Supporting Information

Novel Extension of Meyers' Methodology: Stereoselective Construction of Axially Chiral 7,5-Fused Bicyclic Lactams

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General Experimental

The NMR spectra were recorded on 300 MHz spectrometers. ^1H at 300 MHz and ^{13}C at 75 MHz using CDCl_3 as solvent and with the residual solvent signal ($\delta 7.26$, ^1H ; $\delta 77.0$, ^{13}C) as internal standard unless otherwise indicated. The following abbreviations are used to describe peak pattern: s (singlet), d (doublet), t (triplet), q (quartet). Melting points are uncorrected. Optical rotation were measured at 20°C in CH_2Cl_2 . Analytical thin layer chromatographies were performed on silica gel plates with QF-254 indicator. Dioxane was distilled on sodium-benzophenone. Tetrakis(triphenylphosphine)palladium(0) $[\text{Pd}(\text{PPh}_3)_4]$ was prepared according to Coulson method¹ and stored under nitrogen at -24°C .

2-Iodobenzoic acid ethyl ester (3'a). A solution of 2-iodobenzoic acid (3 g, 12 mmol) in thionyl chloride (30 mL) was stirred at reflux for 2 hours. Thionyl chloride was evaporated under reduced pressure and the residue was dissolved in absolute ethanol (40 mL) at 0°C . The resultant solution was stirred at rt for 12 hours. After evaporation of ethanol, the residue was washed with a 5% aqueous K_2CO_3 solution and extracted with dichloromethane (2 x 20 mL). The combined organic phases were dried (MgSO_4) and the solvent was evaporated under reduced pressure to afford 2-iodobenzoic acid ethyl ester **3'a** as a yellow oil (3.3 g, 99%). ^1H NMR (CDCl_3) δ 7.90 (dd, $J = 1.0$ and 8.0 Hz, 1H), 7.79 (dd, $J = 2.0$ and 8.0 Hz, 1H), 7.32 (td, $J = 1.0$ and 8.0 Hz, 1H), 7.06 (td, $J = 2.0$ and 8.0 Hz, 1H), 4.32 (q, $J = 7.0$ Hz, 2H), 1.33 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 167.0, 141.6, 135.8, 132.8, 131.2, 128.2, 94.3, 62.1, 14.6. IR ν_{max} (KBr) 1726, 1289, 1251, 1134, 1102, 1016, 741 cm^{-1} . Anal. Calcd. for $\text{C}_9\text{H}_9\text{IO}_2$: C, 39.16; H, 3.29. Found: C, 38.85; H, 3.19.

2-Chloroquinoline-3-carboxylic acid ethyl ester (3b). A solution of 2-chloroquinoline-3-carboxylic acid (1.68 g, 8.09 mmol) in thionyl chloride (50 mL) was stirred at reflux for 2 hours. Thionyl chloride was evaporated and the residue was dissolved in CH_2Cl_2 (50 mL) at

¹ Coulson D. R. *Inorganic Synth.* **1972**, 13, 22.

0°C. Distilled triethylamine (3.4 mL, 24.27 mmol) and ethanol (471.2 μ L, 8.09 mmol) were added dropwise. The mixture was stirred at rt for 24 hours under nitrogen atmosphere. The mixture was washed with a 10% aqueous K_2CO_3 solution, the organic layer was dried ($MgSO_4$) and concentrated to afford a yellow solid. Recrystallisation (cyclohexane/ether: 90/10) afforded **3b** (1.64 g, 86%) as a white solid. mp 84-85 °C. 1H NMR ($CDCl_3$) δ 8.59 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 7.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 4.41 (q, J = 7.0 Hz, 2H), 1.39 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 164.9, 148.5, 147.9, 141.8, 132.9, 128.7 (2 C), 128.1, 126.1, 124.8, 62.5, 14.5. IR_{νmax} (KBr) 1725, 1276, 1253, 1202, 1131, 1031, 780 cm^{-1} . Anal. Calcd. for $C_{12}H_{10}ClNO_2$: C, 61.16; H, 4.28; N, 5.94. Found: C, 61.19; H, 4.35; N, 5.97.

