

Supporting Information

Stereocontrol in solid-phase radical reactions: Radical addition to oxime ether anchored
to polymer support

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General Methods. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 200 or 300 MHz and at 50 or 125 MHz, respectively. IR spectra were recorded using FTIR apparatus. Mass spectra were obtained by EI, CI, or SIMS methods. Preparative TLC separations were carried out on precoated silica gel plates (E. Merck 60F₂₅₄). Flash column chromatography was performed using E. Merck Kieselgel 60 (230-400 mesh).

2-(Benzyloxyamino)butanoic acid (3). To a suspension of oxime ether **1** (0.83 mmol/g, 220 mg, 0.18 mmol) in CH_2Cl_2 (6.0 mL) was added Et_2Zn (1.0 M in hexane, 0.93 mL, 0.93 mmol) under a nitrogen atmosphere at $-78\text{ }^\circ\text{C}$. After the reaction mixture was stirred at the same temperature for 30 min, the resin was filtered, washed well with CH_2Cl_2 , AcOEt followed by MeOH and then dried in vacuo. To a flask with the resulting resin **2** was added TFA/ CH_2Cl_2 (1:5, v/v, 5.0 mL) under a nitrogen atmosphere at $20\text{ }^\circ\text{C}$. After the reaction mixture was stirred at the same temperature for 30 min, the reaction mixture was filtered and washed with MeOH/ CHCl_3 (1:11, v/v, 60 mL), and the filtrate was concentrated at reduced pressure. Purification of the residue by Amberlite IR-120B (eluting with MeOH) followed by preparative TLC (MeOH/ CHCl_3 1:10, v/v) afforded the α -amino acid derivative **3** (34 mg, 89%) as a white solid: ^1H NMR

(CD₃OD) δ 7.34-7.26 (5H, m), 4.68 (2H, s), 3.50 (1H, br t, $J=10.2$ Hz), 1.58 (2H, m), 0.95 (3H, t, $J=11.1$ Hz); ¹³C NMR (CD₃OD) δ 177.2, 138.9, 129.4, 129.1, 128.7, 76.9, 66.1, 23.6, 10.7; HRMS calcd for C₁₁H₁₅NO₃ (M⁺) 209.1051, found 209.1064.

4-(*t*-Butyldimethylsiloxymethyl)phenylmethanol (4). To a solution of *p*-xylylene glycol (1.0 g, 7.2 mmol) and imidazole (1.2 g, 18 mmol) in DMF (3 mL) was added dropwise a solution of *t*-butyldimethylsilyl chloride (1.1 g, 7.3 mmol) in DMF (5 mL) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 3 h, the reaction mixture was diluted with Et₂O. The organic phase was washed with water and brine, dried over MgSO₄, and concentrated at reduced pressure. Purification of the residue by flash chromatography (hexane/AcOEt 5:1) afforded **4** (1.1 g, 62%) as a colorless oil and 1,4-di(*t*-butyldimethylsiloxymethyl)benzene (0.26 g, 10%) as a white solid. **4**: IR (CHCl₃) 3608, 3447, 2930, 1514, 1471 cm⁻¹; ¹H NMR (CDCl₃) δ 7.29 (4H, m), 4.73 (2H, s), 4.62 (2H, br s), 0.94 (9H, s), 0.09 (6H, s); ¹³C NMR (CDCl₃) δ 140.7, 139.4, 126.8, 126.1, 65.0, 64.6, 25.8, 18.2, -5.4; HRMS calcd for C₁₄H₂₄O₂Si (M⁺) 252.1544, found 252.1554. 1,4-di(*t*-butyldimethylsiloxymethyl)benzene

: IR (CHCl₃) 2956, 1472 cm⁻¹; ¹H NMR (CDCl₃) δ 7.28 (4H, m), 4.73 (4H, s), 0.94 (18H, s), 0.09 (12H, s); ¹³C NMR (CDCl₃) δ 140.0, 125.9, 64.8, 25.8, 18.3, -5.4; HRMS calcd for C₂₀H₃₈O₂Si₂ (M⁺) 366.2408, found 366.2419.

