The Preparation of 5-hydroxy-1-alkenyboronates from 1-alkynylboronates, Cp_2ZrCl_2 / 2 EtMgBr and aldehydes

Abed Al Aziz Quntar and Morris Srebnik*

Department of Natural Products and Medicinal Chemistry, School of Pharmacy, Hebrew University in Jerusalem, Jerusalem 91120 Israel.

msrebni@md.huji.ac.il

Supporting information

General comments. All reactions were carried out under a nitrogen atmosphere vacuum line and glovebox techniques. Solvents were purified by distillation from appropriate drying agents under a nitrogen atmosphere. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded in $CDCl_3$, ^{11}B NMR (96.24 MHz) was recorded in $CDCl_3$ in the presence of BF_3etharate reference. GCMS analysis were performed on HP GCMS instrument (Model GCD PLUS), with EI detector and 30 m methyl silicone column.

All the aldehydes were commercially purchased and freshly distilled pre use.

General Procedure to 3. To 0.306 g (1.05 mmol) of zirconecene dichloride dissolved in 7 ml of dry THF at -78 ^{0}C was added 1.05 ml of 2M EtMgBr (2.1 mmol) dropwise in a 25 ml round-bottom flask. After stirring for 1hr at -78 ^{0}C, 1 mmol of 1-alkynylboranate was added. The reaction was gradually warmed to 0^{0}C and stirred for 3 hr. Then 2 equiv. of aldehyde were added, the reaction was wormed to 50^{0}C and left stirring overnight. The reaction was worked up with diluted HCl, the product was extracted with diethyl ether (2 X 15ml), separated on silica gel column (90% petroleum ether: 10% diethyl ether), and was analyzed by GCMS, elemental analysis, and NMR spectroscopy.

2a: ^{1}H NMR (300 MHz): δ 0.90 (t, 3H, J_{HH} = 7.2 Hz), 1.02 (t, 3H, J_{HH} = 7.2 Hz), 1.26 (s, 12H), 1.50-1.83 (overlap, 4H), 2.12 (q, 2H, J_{HH} = 7.2), 2.40 (t, 2H, J_{HH} = 7.5 Hz), 5.11 (s, 1H); ^{11}B NMR (96.24 MHZ): δ 28.54; ^{13}C NMR (75.5 MHz): δ 12.17, 13.94, 22.60, 24.79, 31.54, 31.80, 34.65, 82.44, 169.00; MS(EI):m/z (%) 238 (1.9), 219 (2.9), 196 (3.8), 153 (12.5), 139 (63.5), 84 (29.8), 55 (43.3), 43 (91.4), 41 (100), 29 (51.0); Anal. Calcd. for $C_{14}H_{27}BO_2$: C, 70.60; H, 11.43; B, 4.54%. Found: C, 71.10; H, 11.11; B, 4.41%.

2b: ^{1}H NMR (300 MHz): δ 0.90 (t, 3H, J_{HH} = 6.9 Hz), 1.20 (t, 2H, J_{HH} = 7.2 Hz), 1.27 (s, 12H), 1.50-1.85 (overlap, 4H), 2.24 (t, 2H, J_{HH} = 7.2), 2.42 (t, 2H, J_{HH} = 7.2 Hz), ^{11}B NMR (96.24 MHZ): δ 28.55; ^{13}C NMR (75.5 MHz): δ 12.21, 13.99, 22.62, 24.80, 31.56, 31.83, 34.67, 82.47, 169.10; MS(EI):m/z (%) 240 (0.3), 239 (0.3), 198 (2.8), 182 (5.7), 140 (27.9), 101 (22.1), 83 (34.6), 55 (42.3), 43 (82.9), 41 (100), 29 (40.4).

3a: ^{1}H NMR (300 MHz): δ 0.90 (t, 3H, J_{HH} = 6.6 Hz), 1.26 (s, 12H), 1.30-1.43 (overlap, 4H), 1.80-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.40 (t, 2H, J_{HH} = 7.5), 4.68 (dt, 1H, J_{HH} = 5.4), 5.15 (s, 1H), 7.19-7.44 (overlap, 5H); ^{11}B NMR (96.24 MHZ): δ 30.54; ^{13}C NMR (75.5 MHz): δ 13.92, 22.55, 24.78, 31.65, 34.65, 35.09, 37.06, 74.13, 82.53, 125.85, 127.48, 128.39, 144.61, 166.65; MS(EI):m/z (%) 344 (0.5), 329 (1.9), 287 (1.4), 269 (2.0), 246 (3.8), 225 (13.5), 167 (12.5), 143 (58.7), 120 (100), 107 (48.1), 91 (40.0), 79 (89.4), 77 (50.0), 55 (59.6), 41 (64.4), 29 (63.3); Anal. Calcd. for $C_{21}H_{33}BO_3$: C, 73.26; H, 9.66; B, 3.14%. Found: C, 72.88; H, 9.53; B, 2.07%.