2-Chloronicotinic acid ethyl ester (3c). A solution of 2-chloronicotinic acid (1.6 g, 10 mmol) in thionyl chloride (25 mL) was stirred at reflux for 2 hours. Thionyl chloride was evaporated under vacuum and the residue was dissolved in absolute ethanol (40 mL) at 0°C. The reaction mixture was stirred at rt during 12 hours. Ethanol was evaporated, the residue was washed with a 5% aqueous K_2CO_3 solution and extracted with dichloromethane (2 x 20 mL). The organic layer was dried ($MgSO_4$) and evaporated to afford 2-chloronicotinic acid ethyl ester **3c** as a yellow oil (1.8 g, 95%). 1H NMR ($CDCl_3$) δ 8.42 (dd, J = 1.8 and 4.8 Hz, 1H), 8.07 (dd, J = 1.8 and 7.7 Hz, 1H), 7.22 (dd, J = 4.8 and 7.7 Hz, 1H), 4.33 (q, J = 4.0 Hz, 2H), 1.30 (t, J = 4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 164.7, 152.0, 150.1, 140.5, 127.5, 122.4, 62.3, 14.4. IR_{νmax} (KBr) 2984, 1732, 1581, 1403, 1300, 1143, 1066 cm^{-1} . Anal. Calcd. for $C_8H_8ClNO_2$: C, 51.77; H, 4.34; N, 7.55. Found: C, 51.96; H, 4.48; N, 7.38.

2-Acetyl-naphthalen-1-yl trifluoromethanesulfonate (4b). To a solution of 1-hydroxy-2-acetonaphthone (2 g, 10.7 mmol) in dichloromethane (40 mL) under nitrogen, freshly distilled pyridine (2.5 mL, 32 mmol) was added. Trifluoromethane sulfonic anhydride (3.71 mL, 22 mmol) was added dropwise and the resulting solution was allowed to stir at rt for 2 hours. A

white solid precipitated after addition of Et₂O (10 mL). The precipitate was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel (cyclohexane/EtOAc : 9/1) to afford compound **4b** as a brown solid (3.2 g, 95 %). mp 65°C. ¹H NMR (CDCl₃) δ 8.12 (m, 1H), 7.86 (m, 2H), 7.62 (m, 3H), 2.63 (s, 3H). ¹⁹F NMR (CDCl₃) δ -73.46. ¹³C NMR (CDCl₃) δ 198.7, 142.4, 136.5, 129.3, 129.0, 128.9, 128.4, 127.0, 124.8, 122.7, 30.1. IR _νmax (KBr) 1694, 1418, 1205, 1138, 1032, 901, 823, 601 cm⁻¹. Anal. Calcd. for C₁₃H₉F₃O₄S: C, 49.06; H, 2.85. Found: C, 49.18; H, 2.91.

1-[1-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)naphthalen-2-yl]-ethanone (4c). To a solution of aryl triflate **4b** (312 mg, 0.98 mmol) in freshly distilled dioxane (4 mL) was added freshly distilled NEt₃ (0.42 mL, 3 mmol) and Pd(PPh₃)₄ (56 mg, 0.03 mmol). The mixture was degassed with a N₂ flow during 30 min after which time pinacolborane (0.4 mL, 2 mmol) was added dropwise under N₂ and the mixture was heated for 2 hours at 80°C. The solvent was removed *in vacuo* and the residue was purified by chromatography on silica gel (CH₂Cl₂/NEt₃ : 95/5) to afford compound **4c** as a colorless oil (45 mg, 15%). ¹H NMR (CDCl₃) δ 8.08 (m, 1H), 7.87-7.80 (m, 3H), 7.57-7.49 (m, 2H), 2.68 (s, 3H), 1.54 (s, 12H). ¹³C NMR (CDCl₃) δ 200.6, 138.4, 135.7, 135.5, 130.1, 129.8, 128.5, 128.5, 127.1 (2 C), 124.4, 84.3 (2 C), 26.3, 26.1. IR _νmax (KBr) 2980, 1668, 1300 cm⁻¹. HRMS (EI) calcd. for C₁₈H₂₁O₃B: 296.1588, found: 296.1567.