***N*-[4-(*t*-Butyldimethylsiloxymethyl)benzyloxy]phthalimide (5).** To a solution of **4** (7.3 g, 29 mmol) and Et₃N (4.4 mL, 32 mmol) in CH₂Cl₂ (40 mL) was added dropwise mesyl chloride (2.5 mL, 32 mmol) under a nitrogen atmosphere at 0 °C. After the reaction mixture was stirred at the same temperature for 1 h, Et₃N (4.4 mL, 32 mmol) and *N*-hydroxyphthalimide (5.9 g, 58 mmol) were added at 20 °C. After being heated at reflux for 8 h, the solvent was evaporated at reduced pressure. After to the resulting

residue was added AcOEt, the organic phase was washed with 1N NaOH, saturated aqueous NaHCO₃, and water, dried over MgSO₄, and concentrated at reduced pressure. Purification of the residue by recrystallization (hexane/AcOEt) afforded **5** (9.0 g, 79%) as colorless crystals: mp 82-84 °C (hexane/AcOEt); IR (CHCl₃) 2956, 1733, 1469 cm⁻¹; ¹H NMR (CDCl₃) δ 7.68-7.81 (4H, m), 7.50, 7.33 (each 2H, d, *J*=8.0 Hz), 5.20, 4.74 (each 2H, s), 0.93 (9H, s), 0.08 (6H, s); ¹³C NMR (CDCl₃) δ 163.3, 142.6, 134.2, 132.1, 129.7, 128.7, 125.9, 123.3, 79.5, 64.5, 25.7, 18.2, -5.5; HRMS calcd for C₂₂H₂₇NO₄Si (M⁺) 397.1708, found 397.1711. Anal. Calcd for C₂₂H₂₇NO₄Si: C, 66.47; H, 6.85; N, 3.52. Found: C, 66.30; H, 6.82; N, 3.38.

Methyl (*E*)-2-[4-(*t*-Butyldimethylsiloxymethyl)benzyloxyimino]ethanate (6). To a solution of **5** (12 g, 30 mmol) in MeOH (200 mL) was added a solution of hydrazine monohydrate (1.7 g, 33 mmol) in MeOH (10 mL) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h, a solution of 2-hydroxy-2-methoxyacetic acid methyl ester (7.2 g, 60 mmol) in MeOH (10 mL) was added to the reaction mixture at 20 °C. After being stirred at the same temperature for 8 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated at reduced pressure. Purification of the residue by flash chromatography (hexane/AcOEt 10:1) afforded **6** (9.4 g, 93%) as a colorless oil: IR (CHCl₃) 2956, 1737, 1600, 1467 cm⁻¹; ¹H NMR (CDCl₃) δ 7.54 (1H, s), 7.33 (4H, m), 5.28, 4.74 (each 2H, s), 3.85 (3H, s), 0.94 (9H, s), 0.10 (6H, s); ¹³C NMR (CDCl₃) δ 162.3, 141.8, 140.7, 134.3, 128.4, 126.1, 77.9, 64.5, 52.3, 25.8, 18.2, -5.4; HRMS calcd for C₁₇H₂₇NO₄Si (M⁺) 337.1708, found 337.1698.

***N*-[(*E*)-2-(4-(Hydroxymethyl)benzyloxyimino)ethanonyl]bornane-10,2-sultam (7)**
To a solution of (1*R*)-(+)-2,10-camphorsultam (2.0 g, 9.3 mmol) and glyoxylic oxime ether **6** (3.8 g, 11 mmol) in CH₂ClCH₂Cl (40 mL) was added Me₃Al (1.0 M in hexane,