3b: ^{1}H NMR (300 MHz): δ 0.91 (t, 3H, J_{HH} = 6.9 Hz), 1.25 (s, 12H), 1.30-1.43 (overlap, 4H), 1.80-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.33 (s, 3H), 2.39 (t, 2H, J_{HH} = 7.2), 4.63 (dt, 1H, J_{HH} = 6.0), 5.13 (s, 1H), 7.12-7.32 (overlap, 4H); ^{11}B NMR (96.24 MHZ): δ 31.06; ^{13}C NMR (75.5 MHz): δ 13.93, 21.09, 22.58, 24.80, 31.68, 35.18, 36.97, 74.03, 82.54, 125.85, 129.10, 141.63, 166.74; MS(EI):m/z (%) 358 (0.30), 343 (0.31), 283 (1.0), 260 (1.1), 224 (3.8), 157 (18,3), 134 (100), 121 (24.0), 91 (20.2), 76 (18.2), 55 (20.2), 41 (23.1), 29 (14.4); Anal. Calcd. for $C_{22}H_{35}BO_3$: C, 73.74; H, 9.85; B, 3.02%. Found: C, 73.58; H, 9.76; B, 2.88%.

3c: ^{1}H NMR (300 MHz): δ 0.86 (t, 3H, J_{HH} = 6.9 Hz), 1.25 (s, 12H), 1.30-1.43 (overlap, 4H), 1.80-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.39 (t, 2H, J_{HH} = 6.9), 3.80 (s, 3H), 4.62 (dt, 1H, J_{HH} = 6.3), 5.13 (s, 1H), 6.83 (d, 2H, J_{HH} = 8.1 Hz), 7.25 (d, 2H,

J_{HH} = 8.1 Hz); ^{11}B NMR (96.24 MHZ): δ 29.86; ^{13}C NMR (75.5 MHz): δ 13.95, 22.60, 24.82, 31.70, 34.53, 35.21, 36.96, 55.27, 73.82, 82.56, 113.80, 127.17, 136.78, 166.74; MS(EI):m/z (%) 374 (0.40), 356 (0.61), 317 (0.33), 299 (0.92), 274 (1.01), 229 (0.71), 173 (6.80), 150 (100), 137 (36.31), 94 (9.82), 76 (8.02), 55 (18.21), 41 (23.1), 28 (5.82); Anal. Calcd. for $C_{22}H_{35}BO_4$: C, 70.59; H, 9.42; B, 2.89%. Found: C, 70.44; H, 9.50; B, 3.03%.

3d: ^{1}H NMR (300 MHz): δ 0.92 (t, 3H, J_{HH} = 7.2 Hz), 1.18 (d, 3H, J_{HH} = 6.0 Hz), 1.25 (s, 12H), 1.30-1.63 (overlap, 4H), 2.05-2.30 (m, 4H), 2.40 (t, 2H, J_{HH} = 7.2), 3.79 (m, 1H), 5.12 (s, 1H); ^{11}B NMR (96.24 MHZ): δ 30.11; ^{13}C NMR (75.5 MHz): δ 13.94, 22.60, 23.50, 24.80, 31.73, 34.46, 35.19, 37.29, 67.86, 82.55, 166.97; MS(EI):m/z (%) 282 (0.4), 267 (2.9), 255 (10.6), 182 (14.4), 167 (17.3), 138 (16.3), 125 (89.4), 101 (61.5), 95 (60.0), 84 (100), 67 (54.8), 55 (85.6), 43 (67.9), 41 (81.7), 29 (31.7); Anal. Calcd. for $C_{16}H_{31}BO_3$: C, 68.09; H, 11.07; B, 3.83%. Found: C, 67.89; H, 11.16; B, 5.02%.