2'-Acetylbiphenyl-2-carboxylic acid ethyl ester (2a) (General Procedure). To a solution of aryl iodide **3'a** (2.75 g, 10 mmol) or aryl bromide **3a** (2.30 g, 10 mmol) in toluene (150 mL) and ethanol (12 mL), were added boronic acid **4a** (1.64 g, 10 mmol) and an aqueous K₂CO₃ solution (4.14 g in 15 mL of water). The reaction mixture was degassed with a N₂ flow during 30 min. After adding Pd(PPh₃)₄ (580 mg, 5%), the reaction mixture was degassed with N₂ flow for a further 15 min. The mixture was stirred at reflux under N₂ atmosphere during 48

hours and then cooled to rt. The solution was filtered through a plug of celite and toluene was evaporated. Then, Et₂O (100 mL) was added to the resulting aqueous phase. After phase separation, the organic layer was washed with water (50 mL) and dried over MgSO₄. The solvents were evaporated under vacuum, and the residue was purified by flash chromatography (CH₂Cl₂) to afford **2a** (2.44 g, 91% with **3'a**) as a yellow oil. ¹H NMR (CDCl₃) 7.90 (dd, *J* = 1.5 and 8.0 Hz, 1H), 7.63 (dd, *J* = 2.0 and 7.0 Hz, 1H), 7.46-7.31 (m, 4H), 7.11 (dd, *J* = 2.0 and 7.0 Hz, 1H), 7.09 (dd, *J* = 2.0 and 10.0 Hz, 1H), 4.01 (qd, *J* = 1.0 and 7.0 Hz, 2H), 2.07 (s, 3H), 0.93 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (CDCl₃): 202.3, 167.7, 142.8, 141.4, 139.2, 131.9, 131.2, 131.1, 130.6, 130.5, 130.5, 128.6, 128.0, 127.7, 61.2, 29.8, 14.1. IR _νmax (KBr) 2982, 1718, 1689, 1287, 1251, 1131, 1090, 760 cm⁻¹. Anal. Calcd. for C₁₇H₁₆O₃: C, 76.10; H, 6.01. Found: C, 76.18; H, 5.93.

2-(2-Acetylphenyl)quinoline-3-carboxylic acid ethyl ester (2b). According to the general procedure outlined for **2a**, from boronic acid **4a** (1.098 g, 6.7 mmol) and 2-chloroquinoline-3-carboxylic acid ethyl ester **3b** (1.57g, 6.7 mmol). The residue was purified by flash chromatography using a gradient from pure CH₂Cl₂ to pure EtOAc affording **2b** as a yellow solid (1.75 g, 82%). mp 83-84 °C. ¹H NMR (CDCl₃) 8.75 (s, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.78 (dd, *J* = 1.0 and 7.0 Hz; 1H), 7.69 (dt, *J* = 1.0 and 7.0 Hz, 1H), 7.52-7.39 (m, 3H), 7.27 (dd, *J* = 2.0 and 8.0 Hz, 1H), 4.05 (q, *J* = 7.0 and 14.0 Hz, 2H), 2.29 (s, 3H), 1.00 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (CDCl₃) 200.1, 166.3, 160.2, 148.8, 142.2, 139.8, 137.6, 132.1, 132.1, 130.4, 129.7, 129.5, 129.0, 128.5, 127.6, 126.5, 124.7, 61.5, 28.7, 14.2. IR _νmax (KBr) 2928; 1710, 1685, 1264, 1228, 1201, 1097, 1071, 804, 760 cm⁻¹. Anal. Calcd. for C₂₀H₁₇NO₃: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.13; H, 5.47, N, 4.19.

