Intramolecular *O*-Arylation of Phenols with Phenyl Boronic Acids: Application to the Synthesis of Macrocyclic Metalloproteinase Inhibitors

Organic Letters

Supplemental Material

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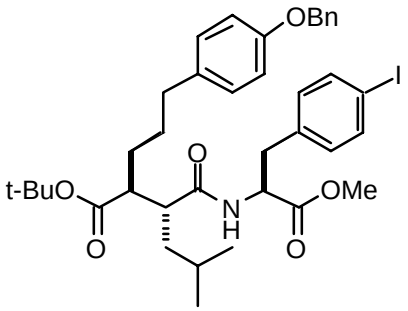
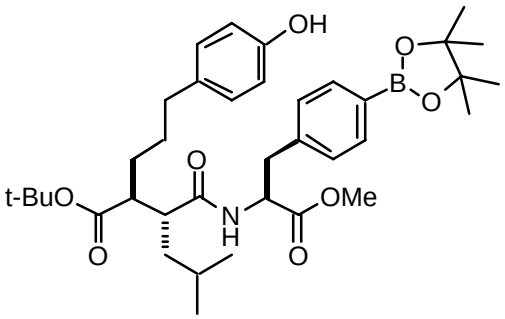


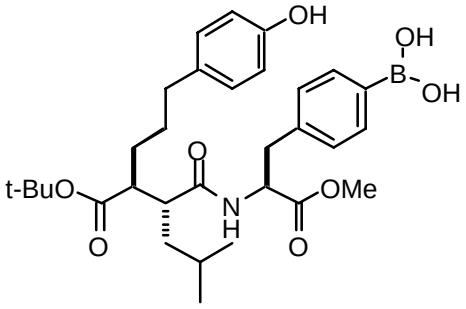
(3a): At 0 °C, *p*-iodo-*L*-phenylalanine methyl ester (1.96 g, 6.43 mmol), NMM (1.51 g, 14.96 mmol) and TBTU (1.44 g, 4.49 mmol) were added sequentially to a solution of the carboxylic acid (1.70 g, 3.74 mmol) in 20 mL of DMF. After warming up to rt for 6 h, the reaction mixture was concentrated and chromatrographed to give the amide (1.94 g, 70%). ^{1}H NMR ($CDCl_3$) δ 7.58 (m, 2H), 7.40(m, 5H), 7.05 (m, 2H), 6.86 (m, 4H), 5.98 (bd, *J* = 8.1 Hz, 1H), 4.99 (s, 2H), 4.92 (m, 1H), 3.71 (s, 3H), 2.98 (m, 2H), 2.46 (m, 3H), 2.30 (m, 1H), 1.70 (m, 2H), 1.66 (m, 2H), 1.44 (s, 9H), 1.26 (m, 2H), 1.02 (m, 1H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.8, 173.4, 171.7, 157.0, 137.7, 137.2, 135.6, 129.3, 128.5, 127.8, 127.4, 114.7, 92.6, 80.8, 70.0, 52.6, 52.4, 49.4, 48.4, 40.5, 37.8, 34.4, 30.4, 29.0, 28.1, 25.8, 23.8, 21.4. IR (cm^{-1}) 3311, 2952, 1723, 1647, 1511, 1240, 1148. ESI (+Na): 764.3. HRMS calcd for $C_{38}H_{48}O_6NI$ ($M + Na^+$) 764.2451, obsd 764.2439.



(**4a**): Potassium acetate (257 mg, 2.62 mmol), pinacol diboron (244 mg, 0.961 mmol) and $PdCl_2$(pddf) catalyst (21 mg, 0.0262 mmol) were added sequentially to a solution of the amide **3a** (648 mg, 0.873 mmol) in 8 mL of DMF. After flushed with N_2, the reaction mixture was sealed and heated to 80°C fo 18 h. The reaction mixture was partitioned between H_2O and EtOAc. The combined organic extract was washed with brine, dried over Na_2SO_4 and concentrated. The residue was chromatographed to give the aryl boronic ester (600 mg, 93% yield). ^{1}H NMR ($CDCl_3$) δ 7.75 (d, *J* = 7.7 Hz, 2H), 7.38 (m, 5H), 7.12 (d, *J*