11 mL, 11 mmol) under a nitrogen atmosphere at 20 °C. After being heated at reflux for 24 h, the reaction mixture was diluted with 1N HCl and then extracted with CH₂Cl₂. The organic phase was washed with water, dried over MgSO₄, and concentrated at reduced pressure. Purification of the residue by flash chromatography (hexane/AcOEt 4:1) afforded the silylated sultam derivative (4.8 g, quantitative) as a colorless oil: $[\alpha]_D^{22} +61.9$ (*c* 2.3, CHCl₃); IR (CHCl₃) 2959, 1693, 1585, 1463 cm⁻¹; ¹H NMR (CDCl₃) δ 8.19 (1H, s), 7.33 (4H, m), 5.29, 4.74 (each 2H, s), 3.98 (1H, dd, *J*=7.1, 5.3 Hz), 3.51, 3.45 (each 1H, d, *J*=13.7 Hz), 2.20-2.00 (2H, m), 1.95-1.82 (3H, m), 1.48-1.28 (2H, m), 1.15, 0.97 (each 3H, s), 0.94 (9H, s), 0.10 (6H, s); ¹³C NMR (CDCl₃) δ 158.9, 141.6, 140.7, 134.2, 128.5, 126.0, 78.0, 65.0, 64.5, 52.8, 48.7, 47.6, 44.5, 38.1, 32.7, 26.1, 25.7, 20.7, 19.6, 18.2, -5.5; HRMS calcd for C₂₆H₄₀N₂O₅SSi (M⁺) 520.2425, found 520.2421. To a solution of the silylated sultam derivative (4.8 g, 9.2 mmol) in EtOH (60 mL) was added pyridinium *p*-toluenesulfonate (4.6 g, 18 mmol) under a nitrogen atmosphere at 20 °C. After being heated at 60 °C for 2 h, the solvent was evaporated at reduced pressure. After to the resulting residue was added CH₂Cl₂, the organic phase was washed with saturated aqueous NaHCO₃, and water, dried over MgSO₄, and concentrated at reduced pressure. Purification of the residue by flash chromatography (hexane/AcOEt 1:1) afforded sultam derivative (3.3 g, 89%) as colorless crystals: mp 139-142 °C (hexane/AcOEt); $[\alpha]_D^{21} +80.0$ (*c* 1.09, CHCl₃); IR (CHCl₃) 3606, 2964, 1693, 1586, 1458 cm⁻¹; ¹H NMR (CDCl₃) δ 8.20 (1H, s), 7.37 (4H, m), 5.30, 4.69 (each 2H, s), 3.98 (1H, dd, *J*=7.2, 5.8 Hz), 3.51, 3.46 (each 1H, d, *J*=13.8 Hz), 2.12-2.05 (2H, m), 1.96-1.87 (3H, m), 1.47-1.26 (2H, m), 1.15, 0.97 (each 3H, s); ¹³C NMR (CDCl₃) δ 158.9, 141.1, 140.8, 135.0, 128.7, 126.9, 77.9, 65.0, 64.7, 52.9, 48.7, 47.7, 44.5, 38.1, 32.7, 26.2, 20.7, 19.7; HRMS calcd for C₂₀H₂₆N₂O₅S (M⁺) 406.1561, found 406.1560. Anal. Calcd for C₂₀H₂₆N₂O₅S: C, 59.09; H, 6.45; N, 6.89; S, 7.89. Found: C, 59.04; H, 6.69; N,

6.90; S, 7.96.

Attachment of oxime ether 7 to Carboxypolystyrene HL resin.

To a suspension of Carboxypolystyrene HL resin (1.18 mmol/g, 12 g, 14 mmol) in CH_2Cl_2 (200 mL) were added oxime ether **7** (8.1 g, 20 mmol), DCC (8.5 g, 41 mmol) and DMAP (0.83 g, 6.8 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h and then stood for 11 h, the resin was filtered, washed well with CH_2Cl_2 , AcOEt followed by MeOH and then dried in vacuo.

Attachment of the sultam derivative to Wang resin. To a solution of **7** (7.2 g, 18 mmol) in pyridine (15 mL) was added glutaric anhydride (2.0 g, 18 mmol) under a nitrogen atmosphere at 20 °C and the reaction mixture was then heated at 80 °C for 1 h. After glutaric anhydride (2.0 g, 18 mmol) was added to the reaction mixture, which was then heated at 80 °C for 1 h, glutaric anhydride (2.0 g, 18 mmol) was added to the reaction mixture. After being heated at 80 °C for 2 h, the reaction mixture was diluted with AcOEt and then was washed with 5% HCl, water, brine, dried over MgSO_4 , and concentrated at reduced pressure. Purification of the residue by flash chromatography (hexane/AcOEt 3:2) afforded the acid derivative (9.1 g, 99%) as a colorless oil: $[\alpha]_D^{21} +67.1$ (c 0.92, CHCl_3); IR (CHCl_3) 3684, 2969, 1732, 1586, 1519 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.20 (1H, s), 7.40-7.31 (4H, m), 5.31, 5.11 (each 2H, s), 3.98 (1H, dd, $J=6.8$, 5.6 Hz), 3.52, 3.46 (each 1H, d, $J=14.0$ Hz), 2.45-2.36 (4H, m), 2.13-1.90 (7H, m), 1.48-1.36 (2H, m), 1.16, 0.98 (each 3H, s); ^{13}C NMR (CDCl_3) δ 178.1, 172.5, 159.0, 140.9, 135.9, 128.7, 128.3, 77.7, 65.8, 65.1, 52.9, 48.8, 47.7, 44.6, 38.1, 33.0, 32.8, 26.2, 20.7, 19.73, 19.67; HRMS calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_8\text{S}$ (M^+) 520.1877, found 520.1903. To a suspension of Wang resin (0.83 mmol/g, 6.0 g, 5.0 mmol) in CH_2Cl_2 (100 mL) were added the acid derivative (5.2 g, 10 mmol), DCC (5.1 g, 25 mmol) and DMAP (0.3 g,

2.5 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h and then stood for 11 h, the resin was filtered, washed well with CH₂Cl₂, AcOEt followed by MeOH and then dried in vacuo.

