s, 1H); **^{13}C NMR** (CDCl_3 , 100 MHz) δ 14.2, 23.5, 24.3, 34.0, 35.6, 60.3, 67.9, 128.4, 128.7 (2C), 134.9, 151.5, 173.4, 174.0; **IR** (polymer) 1773, 1719, 1678, 1637, 1518, 1241, 772, 730, 698 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_5 = 307.1420$, found 307.1428.

(4-[1,3]Dioxan-2-yl-butyryl)-carbamic acid benzyl ester

MW: $\text{C}_{16}\text{H}_{21}\text{NO}_5 = 307.34$; **^1H NMR** (CDCl_3 , 400 MHz) δ 1.27-1.33 (m, 1H), 1.61-1.66 (m, 2H), 1.71-1.79 (m, 2H), 1.98-2.10 (m, 1H), 2.75 (t, $J = 7.2$ Hz, 2H), 3.72 (m, 2H), 4.04-4.08 (m, 2H), 4.52 (t, $J = 5.0$ Hz, 1H), 5.15 (s, 2H), 7.32-7.37 (m, 5H), 7.50 (br s, 1H); **^{13}C NMR** (CDCl_3 , 100 MHz) δ 18.7, 25.8, 34.1, 35.8, 66.8, 67.8, 101.9, 128.4, 128.7, 135.0, 151.4, 173.9; **IR** (polymer) 1773, 1677, 1637, 1509, 1233, 1094, 986, 773, 730 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_5 = 307.1420$, found 307.1412.

(2-Cyclohexyl-acetyl)-carbamic acid benzyl ester

MW: $\text{C}_{16}\text{H}_{21}\text{NO}_3 = 275.34$; **^1H NMR** (CDCl_3 , 400 MHz) δ 0.86-1.31 (m, 6H), 1.66-1.77 (m, 4H), 1.78-1.86 (m, 1H), 2.61 (d, $J = 2.1$ Hz, 2H), 5.15 (s, 2H), 7.35-7.47 (m, 6H); **^{13}C NMR** (CDCl_3 , 100 MHz) δ 26.0, 26.1, 33.0, 34.2, 43.5, 67.7, 128.4, 128.6,

128.7, 135.0, 151.4, 172.4; **IR** (polymer) 1684, 1522, 1212, 1127, 1026, 741, 698 cm⁻¹; **HRMS** (M⁺) calcd for C₁₆H₂₁NO₃ = 275.1521, found 275.1518.

(3-Methyl-5-phenyl-pentanoyl)-carbamic acid benzyl ester

MW: C₂₀H₂₃NO₃ = 325.40; **¹H NMR** (CDCl₃, 400 MHz) δ 1.01 (d, *J* = 6.7 Hz, 3H), 1.49-1.56 (m, 1H), 1.65-1.74 (m, 1H), 2.05-2.13 (m, 1H), 2.54-2.69 (m, 3H), 2.78 (dd, *J* = 16.0 Hz, 5.8 Hz, 1H), 5.15 (s, 2H), 7.15-7.39 (m, 11H); **¹³C NMR** (CDCl₃, 100 MHz) δ 19.6, 29.4, 33.3, 38.5, 43.1, 67.8, 125.7, 127.6, 128.4 (2C), 128.7, 134.4, 134.9, 142.4, 151.4, 173.5; **IR** (polymer) 1685, 1523, 1499, 1197, 1157, 1026, 744, 698 cm⁻¹; **HRMS** (M⁺) calcd for C₂₀H₂₃NO₃ = 325.1678, found 325.1678.