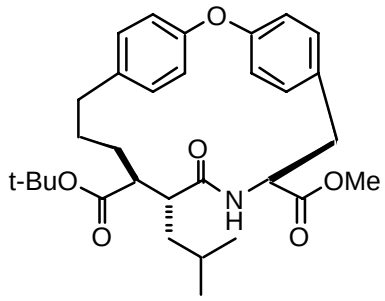
= 7.7 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.99 (bd, *J* = 8.1 Hz, 1H), 4.97 (s, 2H), 4.96 (m, 1H), 3.70 (s, 3H), 3.06 (d, *J* = 5.9 Hz, 2H), 2.45 (m, 3H), 2.33 (m, 1H), 1.70 (m, 2H), 1.50 (m, 2H), 1.42 (s, 9 H), 1.35 (m, 2H), 1.29 (s, 12H), 1.01 (m, 1H), 0.84 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.8, 173.4, 171.9, 156.9, 139.1, 135.1, 134.5, 129.3, 128.5, 127.8, 127.4, 114.7, 83.8, 80.7, 70.0, 52.7, 52.3, 49.6, 48.4, 40.5, 38.4, 34.5, 30.6, 29.2, 28.1, 25.8, 24.8, 23.8, 21.4. IR (cm^{-1}) 2952, 1725, 1648, 1511, 1361, 1146. ESI (+Na): 764.5. HRMS (Compound decomposed to free boronic acid.) calcd for $C_{38}H_{50}O_8NB$ ($M + H^+$) 660.3719, obsd 660.3726.

A solution of the aryl boronic ester (500 mg, 0.675 mmol) in anhydrous MeOH (20 mL) and EtOAc (30 mL) was treated with Pd-C (50 mg, 10% wt equiv) and stirred under hydrogen atmosphere (1atm) at 25°C for 16 h. The reaction mixture was filtered, concentrated and dried under vacuum to give **4a** (422 mg, 96%). ^{1}H NMR ($CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.02 (bd, *J* = 8.1 Hz, 1H), 5.96 (bs, 1H), 4.96 (m, 1H), 3.70 (s, 3H), 3.07 (d, *J* = 6.2 Hz, 2H), 2.45 (m, 3H), 2.33 (m, 1H), 1.67 (m, 2H), 1.47 (m, 2H), 1.43 (s, 9H), 1.30 (s, 12H), 1.26 (m, 2H), 1.05 (m, 1H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.1, 173.8, 171.8, 154.3, 139.0, 135.1, 135.0, 133.5, 129.2, 128.5, 115.3, 83.8, 80.9, 52.8, 52.3, 49.6, 48.4, 40.5, 38.2, 34.6, 30.7, 29.3, 28.0, 25.7, 24.8, 23.8, 21.4. IR (cm^{-1}) 3316, 2977, 1725, 1650, 1516, 1362, 1146. HRMS (Compound decomposed to free boronic acid.) calcd for $C_{31}H_{44}O_8NB$ ($M + H^+$) 570.3238, obsd 570.3239.

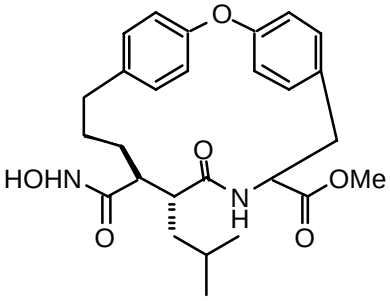


(**5a**): Aqueous HCl (2N, 14 mL) and benzoboronic acid (16 mg, 0.131 mmol) was added to a solution of **4a** (80 mg, 0.123 mmol) in THF (8 mL) and MeOH (3 mL). After 18 h at rt, the reaction mixture was partitioned between H_2O and EtOAc. The combined organic extract was washed sequentially with saturated $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated (another portion of benzoboronic acid (16 mg) was added during the concentration). Flash chromatography afforded the boronic acid **5a** (40 mg, 57% yield) and the recoveded the boronic ester **4a** (20 mg, 25%). The calibrated yield from the boronic ester