2-(2-Acetylphenyl)nicotinic acid ethyl ester (2c). According to the general procedure outlined for **2a**, from boronic acid **4a** (1.64 g, 10 mmol) and ethyl 2-chloronicotinate **3c** (1.85

g, 10 mmol). The residue was purified by flash chromatography (EtOAc) to afford **2c** as a yellow oil (2.1 g, 71%). ^1H NMR (CDCl_3) δ 8.66 (dd, $J = 2.0$ and 5.0 Hz, 1H), 8.23 (dd, $J = 2.0$ and 8.0 Hz, 1H), 7.77 (dd, $J = 2.0$ and 8.0 Hz, 1H), 7.45 (m, 2H), 7.30 (dd, $J = 4.5$ and 8.0 Hz, 1H), 7.19 (dd, $J = 2.0$ and 7.0 Hz, 1H), 4.02 (q, $J = 7.0$ Hz, 2H), 2.30 (s, 3H), 0.96 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 200.3, 166.4, 161.1, 151.9, 141.5, 138.6, 137.7, 131.8, 130.2, 129.3, 128.5, 126.5, 122.3, 61.5, 28.9, 14.1. IR ν_{max} (KBr) 2983, 1722; 1686, 1427, 1285, 1138, 762 cm^{-1} . Anal. Calcd. for $\text{C}_{16}\text{H}_{15}\text{NO}_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.45; H, 5.62; N, 5.27.

2-(2-Acetyl-naphtalen-1-yl)nicotinic acid ethyl ester (2d) (“one-pot” procedure). To a solution of aryl triflate **4b** (2g, 6.28 mmol) in freshly distilled dioxane (80 mL), were added freshly distilled NEt_3 (2.62 mL, 18.84 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (580 mg, 0.5 mmol). The mixture was degassed with a N_2 flow for 30 min. Pinacolborane (1.82 mL, 12.6 mmol) was added dropwise under N_2 and the mixture was heated for 2 hours at 80°C after which time the mixture was allowed to cooled to rt. Distilled water (15 mL), $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$ (5.93 g, 18.84 mmol), 2-chloronicotinic acid ethyl ester **3c** (1.16 g, 6.28 mmol) and dioxane (20 mL) were added. The mixture was degassed with N_2 flow for 15 minutes, heated at reflux for 24 hours and then cooled to rt. Water (30 mL) and EtOAc (30 mL) were added. After phase separation, the organic layer was collected, dried (MgSO_4) and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (EtOAc/cyclohexane : 8:2) to give the title keto-ester **2d** as an yellow oil. ^1H NMR (CDCl_3) δ 8.82 (dd, $J = 2.0$ and 5.0 Hz, 1H), 8.43 (dd, $J = 2.0$ and 8.0 Hz, 1H), 7.96-7.85 (m, 3H), 7.52-7.44 (m, 2H), 7.35 (td, $J = 1.0$ and 8.0 Hz, 1H), 7.14 (d, $J = 9.0$ Hz, 1H), 3.84 (q, $J = 7.0$ Hz, 2H), 2.39 (s, 3H), 0.67 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 200.6, 165.8, 159.8, 152.6, 140.0, 138.7, 135.2, 133.8, 132.4, 128.7, 128.4, 128.2, 128.0, 127.4, 127.1, 125.3, 122.7, 61.3, 29.6, 13.7. IR ν_{max} (KBr) 1712, 1682, 1299, 811 cm^{-1} . HRMS (EI) calcd. for $\text{C}_{20}\text{H}_{17}\text{NO}_3$: 319.1186, found: 319.1207.