[2-(2-Oxo-hexahydro-cyclopenta[b]furan-6-yl)-acetyl]-carbamic acid benzyl ester

MW: C₁₇H₁₉NO₅ = 317.34; *exo* : *endo* = 10 : 1 (from ¹H NMR ratio); **¹H NMR** (CDCl₃, 400 MHz) δ 1.36-1.50 (m, 2H), 1.98-2.10 (m, 2H), 2.29 (dd, *J* = 18.1 Hz, 2.7 Hz, 1H), 2.59-2.63 (m, 1H), 2.29 (dd, *J* = 9.8 Hz, 18.1 Hz, 1H), 2.85-2.8 (m, 3H), 4.66 (dd, *J* = 7.1 Hz, 3.1 Hz, 0.91H), 5.01 (t, *J* = 6.1 Hz, 0.09H), 5.15 (s, 2H), 7.31-7.38 (m, 5H), 7.69 (br s, 1H); **¹³C NMR** (CDCl₃, 100 MHz) δ 30.2, 31.9, 35.7, 37.8, 38.0, 42.0, 68.0, 89.7, 128.4, 128.7, 128.8, 134.8, 151.6, 172.7, 177.2; **IR** (polymer) 1771, 1685, 1508, 1202, 1021, 777, 737, 700 cm⁻¹; **HRMS** (M⁺) calcd for C₁₇H₁₉NO₅ = 317.1263, found 317.1262.

(2-Adamantan-1-yl-acetyl)-carbamic acid benzyl ester

MW: C₂₀H₂₅NO₃ = 327.42; **¹H NMR** (CDCl₃, 400 MHz) δ 1.64-1.67 (m, 11H), 1.95 (s, 4H), 2.62 (s, 2H), 5.15 (s, 2H), 7.16-7.46 (m, 6H); **¹³C NMR** (CDCl₃, 100 MHz) δ 28.6, 33.6, 36.7, 42.2, 49.1, 67.7, 128.4, 128.7 (2C), 134.6, 151.3, 172.5; **IR**

(polymer) 1637, 1508, 1194, 1127, 776, 717, 698 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_3 = 327.1834$, found 327.1833.

[2-(2-Ethoxy-hexahydro-cyclopenta[b]furan-4-yl)-acetyl]-carbamic acid benzyl ester (12)

MW: $\text{C}_{19}\text{H}_{25}\text{NO}_5 = 347.41$; : = 1 : 1 (from ^1H NMR ratio); **^1H NMR** (benzene- d_6 , 400 MHz) δ 1.07 (t, $J = 7.1$ Hz, 1.5H), 1.11 (t, $J = 7.0$ Hz, 1.5H), 1.16-1.21 (m, 1H), 1.59-1.65 (m, 1H), 1.77-1.92 (m, 3H), 2.02-2.27 (m, 3H), 2.45-2.68 (m, 2H), 3.22-3.32 (m, 1H), 3.70-3.79 (m, 1H), 4.49-4.53 (m, 1H), 4.80 (d, $J = 1.0$ Hz, 2H), 5.03 (d, $J = 5.2$ Hz, 0.5H), 5.07 (d, $J = 4.9$ Hz, 0.5H), 7.05-7.11 (m, 5H), 7.76-7.77 (m, 1H); **^{13}C NMR** (benzene- d_6 , 100 MHz) δ 15.2, 15.3, 30.5, 31.3, 31.6, 34.0, 39.2, 40.0, 40.6, 41.6, 41.9, 42.1, 48.1, 48.5, 62.1, 62.4, 67.2 (2C), 83.5, 86.4, 105.2, 105.6, 127.1, 128.2, 128.3, 128.4 (3C), 128.5 (2C), 130.1, 134.6, 135.5, 135.6, 151.6, 173.0, 173.1; **IR** (polymer) 1762, 1700, 1654, 1508, 1376, 1201, 1083, 1042, 1012, 776, 743, 699 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_5 = 347.1733$, found 347.1731.

Preparation of lactone¹⁾

1) Paquette, L. A.; Kang, H-J.; Ra, C. S. *J. Am. Chem. Soc.* **1992**, *114*, 7387.