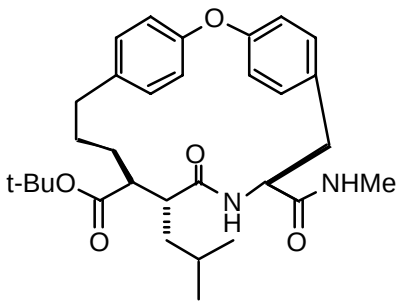
is 76%. ^{1}H NMR ($CDCl_3$) δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.42 (d, *J* = 8.4 Hz, 2H), 5.15 (m, 1H), 3.83 (s, 3H), 3.40 (m, 1H), 3.82 (m, 1H), 2.36 (m, 3H), 2.16 (m, 1H), 1.69 (m, 2H), 1.39 (s, 9H), 1.26 (m, 4H), 1.00 (m, 1H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.5, 172.0, 154.6, 141.2, 135.9, 133.1, 128.8, 115.3, 81.2, 53.2, 52.7, 49.1, 48.8, 40.7, 39.2, 35.1, 31.3, 29.5, 28.0, 25.7, 23.9, 21.4. HRMS calcd for $C_{31}H_{44}O_8NB$ ($M + H^+$) 570.3238, obsd 570.3228.



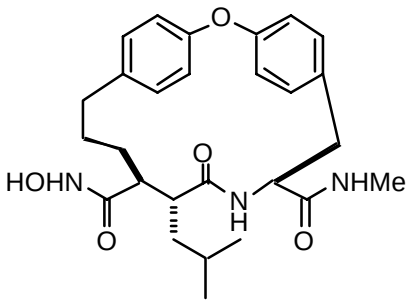
(**6a**): Activated 4A molecular sieves (100 mg), Et_3N (1 mL), and $Cu(OAc)_2$ were added sequentially to a solution of **5a** (30 mg, 0.0527 mmol) in 20 mL of dry CH_2Cl_2. The reaction mixture was flushed with N_2 and sealed. After 48 h at rt, the reaction mixture was filtered through celite, concentrated and chromatographed to give the cyclized product **6a** (15 mg, 54% yield). ^{1}H NMR ($CDCl_3$) δ 7.07 (m, 8H), 5.25 (bd, *J* = 8.4 Hz, 1H), 4.58 (m, 1H), 3.74 (s, 3H), 3.30 (dd, *J* = 3.7, 13.9 Hz, 1H), 2.78 (m, 1H), 2.52 (m, 1H), 2.30 (m, 1H), 2.05 (m, 1H), 1.86 (m, 1H), 1.59 (m, 1H), 1.51 (m, 2H), 1.44 (s, 9H), 1.41 (m, 2H), 1.08 (m, 1H), 0.83 (m, 6H), 0.24 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 174.2, 173.8, 172.4, 161.4, 160.3, 137.9, 132.4, 130.0, 122.5, 80.4, 53.9, 52.4, 48.3, 46.9, 40.3, 37.4, 34.5, 28.6, 28.1, 25.3, 23.7, 21.6. IR (cm^{-1}) 2825, 1724, 1509, 1154. HRMS calcd for $C_{31}H_{41}O_6N$ ($M + H^+$) 524.3012, obsd 524.2997.



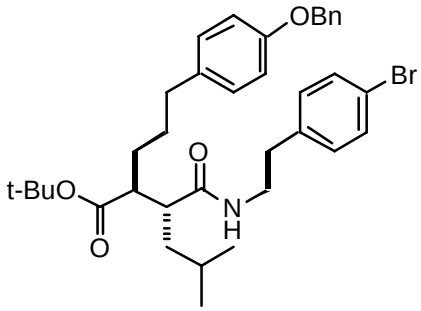
(**7a**): Trifluoroacetic acid (1 mL) was added dropwise to a solution of **6a** (8 mg, 0.0153 mmol) in 1 mL of CH_2Cl_2 at 0 °C. After 10 min, the reaction mixture was slowly warmed up. After 2 h at rt, the mixture was concentrated in vacuo and dried thoroughly under vacuum to give the crude carboxylic acid. At 0 °C, BOP-Cl (8 mg, 0.018 mmol), DIEA (10 mg, 0.0775 mmol) and $HONH_2$·HCl (2 mg, 0.029 mmol) were added sequentially to a solution of the crude carboxylic acid (7 mg, 0.0150 mmol) in 1 mL of DMF. After warming up to rt for 2 h, the mixture was concentrated to remove DMF and excess DIEA. The residue was purified over reverse phase HPLC to give the hydroxylamic acid **7a** (5 mg, 68% yield) as a white solid. ^{1}H NMR (CD_3OD) δ 7.08 (m, 8H), 4.61 (dd, *J* =4.2, 12.7 Hz, 1H), 3.69 (s, 3H), 3.25 (m, 1H), 2.80 (m, 1H), 2.67 (m, 1H), 2.29 (m, 1H), 2.05 (m, 1H), 1.13 (m, 2H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.48 (m, 1H). ^{13}C NMR (CD_3OD) δ 176.2, 175.7, 173.5, 162.5, 162.0, 138.9, 134.5, 131.3, 123.5, 55.0, 52.7, 47.6, 46.9, 41.1, 36.7, 35.6, 29.6, 28.9, 26.1, 24.3, 22.1.



