Supporting Information

for

Direct Mono-*N*-Methylation of Solid-Supported Amino Acids: A Useful Application of the Matteson Rearrangement of α-Aminoalkylboronic Esters

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Representative procedure. Note: we have found that with some batches of commercial resin-bound amino acids it may be advisable to cap unreacted sites before use (benzoyl chloride, pyridine, methylene chloride, 2 hours). A portion of Fmoc-Val-HMPB-BHA (sasrin) resin (300 mg, 0.45 mmol/g, 0.135 mmol) in a polypropylene fritted vessel was treated with a solution of 20% piperidine/DMF (1× 5 mL for 3 min, 1× 5 mL for 40 min), then rinsed several times with anhydrous DMF. The resin was then suspended in 2.5 mL of DMF/*t* -amyl alcohol (9:1) followed by addition of diisopropylethylamine (120 μL, 0.68 mmol) and pinacol chloromethylboronic ester (112 μL, 0.68 mmol). The suspension was reacted on an orbital shaker for 20 hours at room temperature. The resin was washed successively with DMF (3×), THF (3×) , and 4:1 THF-aq. pH 8 buffer (3×). To the resin suspended in 4:1 THF-aq. pH 8 buffer (3 mL) was then added hydrogen peroxide (30% aq. solution, 80 mL, ca. 5 equiv.). The mixture was shaken for 5 minutes on a vortexer then the resin was washed several times with 4:1 THF-water. The resin was rinsed successively with THF (2×), DMF-Et_3N (1×), DMF (2×), CH_2Cl_2 (5x), then dried under high vacuum for >12 hours to give 0.29 g of resin product (theoretical loading = 0.49 mmol/g). A sample (0.150 g, 0.074 mmol) was treated with a 1% solution of trifluoroacetic acid in dichloromethane (2 mL). The suspension was stirred for 20 minutes, then filtered through glass wool, and rinsed with 1% TFA-CH_2Cl_2 (5 × 1 mL). The combined filtrates were concentrated to

dryness and the resulting oil was dried in vacuo for 15 hours. The resulting *N*-methyl-valine trifluoroacetate salt was obtained as a yellowish oil (18 mg, 95%) that can be precipitated with ether from a concentrated methanol solution.

Other cleavage procedures:

1) Sasrin resin. For residues containing Boc or *t*-butyl protected side chains: the filtrate are evaporated at low temperature (ca. 5 °C) or neutralized with a slight excess of pyridine (as a solution in CH_2Cl_2) added in the receiving flask in the filtration and rising steps.

2) Wang resin. A cleavage TFA-CH_2Cl_2-H_2O cleavage cocktail (85:10:5) was employed. The suspension was stirred for ca. 1-2 hours, filtered, rinsed with TFA, and concentrated.

Spectroscopic data. All model amino acids used are commercially available and were thus characterized only by electrospray mass spectrometry and proton NMR (CD_3OD, 300 MHz).
2a. ^{1}H NMR δ (ppm): 3.83 (1H, d, *J* = 4.5 Hz, α-CH), 2.72 (3H, s, N-CH_3), 2.30 (1H, m, C*H*$(CH_3)_2$), 1.15 (3H, d, *J* = 6.5 Hz, CH(C*H*$_3)_2$),), 1.05 (3H, d, *J* = 6.5 Hz, CH(C*H*$_3)_2$). ES-MS (+ve): 132 [MH^+].
2c. ^{1}H NMR δ (ppm): 7.35-7.15 (5H, m, -Ph), 4.25 (1H, t, *J* = 6.5 Hz, α-CH), 3.40-3.20 (2H, m, -CH_2Ph), 2.72 (3H, s, N-CH_3). ES-MS (+ve): 180 [MH^+].

2d. ^{1}H NMR δ (ppm): 3.92 (1H, m, α-CH), 2.73 (3H, s, N-CH_3), 2.0-1.6 (3H, m, C*H*$_2$C*H*(CH_3)$_2$), 1.02 (3H, d, *J* = 7 Hz, CH(C*H*$_3$)$_2$), 0.99 (3H, d, *J* = 7 Hz, CH(C*H*$_3$)$_2$). ES-MS (+ve): 146 [MH^+].

2e. ^{1}H NMR δ (ppm): 7.20 (2H, d, *J* = 9 Hz, -Ar), 6.98 (2H, d, *J* = 9 Hz, -Ar), 4.20 (1H, t, *J* = 6 Hz, α-CH), 3.30-3.10 (2H, m, -CH_2Ph), 2.71 (3H, s, N-CH_3), 1.33 (9H, s, C(CH_3)$_3$). ES-MS (+ve): 252 [MH^+].

2f. ^{1}H NMR δ (ppm): 4.14 (1H, d, *J* = 5 Hz, α-CH), 3.01 (2H, m, CH_2CO-*t*-Bu), 2.76 (3H, s, N-CH_3), 1.46 (9H, s, C(CH_3)$_3$). ES-MS (+ve): 204 [MH^+].