3e: ^{1}H NMR (300 MHz): δ 0.88 (t, 3H, J_{HH} = 7.5 Hz), 0.97 (t, 3H, J_{HH} = 7.2 Hz), 1.25 (s, 12H), 1.20-2.10 (overlap, 10H), 2.04 (t, 2H, J_{HH} = 7.8), 4.09 (m, 1H), 5.13 (s, 1H); ^{11}B NMR (96.24 MHZ): δ 30.02; ^{13}C NMR (75.5 MHz): δ 13.95, 14.00, 22.61, 23.52, 24.80, 31.73, 34.46, 35.19, 37.29, 71.00, 82.57, 166.87; MS(EI):m/z (%) 296 (0.5), 281 (3.1), 267 (20.8), 237 (15.7), 169 (18.4), 139 (16.3), 125 (77.8), 87 (20.1), 84 (112.3), 57 (19.8), 43 (80.0), 41 (79.9), 29 (100); Anal. Calcd. for $C_{17}H_{33}BO_3$: C, 68.92; H, 11.23; B, 3.65%. Found: C, 68.80; H, 11.14; B, 3.47%.

3f: ^{1}H NMR (300 MHz): δ 1.26 (s, 12H), 1.88 (t, 2H, J_{HH} = 8.1), 1.93-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.51 (t, 2H, J_{HH} = 7.8), 3.50 (t, 2H, J_{HH} = 6.9), 4.68 (dt, 1H, J_{HH} = 7.2), 5.21 (s, 1H), 7.23-7.49 (overlap, 5H); ^{11}B NMR (96.24 MHZ): δ 29.87; ^{13}C NMR (75.5 MHz): δ 24.81, 32.40, 53.06, 36.96, 44.83, 46.65, 74.03, 82.76, 125.83, 127.60, 128.47, 144.46, 164.43; MS(EI):m/z (%) 367 (0.3), 366 (0.4), 365 (0.4), 364 (1.2), 329 (0.8), 208 (10.8), 156 (13.7), 105 (100), 77 (80.1), 43 (33.3), 41 (45.1), 29 (10.8); Anal. Calcd. for $C_{20}H_{30}BClO_3$: C, 65.86; H, 8.29; Cl, 9.72; B, 2.96%. Found: C, 65.55; H, 8.19; Cl, 9.66; B, 3.12%.

3g: ^{1}H NMR (300 MHz): δ 1.25 (s, 12H), 1.89 (t, 2H, J_{HH} = 8.2), 1.93-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.29 (s, 3H), 2.50 (t, 2H, J_{HH} = 7.7), 3.51 (t, 2H, J_{HH} = 6.8), 4.68 (dt, 1H, J_{HH} = 7.2), 5.21 (s, 1H), 7.15-7.40 (overlap, 4H); ^{11}B NMR (96.24 MHZ): δ 29.95; ^{13}C NMR (75.5 MHz): δ 24.81, 32.40, 35.06, 35.88, 36.96, 44.83, 46.65, 74.03, 82.76, 125.78, 129.80, 142.40, 163.44; MS(EI):m/z (%) 381 (6.8), 379 (4.9), 378 (3.9), 377 (16.6), 376 (4.5), 361 (2.0), 299 (10.0), 267 (15.7), 248 (19.6), 213 (17.6), 199 (33.3), 147 (40.2), 135 (27.5), 121 (71.6), 91 (54.9), 59 (47.4), 41 (100), 29 (12.7); Anal. Calcd. for $C_{21}H_{32}BClO_3$: C, 66.60; H, 8.52; Cl, 9.36; B, 2.85%. Found: C, 66.52; H, 8.39; Cl, 9.28; B, 2.77%.

3h: ^{1}H NMR (300 MHz): δ 1.25 (s, 12H), 1.88 (t, 2H, J_{HH} = 8.2), 1.93-1.95 (m, 2H), 2.05-2.18 (m, 2H), 2.50 (t, 2H, J_{HH} = 8.2), 3.51 (t, 2H, J_{HH} = 6.8), 3.90 (s, 3H), 4.68 (dt, 1H, J_{HH} = 7.1), 5.21 (s, 1H), 7.15-7.40 (2d, 4H); ^{11}B NMR (96.24 MHZ): δ 30.15; ^{13}C NMR (75.5 MHz): δ 24.87, 32.40, 35.03, 35.85, 36.94, 46.67, 54.5, 74.14, 82.76, 115.4, 127.68, 135.80, 142.40, 162.33; MS(EI):m/z (%) 397 (0.6), 396 (0.7), 395 (0.7), 394 (2.6), 379 (3.1), 365 (5.0), 363 (2.5), 359 (6.7), 257 (12.5), 137 (30.1), 107

(30.4), 90 (100), 76 (34.3), 41 (66.9), 29 (30/1); Anal. Calcd. for $C_{21}H_{32}BClO_4$: C, 63.90; H, 8.17; Cl, 8.98; B, 2.74%. Found: C, 63.68; H, 8.04; Cl, 8.84; B, 2.85%.