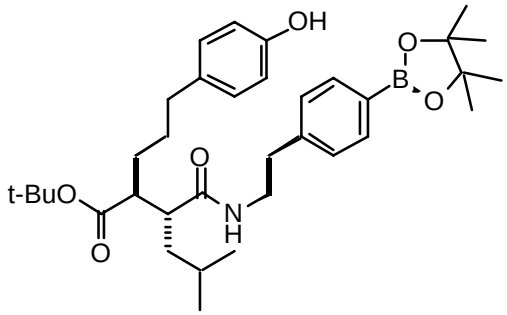
(**6d**): The procedure described for **6a** was employed (52% yield). ^{1}H NMR ($CDCl_3$) δ 7.07 (m, 8H), 6.37 (bs, 1H), 5.41 (bd, *J* = 7.8 Hz, 1H), 4.42 (m, 1H), 3.10 (dd, *J* = 4.0, 14.7 Hz, 1H), 2.81 (m, 1H), 2.75 (d, *J* = 4.8 Hz, 3H), 2.30 (m, 1H), 2.04 (m, 1H), 1.78 (m, 1H), 1.48 (m, 1H), 1.45 (s, 9H), 1.33 (m, 2H), 1.07 (m, 1H), 0.85 (m,2H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.2 Hz, 3H), 0.19 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 174.7, 174.0, 171.7, 161.2, 160.3, 137.7, 132.9, 130.0, 122.5, 80.5, 54.5, 48.2, 47.0, 40.5, 35.9, 34.5, 28.6, 28.1, 26.1, 25.4, 23.8, 21.5. IR (cm^{-1}) 3301, 2930, 1724, 1643, 1496, 1152. HRMS calcd for $C_{31}H_{42}O_5N_2$ ($M + H^+$) 523.3172, obsd 523.3175.



(**7d**): The procedure described for **7a** was employed (65% yield). ^{1}H NMR (CD_3OD) δ 7.09 (m, 8H), 4.48 (dd, *J* = 3.9, 12.5 Hz, 1H), 3.02 (dd, *J* = 3.9, 14.4 Hz, 1H), 3.82 (m, 1H), 2.73 (m, 1H), 2.69 (s, 3H), 2.27 (m, 1H), 2.06 (m, 1H), 1.95 (m, 1H), 1.55 (m, 1H), 141 (m, 2H), 1.36 (m, 1H), 1.11 (m, 2H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.6 Hz, 3H), 0.45 (m, 1H). ^{13}C NMR (CD_3OD) δ 175.9, 174.3, 162.4, 162.0, 138.9, 134.7, 131.3, 123.4, 55.9, 47.8, 47.0, 41.4, 37.4, 35.5, 29.7, 29.0, 26.3, 26.2, 24.4, 22.1. IR (cm^{-1}) 3311, 2955, 1677, 1496, 1189. ESI (+Na): 504.4. HRMS calcd for $C_{27}H_{35}O_5N_3$ ($M + H^+$) 482.2669, obsd 482.2671.

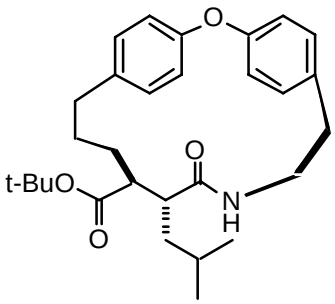


(**3b**): The procedure described for **3a** was employed (61% yield). ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 7H), 7.05 (m, 4H), 6.88 (m, 2H), 4.97 (s, 2H), 3.48 (m, 2H), 2.72 (m, 2H), 2.51 (m, 3H), 2.22 (m, 1H), 1.70 (m, 1H), 1.56 (m, 3H), 1.43 (s, 9H), 0.99 (m, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.2, 173.6, 157.0, 137.7, 137.2, 134.4, 131.7, 130.4, 129.3, 128.5, 127.8, 127.4, 114.7, 80.8, 70.0, 49.6, 48.5, 40.4, 40.2, 35.2, 34.6, 30.6, 29.1, 28.1, 26.0, 23.8, 21.5. IR (cm^{-1}) 3305, 2953, 1724, 1643, 1511, 1241, 1148. HRMS calcd for $C_{36}H_{46}O_4NBr$ ($M + H^+$) 636.2688, obsd 636.2708.