***N*-[*(2R)*-2-(4-(Hydroxymethyl)benzyloxyamino)butanonyl]bornane-10,2-sultam**

(10). To a suspension of oxime ether **8** (0.77 mmol/g, 250 mg, 0.19 mmol) in CH₂Cl₂ (6.0 mL) was added Et₃B (1.0 M in hexane, 1.5 mL, 1.5 mmol) under a nitrogen atmosphere at -78 °C. After the reaction mixture was stirred at the same temperature for 30 min, the resin was filtered, washed well with CH₂Cl₂ and AcOEt and then dried in vacuo. To a flask with the resulting resin in THF/MeOH (2:1, 12 mL) was added K₂CO₃ (207 mg, 1.5 mmol) under a nitrogen atmosphere at 20 °C. After being stirred at the same temperature for 1.5 h, the reaction mixture was filtered and washed with MeOH, and the filtrate was concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane/AcOEt 1:1) afforded the α-amino acid derivative **10** (4 mg, 5%) as a colorless oil: [α]_D²⁰ +137.37 (*c* 0.99, CHCl₃); IR (CHCl₃) 3640, 2966, 1693, 1458 cm⁻¹; ¹H NMR (CDCl₃) δ 7.38-7.24 (4H, m), 4.68, 4.63 (each 1H, d, *J*=11.7 Hz), 4.62 (3H, s), 4.26 (1H, dd, *J*=7.9, 4.8 Hz), 3.91 (1H, br t, *J*=6.2 Hz), 3.454, 4.451 (each 1H, d, *J*=14.0 Hz), 2.05 (2H, br d, *J*=6.5 Hz), 1.95-1.75 (3H, m), 1.72-1.28 (4H, m), 1.11, 0.95 (each 3H, s), 0.94 (3H, t, *J*=7.5 Hz); ¹³C NMR (CDCl₃) δ 173.8, 140.2, 136.9, 128.7, 126.7, 75.2, 64.7, 64.1, 52.7, 48.4, 47.5, 44.3, 38.0, 32.5, 26.1, 23.7, 20.5, 19.6, 10.3; HRMS calcd for C₂₂H₃₂N₂O₅S (M⁺) 436.2030, found 436.2032.

Ethyl radical addition to oxime ether 9. To a suspension of oxime ether **9** (0.83 mmol/g, 200 mg, 0.166 mmol) in CH₂Cl₂ (10 mL) was added Et₃B or Et₂Zn (1.0 M in hexane, 0.83 mL, 0.83 mmol) under a nitrogen atmosphere at -78 °C. After the reaction mixture was stirred at the same temperature for 30 min, the resin was filtered, washed well with CH₂Cl₂ and AcOEt, and then dried in vacuo. To a flask with the resulting resin

was added TFA/CH₂Cl₂ (1:5, v/v, 5.0 mL) under a nitrogen atmosphere at 20 °C. After being stirred at the same temperature for 30 min, the reaction mixture was filtered and washed with CH₂Cl₂ (50 mL), and the filtrate was concentrated at reduced pressure. After the resulting residue was added CH₂Cl₂, the organic phase was washed with diluted aqueous NaHCO₃, and water, dried over MgSO₄, and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane/AcOEt 2:3, 2-fold development) afforded the α-amino acid derivative **11a** (68 mg, 74%) in the case of Et₃B or (61 mg, 67%) in the case of Et₂Zn. $[\alpha]_D^{19} +70.0$ (c 0.97, CHCl₃); IR (CHCl₃) 2965, 1731, 1457 cm⁻¹; ¹H NMR (CDCl₃) δ 7.36, 7.30 (each 2H, br d, *J*=7.5 Hz), 5.10 (2H, s), 4.72, 4.66 (each 1H, d, *J*=11.7 Hz), 4.28 (1H, dd, *J*=7.8, 4.8 Hz), 3.96 (1H, br t, *J*=6.3 Hz), 3.51, 3.48 (each 1H, d, *J*=14.1 Hz), 2.48-2.36 (4H, m), 2.13-1.80 (7H, m), 1.75-1.23 (4H, m), 1.12, 0.97 (each 3H, s), 0.95 (3H, t, *J*=7.5 Hz); ¹³C NMR (CDCl₃) δ 178.2, 173.7, 172.5, 137.8, 135.0, 128.6, 127.9, 75.1, 66.0, 64.8, 64.1, 52.8, 48.4, 47.6, 44.4, 38.1, 33.0, 32.7, 32.5, 26.2, 23.7, 20.5, 19.7, 19.6, 10.3; SIMS calcd for C₂₇H₃₈N₂O₈S - H (negative, M⁺ - H) 549.3332, found 549.3320.