[2-(2-Hydroxy-hexahydro-cyclopenta[b]furan-4-yl)-acetyl]-carbamic acid benzyl ester (12a)

A stirred THF solution (3 mL) of **12** (52 mg, 0.15 mmol) was treated with 10% HCl (1.5 mL) at room temperature. After being stirred for 4h at room temperature, the reaction mixture was diluted with ethyl acetate (10 mL), quenched with aqueous sodium bicarbonate and washed with water and brine. The organic layer was dried over anhydrous MgSO_4 , filtered and concentrated under reduced pressure. The crude

product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1 : 1) to give product **12a** (46 mg, 0.14 mmol, 95%).

MW: C₁₇H₂₁NO₅ = 319.35; **¹H NMR** (benzene-*d*₆, 400 MHz) δ 1.12-1.16 (m, 1H), 1.53-1.65 (m, 1H), 1.71-1.89 (m, 3H), 2.06-2.27 (m, 3H), 2.44-2.65 (m, 2H), 4.39-4.43 (m, 0.3H), 4.60-4.64 (m, 0.7H), 4.80 (d, *J* = 1.3 Hz, 2H), 5.30 (d, *J* = 4.8 Hz, 0.3H), 5.36 (d, *J* = 4.7 Hz, 0.7H), 7.05-7.11 (m, 5H), 7.31-7.32 (m, 1H); **¹³C NMR** (benzene-*d*₆, 100 MHz) δ 30.7, 31.6, 31.9, 34.3, 39.8, 40.8 (2C), 41.7, 42.1, 42.2, 48.1, 49.0, 67.4, 67.5, 83.9, 86.6, 100.2, 100.6, 127.4, 128.6, 128.7 (3C), 135.7, 151.8, 173.1; **IR** (polymer) 2945, 1765, 1700, 1519, 1456, 1201, 1071, 1023, 776, 736, 699 cm⁻¹; **HRMS** (M⁺) calcd for C₁₇H₂₁NO₅ = 319.1420, found 319.1405.

[2-(2-Oxo-hexahydro-cyclopenta[b]furan-4-yl)-acetyl]-carbamic acid benzyl ester (12b)

To a stirred solution of **12a** (32 mg, 0.1 mmol) in dichloromethane (3 mL) was added 4-methylmorpholine *N*-oxide (NMO, 23 mg, 0.2 mmol) and tetrapropylammonium perruthenate (TPAP, 4 mg, 0.01 mmol). After being stirred for 30 min at room temperature, the solvent was evaporated under reduced pressure. The crude product was purified by passing through a short column of silica gel (ethyl acetate : *n*-hexane = 1 : 2) to give product **12b** (24 mg, 0.075 mmol, 75%).

MW: C₁₇H₁₉NO₅ = 317.34; **¹H NMR** (benzene-*d*₆, 400 MHz) δ 0.78-0.85 (m, 1H), 1.42-1.55 (m, 3H), 1.60-1.66 (m, 1H), 1.76-1.81 (m, 1H), 2.15 (d, *J* = 6.1 Hz, 2H), 2.29 (dd, *J* = 16.7, 7.4 Hz, 1H), 2.42 (dd, *J* = 16.6, 6.7 Hz, 1H), 4.13-4.17 (m, 1H), 4.78 (d, *J* = 1.2 Hz, 2H), 6.94 (d, *J* = 5.5 Hz, 1H), 7.05-7.13 (m, 5H); **¹³C NMR** (benzene-*d*₆, 100 MHz) δ 29.7, 31.2, 34.1, 39.9, 41.1, 44.2, 66.9, 84.0, 126.7, 127.9, 128.0, 128.1 (2C), 134.8, 151.1, 171.8, 175.0; **IR** (polymer) 1753, 1687, 1509, 1456, 1196, 1072, 1026, 818, 750, 700 cm⁻¹; **HRMS** (M⁺) calcd for C₁₇H₁₉NO₅ = 317.1263, found 317.1268.