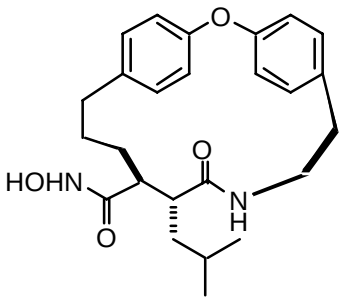
(**4b**): The Pd(0) catalyzed coupling procedure described for **4a** was employed (83% yield). ^{1}H NMR ($CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.39 (m, 5H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.98 (s, 2H), 3.53 (m, 2H), 2.78 (m, 2H), 2.47 (m, 3H), 2.18 (m, 1H), 1.70 (m, 1H), 1.53 (m, 5H), 1.42 (s, 9H), 1.33 (s, 12H), 1.02 (m, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.1, 173.5, 157.0, 142.1, 137.3, 135.2, 135.1, 134.5, 129.3, 128.5, 128.1, 127.8, 127.4, 114.7, 83.7, 80.6, 70.0, 49.7, 48.6, 40.4, 40.2, 36.1, 34.6, 30.7, 29.2, 28.1, 25.9, 24.8, 23.8, 21.5. IR (cm^{-1}) 3304, 2976, 1724, 1643, 1511, 1362, 1146. HRMS calcd for $C_{42}H_{58}O_6NB$ ($M + H^+$) 684.4435, obsd 684.4451.

The hydrogenation procedure described for **4a** was employed (quantitative yield). ^{1}H NMR ($CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 3.49 (m, 2H), 2.72 (m, 2H), 2.40 (m, 3H), 2.13 (m, 1H), 1.63 (m, 1H), 1.41 (m, 5H), 1.35 (s, 9H), 1.26 (s, 12H), 0.75 (d, *J* = 6.6 Hz, 3H), 0.70 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.3, 174.0, 154.4, 141.9, 141.2, 135.2, 133.5, 129.2, 128.1, 115.3, 83.8, 80.9, 49.6, 48.6, 40.3, 35.9, 34.6, 30.7, 29.2, 28.1, 25.9, 24.8, 23.8, 21.5. IR (cm^{-1}) 3312, 2976, 1646, 1516, 1362, 1146. HRMS calcd for $C_{35}H_{42}O_6NB$ (Compound decomposed to free boronic acid.) ($M + H^+$) 512.3183, obsd 512.3176.

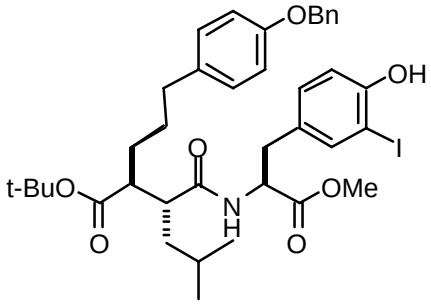


(**6b**): The procedure described for **6a** was employed (43% yield). ^{1}H NMR ($CDCl_3$) δ 7.08 (m, 8H), 3.54 (m, 1H), 3.3 (m, 1H), 2.89 (m, 1H), 2.78 (m, 1H), 2.52 (m, 1H), 2.30 (m, 1H), 1.95 (m, 1H), 1.79 (m, 1H), 1.50 (m, 5H), 1.43 (s, 9H), 0.96 (m, 1H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 3H), 0.24 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 174.1, 173.6, 161.1,