2'-Acetylbiphenyl-2-carboxylic acid (5a)² (**General Procedure**). To a solution of keto-ester **2a** (1.85 g, 6.9 mmol) in ethanol (40 mL), was added 10 M NaOH (4.2 mL) at 0°C. The mixture was stirred for 24 hours at rt after which time ethanol was evaporated under vacuum. Water (10 mL) was added and the resulting aqueous layer was washed with CH₂Cl₂ (20 mL). After treatment with 1 M HCl (pH = 3), the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were dried (MgSO₄) and concentrated *in vacuo* to afford **5a** (1.59 g, 96%) as a white solid. mp 218°C. ¹H NMR (CDCl₃) 7.99 (dd, *J* = 1.0 and 8.0 Hz, 1H), 7.71 (dd, *J* = 1.0 and 7.0 Hz, 1H), 7.56-7.40 (m, 4H), 7.16 (m, 2H), 2.25 (s, 3H). ¹³C NMR (CDCl₃) 202.9, 171.9, 143.2, 140.9, 138.7, 132.6, 131.4, 131.2, 131.0, 130.8, 129.4, 128.5, 128.0, 127.9, 29.5. IR _ν_{max} (KBr) 2998, 2819, 2656, 2552, 1690, 1312, 1249, 958, 762 cm⁻¹. Anal. Calcd. for C₁₅H₁₂O₃: C, 74.99; H, 5.05. Found: C, 74.91; H, 4.99.

2-(2-Acetylphenyl)nicotinic acid (5c). According to the general procedure outlined for **5a**, from keto-ester **2c** (1.85 g, 6.9 mmol) to afford the desired keto-acid **5c** (1.26 g, 76%) as a white solid. mp 164°C. ¹H NMR (CD₃OD) 9.06 (d, *J* = 6.0 Hz, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 8.0 Hz, 1H), 7.75-7.56 (m, 3H), 1.96 (s, 3H). IR (KBr) 3447, 3392, 1619, 1383, 1186, 1141 cm⁻¹. Anal. Calcd. for C₁₄H₁₁NO₃: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.75; H, 4.56; N, 5.89.

2-(2-Acetyl-naphthalen-1-yl)-nicotinic acid (5d). According to the general procedure outlined for **5a**, from keto-ester **2d** (525 mg, 1.64 mmol) to afford the desired keto-acid **5d** as a white solid (382 mg, 80 %). mp 156°C. ¹H RMN (acetone-d₆) δ 8.84 (d, *J* = 4.0 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.00 (m, 3H), 7.62 (m, 2H), 7.41 (t, *J* = 7.0 Hz, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 2.29 (s, 3H). ¹³C RMN (CDCl₃) δ 200.8, 167.1, 160.5, 153.2, 140.7, 139.5, 135.9 (2

² Muto, S.; Bruce, T. C. *J. Am. Chem. Soc.* **1980**, *102*, 4472-4480.

C), 135.6, 133.4, 129.2, 129.2, 128.6, 127.9 (2 C), 126.3, 123.8, 31.0. IR $\nu_{\max}$ (KBr): 2925, 1720, 1686, 1577, 1241, 810, 776 cm^{-1} . Anal. Calcd. for $\text{C}_{18}\text{H}_{13}\text{NO}_3$: C, 74.22; H, 4.50; N, 4.81. Found: C, 74.25; H, 4.51, N, 4.77.

7.9181
7.9143
7.8917
7.8879
7.7260
7.7197
7.6996
7.6946
7.3456
7.3419
7.3205
7.3168
7.2954
7.2904
7.0908
7.0845
7.0657
7.0582
7.0393
7.0331

4.3592
4.3354
4.3115
4.2877

1.3577
1.3339
1.3100

^1H NMR (300 MHz, CDCl_3)

^1H NMR (300 MHz, CDCl_3)

NOESY : 21% of (*aR*,3*R*,13*bS*)-**1a** and 79% of (*aS*,3*R*,13*bR*)-**1a**.

See next page for zoom of marked region.

Zoom of NOESY : 21% of (*aR*,3*R*,13*bS*)-**1a** and 79% of (*aS*,3*R*,13*bR*)-**1a**.

^1H NMR (300 MHz, CDCl_3)