From the ^1H - ^1H COSY NMR spectrum and the decoupling technique, an NOE experiment of **12b** showed 4.6% NOE between H_a (1.76-1.81 ppm) and H_c (2.26-2.45 ppm), but H_a (1.76-1.81 ppm) and H_b (1.50-1.55 ppm) showed no NOE effect, indicating that the stereochemistry of a major isomer is *trans*-geometry.²⁾

2) (a) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765. (b) Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500. (c) Busato, S.; Scheffold, R. *Helv. Chim. Acta.* **1994**, *77*, 92.

3-(1-Benzenesulfonyl-3-benzyloxycarbonylamino-3-oxo-propyl)-cyclopentane-1,1-dicarboxylic acid diethyl ester (14)

MW: $\text{C}_{28}\text{H}_{33}\text{NO}_9\text{S}$ = 559.63; ^1H NMR (CDCl_3 , 400 MHz) δ 1.17-1.1.23 (m, 6H), 1.31-1.46 (m, 1H), 1.87-2.26 (m, 4H), 2.45-2.54 (m, 2H), 2.88 (dt, J = 18.6 Hz, 3.2 Hz, 1H), 3.52-3.64 (m, 1H), 3.99-4.05 (m, 1H), 4.09-4.17 (m, 4H), 5.15(d, J = 2.9 Hz, 2H), 7.34-7.88 (m, 11H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9, 14.0, 28.4, 30.6, 32.3, 32.7, 33.3, 36.3, 38.0, 38.6, 59.3 (2C), 61.5 (2C), 61.6 (2C), 62.5 (2C), 68.1, 128.5 (2C), 128.7, 128.8, 128.9, 129.2, 133.8, 134.7 (2C), 137.9, 138.1, 151.2, 151.3, 171.8, 172.0, 172.1; **IR** (polymer) 1718, 1654, 1508, 1448, 1369, 1304, 1261, 1200, 1146, 1084, 1025, 738, 692, 598 cm^{-1} ; **HRMS** (M^+) calcd for $\text{C}_{28}\text{H}_{33}\text{NO}_9\text{S}$ = 559.1876, found 559.1877.

(E)-3-(3-Benzyloxycarbonylamino-3-oxo-propenyl)-cyclopentane-1,1-dicarboxylic acid diethyl ester (15) To a solution of **14** (112 mg, 0.2 mmol) in methylene chloride (1.0 mL) were added triethylamine (28 μl , 0.2 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 36 μl , 0.24 mmol) at 0°C. After being stirred for 30min at room temperature, the solvent was evaporated under the reduced pressure.

The residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give the product **15** (66 mg, 0.16 mmol, 80%) as a *E* isomer.

MW: C₂₂H₂₇NO₇ = 417.45; **¹H NMR** (CDCl₃, 400 MHz) δ 1.19-1.25 (m, 6H), 1.54-1.62 (m, 1H), 1.91-1.99 (m, 2H), 2.16-2.23 (m, 1H), 2.33-2.41 (m, 1H), 2.49-2.54 (m, 1H), 2.79-2.86 (m, 1H), 4.13-4.20 (m, 4H), 5.16 (s, 2H), 6.82 (dd, *J* = 15.4 Hz, 0.9 Hz, 1H), 7.03 (dd, *J* = 15.4 Hz, 7.8 Hz, 1H), 7.33-7.37 (m, 5H), 7.42 (br s, 1H); **¹³C NMR** (CDCl₃, 100 MHz) δ 14.0, 31.9, 33.8, 39.8, 42.5, 60.1, 61.5, 67.9, 120.6, 128.4, 128.7, 134.9, 151.5, 152.6, 165.6, 172.0, 172.2; **IR** (polymer) 1726, 1685, 1638, 1508, 1368, 1268, 1199, 776, 736, 699 cm⁻¹; **HRMS** (M⁺) calcd for C₂₂H₂₇NO₇ = 417.1788, found 417.1776.