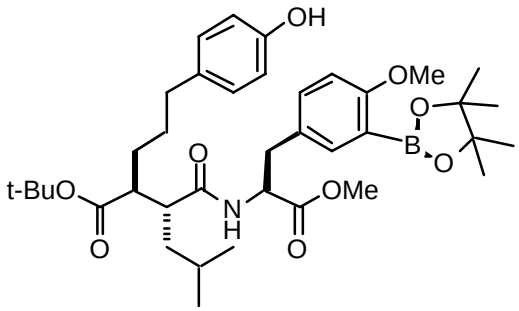
160.4, 137.9, 134.8, 129.8, 122.5, 80.4, 48.2, 47.5, 40.7, 39.7, 35.9, 34.5, 34.0, 28.4, 28.3, 28.1, 25.8, 23.6, 21.6. IR (cm^{-1}) 2927, 1719, 1646, 1508, 1492, 1183, 1152. HRMS calcd for $C_{29}H_{39}O_4N$ ($M + H^+$) 466.2957, obsd 466.2969 .



(**7b**): The procedure described for **7a** was employed (70% yield). ^1H NMR (CD_3OD) δ 7.06 (m, 8H), 3.66 (dt, *J* = 3.2, 13.4 Hz, 1H), 3.02 (dt, *J* = 3.7, 13.4 Hz, 1H), 2.88 (dt, *J* = 3.1, 14.4 Hz, 1H), 2.80 (dt, *J* = 4.4, 13.2 Hz, 1H), 2.61 (dt, *J* = 4.2, 14.4 Hz, 1H), 2.24 (m, 1H), 2.04 (m, 1H), 1.98 (m, 1H), 1.31 (m, 5H), 1.10 (m, 1H), 0.82 (d, *J* = 6.4 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.05 (m, 1H). ^{13}C NMR (CD_3OD) δ 177.1, 173.7, 162.5, 162.1, 139.0, 136.8, 131.1, 123.3, 47.8, 46.9, 43.0, 42.4, 35.0, 33.8, 29.5, 29.2, 26.6, 24.5, 22.2. IR (cm^{-1}) 2929, 1678, 1509, 1205, 1157. ESI (+Na): 447.3. HRMS calcd for $C_{25}H_{32}O_4N_2$ ($M + Na^+$) 447.2233, obsd 447.2238.



(**3c**): The procedure described for **3c** was employed (72% yield). ^1H NMR ($CDCl_3$) δ 7.38 (m, 5H), 7.11 - 6.80 (m, 7H), 4.97 (s, 2H), 4.89 (m, 1H), 3.71 (s, 3H), 2.93 (m, 2H), 2.49 (m, 3H), 2.30 (m, 1H), 1.68 (m, 1H), 1.53 (m, 3H), 1.44 (s, 9H), 1.23 (m, 2H), 1.08 (m, 1H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.9, 173.5, 171.8, 157.0, 154.6, 138.9, 137.2, 134.4, 130.7, 129.8, 129.3, 128.5, 127.8, 127.4, 115.1, 114.7, 85.4, 80.9, 70.0, 52.9, 524, 49.5, 48.4, 40.4, 36.9, 34.4, 30.6, 29.1, 28.1, 25.8, 23.8, 21.5. IR (cm^{-1}) 3304, 2954, 1724, 1647, 1511, 1367, 1238, 1150. HRMS calcd for $C_{38}H_{48}O_7NI$ ($M + H^+$) 758.2554, obsd 758.2538.