Alkyl radical addition to oxime ether 9. To a suspension of oxime ether **9** (0.83 mmol/g, 200 mg, 0.166 mmol) in RI/toluene (4:1, v/v, 5 mL) was added Et₃B or Et₂Zn (1.0 M in hexane, 0.83 mL, 0.83 mmol) under a nitrogen atmosphere at 0 °C. After the reaction mixture was stirred at the same temperature for 15 min, Et₃B or Et₂Zn (1.0 M in hexane, 0.83 mL, 0.83 mmol) was added to the reaction mixture. After the reaction mixture was stirred at the same temperature for 15 min, the resin was filtered, washed well with CH₂Cl₂ and AcOEt, and then dried in vacuo. To a flask with the resulting resin was added TFA/CH₂Cl₂ (1:5, v/v, 5.0 mL) under a nitrogen atmosphere at 20 °C. After being stirred at the same temperature for 30 min, the reaction mixture was filtered and washed with CH₂Cl₂ (50 mL), and the filtrate was concentrated at reduced pressure.

After to the resulting residue was added CH_2Cl_2 , the organic phase was washed with diluted aqueous NaHCO_3 , and water, dried over MgSO_4 , and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane/AcOEt 3:2, 3-fold development) afforded the α -amino acid derivative **11b** or **11c**. **11b**, $[\alpha]^{19}_{\text{D}} +59.1$ (*c* 1.0, CHCl_3); IR (CHCl_3) 2966, 1732, 1456 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.36, 7.30 (each 2H, br d, $J=7.8$ Hz), 5.10 (2H, s), 4.69, 4.62 (each 1H, d, $J=12.0$ Hz), 4.14 (1H, br d, $J=5.1$ Hz), 3.97 (1H, br t, $J=6.3$ Hz), 3.51, 3.47 (each 1H, d, $J=13.5$ Hz), 2.48-2.37 (4H, m), 2.14-1.82 (8H, m), 1.48-1.28 (2H, m), 1.12, 0.97 (each 3H, s), 1.00, 0.86 (each 3H, d, $J=6.9$ Hz); ^{13}C NMR (CDCl_3) δ 178.4, 174.0, 172.5, 137.9, 134.9, 128.7, 127.9, 75.0, 67.9, 66.0, 64.9, 52.9, 48.2, 47.5, 44.4, 38.3, 33.0, 32.7, 32.6, 30.0, 26.2, 20.5, 19.7, 19.6, 17.6; HRMS calcd for $\text{C}_{28}\text{H}_{40}\text{N}_2\text{O}_8\text{S} + \text{H}$ ($\text{M}^+ + \text{H}$) 565.2582, found 565.2572. **11c**, $[\alpha]^{19}_{\text{D}} +50.0$ (*c* 0.98, CHCl_3); IR (CHCl_3) 2933, 1731, 1451 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.35, 7.29 (each 2H, br d, $J=8.1$ Hz), 5.10 (2H, s), 4.68, 4.61 (each 1H, d, $J=12.0$ Hz), 4.14 (1H, m), 3.97 (1H, br t, $J=6.3$ Hz), 3.51, 3.46 (each 1H, d, $J=14.4$ Hz), 2.48-2.37 (4H, m), 2.17-1.79 (7H, m), 1.78-0.95 (13H, m), 1.13, 0.97 (each 3H, s); ^{13}C NMR (CDCl_3) δ 178.2, 173.9, 172.5, 138.0, 134.9, 128.7, 127.9, 74.9, 67.7, 66.0, 64.9, 52.9, 48.2, 47.5, 44.4, 39.7, 38.3, 33.0, 32.7, 32.6, 29.6, 28.6, 26.2, 26.1, 26.0, 25.8, 20.4, 19.8, 19.6; HRMS calcd for $\text{C}_{31}\text{H}_{44}\text{N}_2\text{O}_8\text{S} + \text{H}$ ($\text{M}^+ + \text{H}$) 605.2894, found 605.2900.