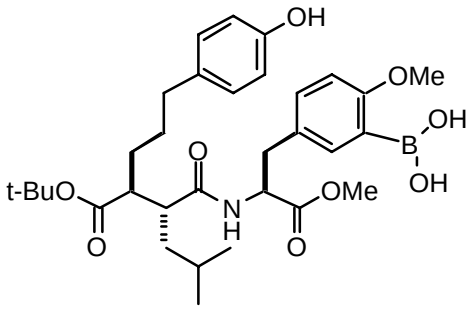


(**4e**): (Trimethylsilyl)diazomethane (2 M in hexane, 3 mL) was added dropwise over 2 h to a solution of **3c** (200 mg, 0.264 mmol) in 4 mL of MeOH at rt. After 30 min at rt, the reaction mixture was concentrated and chromatographed to give O-methylated **3c** (181 mg, 89% yield). ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 1H), 7.31 (m, 5H), 6.97 (m, 3H), 6.80 (m, 2H), 6.60 (m, 1H), 4.89 (s, 2H), 4.82 (m, 1H), 3.71 (s, 3H), 3.64 (s, 3H), 2.87 (m, 2H), 2.42 (m, 3H), 2.36 (m, 1H), 1.60 (m, 1H), 1.48 (m, 3H), 1.37 (s, 9H), 1.18 (m, 2H), 0.99 (m, 1H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.8, 173.3, 171.8, 157.3, 157.0, 140.1, 137.2, 134.4, 130.1, 129.3, 128.5, 127.8, 127.4, 114.7, 110.8, 86.0, 80.8, 70.0, 56.3, 52.8, 52.3, 49.5, 48.4, 40.4, 36.9, 34.4, 30.6, 29.1, 28.1, 25.8, 23.8, 21.5. IR (cm^{-1}) 3317, 2953, 1724, 1511, 1492, 1254, 1148. ESI (+Na): 794.4. HRMS calcd for $C_{39}H_{50}O_7N_2I$ ($M + H^+$) 772.2697, obsd 772.2693.

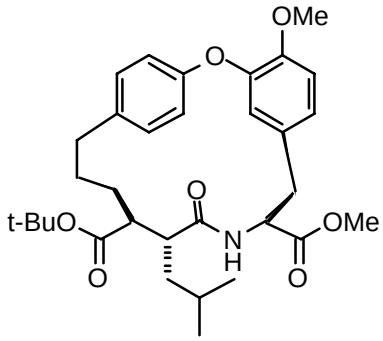
The Pd (0) catalyzed cross coupling procedure described for **4a** was employed (60% yield). ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 6H), 7.07 (m, 3H), 6.87 (m, 3H), 6.47 (m, 2H), 6.74 (m, 1H), 5.99 (bd, *J* = 8.4 Hz, 1H), 4.97 (s, 2H), 4.91 (m, 1H), 3.75 (s, 3H), 2.99 (m, 2H), 2.48 (m, 3H), 2.30 (m, 1H), 1.49 (m, 3H), 1.43 (s, 9H), 1.33 (s, 12H), 1.18 (m, 2H), 1.00 (m, 1H), 0.84 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.8, 173.3, 172.0, 163.4, 156.9, 137.5, 134.5, 133.1, 129.2, 128.3, 127.8, 127.4, 127.1, 114.7, 110.6, 83.5, 80.6, 70.0, 55.7, 52.9, 52.1, 49.6, 48.5, 40.5, 37.3, 34.4, 30.6, 29.1, 28.1, 25.8, 24.8, 23.9, 21.4. IR (cm^{-1}) 2953, 1725, 1511, 1351, 1250, 1146. ESI (+Na): 794.6. HRMS calcd for $C_{39}H_{52}O_9NB$ (Compound decomposed to free boronic acid.) ($M - H^+$) 688.3643, obsd 688.3647.

The hydrogenation procedure described for **4a** was employed (93% yield). ^{1}H NMR ($CDCl_3$) δ 7.44 (bs, 1H), 7.14 (m, 1H), 6.92 (m, 2H), 6.73 (m, 4H), 6.12 (bd, *J* = 8.3 Hz, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 3.94 (m, 2H), 2.41 (m, 4H), 1.67 (m, 1H), 1.53 (m, 3H), 1.41 (s, 9H), 1.32 (s, 12H), 1.05 (m, 3H), 0.82 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 174.0, 173.6, 172.0, 163.4, 154.4, 137.6, 133.3, 133.1, 129.2, 127.1, 115.2, 110.6, 87.3, 80.8, 55.6, 53.1, 58.2, 49.5, 48.4,

40.7, 37.3, 34.3, 30.5, 29.0, 28.1, 25.8, 24.8, 23.8, 21.4. IR (cm^{-1}) 2976, 1725, 1516, 1496, 1251, 1147. HRMS calcd for $C_{32}H_{46}O_9NB$ (Compound decomposed to free boronic acid.) (M - H^+) 598.3215, obsd 598.3204.

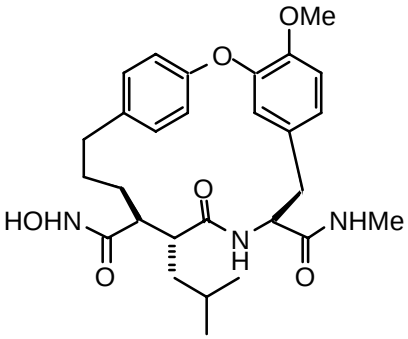


(**5e**): The procedure described for **5a** was employed. The boronic acid yield was 61% and the recovered boronic ester was 16%. The calibrated yield from the boronic acid is 73%. ^1H NMR ($CDCl_3$) δ 7.67 (d, *J* = 2.2 Hz, 1H), 7.12 (m, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.72 (m, 2H), 6.62 (d, *J* = 8.4 Hz, 2H), 6.15 (d, *J* = 8.4 Hz, 2H), 4.96 (m, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.09 (m, 1H), 2.84 (m, 1H), 2.45 - 2.13 (m, 4H), 1.63 (m, 1H), 1.34 (s, 9H), 1.19 (m, 5H), 0.92 (m, 1H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 174.4, 173.9, 172.1, 163.6, 154.3, 137.3, 133.5, 129.2, 128.3, 115.2, 110.0, 81.0, 55.4, 52.9, 52.3, 49.3, 48.4, 40.5, 37.3, 34.5, 30.6, 29.1, 28.0, 25.7, 23.8, 21.4. IR (cm^{-1}) 3352, 1726, 1652, 1515, 1492, 1368, 1151. ESI (+Na): 622.5. HRMS calcd for $C_{32}H_{46}O_9NB$ (M - H^+) 598.3187, obsd 598.3189.



(**6e**): The cyclization procedure described for **6a** was employed (52% yield). ^1H NMR ($CDCl_3$) δ 7.23 (m, 2H), 7.15 (m, 1H), 7.00 (m, 1H)), 6.82 (d, *J* = 8.1 Hz, 1H), 6.61 (m, 1H), 6.26 (d, *J* = 2.2 Hz, 1H), 5.96 (d, *J* = 5.9 Hz, 1H), 4.72 (m, 1H), 3.94 (s, 3H), 3.67 (s, 3H), 2.95 (m, 3H), 2.50 (m, 1H), 2.09 (m, 1H), 1.82 (m, 3H), 1.51 (m, 1H), 1.40 (s, 9H), 1.33

(m, 2H), 1.10 (m, 1H), 0.83 (d, *J* = 6.2 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.1, 172.8, 171.5, 154.1, 149.7, 138.7, 130.4, 129.9, 129.0, 123.2, 122.6, 121.7, 116.3, 111.8, 80.4, 56.0, 53.7, 52.1, 47.7, 46.9, 37.1, 36.0, 35.8, 30.5, 28.1, 26.9, 26.0, 23.8, 21.4.



(**7e**): The amination procedure described for **4d** was employed (80% yield). ^{1}H NMR ($CDCl_3$) δ 7.22 (m, 2H), 7.02 (m, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.50 (m, 1H), 6.24 (d, *J* = 6.6 Hz, 1H), 6.16 (d, *J* = 2.2 Hz, 1H), 4.48 (m, 1H), 3.92 (s, 3H), 3.12 (m, 1H), 2.88 (m, 1H), 2.74 (d, *J* = 4.8 Hz, 3H), 2.51 (m, 1H), 2.13 (m,.1H), 1.96 (m, 1H), 1.78 (m, 1H), 1.66 (m, 2H), 1.55 (m, 1H), 1.44 (s, 9H), 1.33 (m, 1H), 1.16 (m, 3H), 0.78 (d, *J* = 6.2 Hz, 3H), 0.76 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.9, 173.4, 170.7, 154.1, 150.0, 147.9, 138.4, 130.2, 130.0, 123.0, 122.2, 122.0, 115.9, 111.6, 80.4, 56.0, 54.7, 47.6, 47.4, 37.6, 37.5, 35.2, 29.8, 28.1, 27.6, 25.9, 26.0, 23.6, 21.6.

The hydroxyamic acid preparation procedure described for **7a** was employed (66% yield). ^{1}H NMR (CD_3OD) δ 8.03 (d, *J* = 6.6 Hz, 1H), 7.23 (m, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.95 (m, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.21 (d, *J* = 1.8 Hz, 1H), 4.18 (m, 1H), 3.87 (s, 3H), 2.86 (m, 3H), 2.64 (s, 3H), 2.51 (m, 1H), 2.39 (m, 1H), 2.08 (m, 1H), 1.74 (m, 1H), 1.55 (m, 2H), 1.46 (m, 2H), 1.03 (m, 2H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H).