SUPPLEMENTARY INFORMATION

Rhodium-Catalyzed Addition of Arylboronic Acids to Isatins: An Entry to Diversity in 3-Aryl-3-Hydroxyoxindoles

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General remarks:

All air- and moisture-sensitive manipulations were carried out under a dry nitrogen atmosphere using standard Schlenk techniques. 1,4-Dioxane was distilled from sodium before use. ^1H -NMR, and ^{13}C -NMR spectra were recorded on a Varian 300 (300 and 75 MHz) in CDCl_3 . Chemical shifts (δ) are quoted in ppm using residual solvent as internal standard (δ_{C} 77.0 and δ_{H} 7.26 for CDCl_3). Mass spectra (HRMS) were recorded on an AEI MS-902. Optical rotations were measured on a Schmidt and Haensch Polartronic MH8. $\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2$ was purchased from Strem and used without further purification. All other chemicals were purchased from Acros or Aldrich and used as received. Flash chromatography was performed using silica gel 60 Å (Merck, 230-400 mesh). Ligand **L** was prepared according to a literature procedure.¹

Catalytic Addition Reactions:

General Procedure for Table 1

In a flame dried Schlenk tube flushed with nitrogen, 1.55 mg (6.0 μmol , 3 mol%) of $\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2$ and 3.7 μL (14.0 μmol , 7 mol%) of triphenylphosphite were dissolved in 2 mL of acetone. After stirring for 5 min at room temperature, 0.2 mmol of substrate **1** and 0.4 mmol of arylboronic acid **2** were added and the resulting mixture was stirred at reflux temperature. After 4 h the reaction mixture was cooled to RT and the solvent evaporated under reduced pressure. Products **3** were purified by column chromatography using eluent conditions reported for TLC.

Table 1, entry 1: 3-Phenyl-3-hydroxyoxindole **3a**

Yield: 91%. TLC conditions: (CH_2Cl_2 /ethyl acetate: 80/20) R_f = 0.24. ^1H NMR (DMSO-d_6) δ = 10.26 (s, 1H), 7.19-7.08 (m, 6H), 6.96 (d, J = 7.0 Hz, 1H), 6.81 (dt, J = 7.7 Hz, J = 0.7 Hz, 1H), 6.76 (d, J = 7.7 Hz, 1H), 6.48 (s, 1H); ^{13}C NMR (DMSO-d_6) δ = 178.44, 141.92, 141.52, 133.72, 129.20, 128.04, 127.38, 125.39, 124.75, 122.01, 109.8, 77.28. HRMS calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_2$: m/z 225.0790, found: 225.0795. Anal. calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_2$: 74.6 (C), 4.93 (H), 6.22 (N), found: 74.6 (C), 5.01 (H), 6.28 (N). Spectral and physical data are in accordance with literature.²

Table 1, entry 2: 5-Methyl-3-phenyl-3-hydroxyoxindole **3b**

Yield: 79%. mp 212.0°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) *R_f* = 0.29. ¹H NMR (DMSO-d₆) δ = 10.15 (s, 1H), 7.19-7.10 (m, 5H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.76 (s, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 6.42 (d, *J* = 1.5 Hz, 1H), 2.06 (s, 3H); ¹³C NMR (DMSO-d₆) δ = 178.51, 141.67, 139.41, 133.86, 130.87, 129.37, 128.04, 127.31, 125.34, 125.26, 109.58, 77.41, 20.60. HRMS calcd for C₁₅H₁₃NO₂: *m/z* 239.0946, found: 239.0952. Anal. calcd for C₁₅H₁₃NO₂: 75.3 (C), 5.48 (H), 5.86 (N), found: 75.0 (C), 5.65 (H), 5.56 (N). Spectral and physical data are in accordance with literature.²

Table 1, entry 3: 5-Chloro-3-phenyl-3-hydroxyoxindole **3c**

Yield: 99%. mp 240.4°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) *R_f* = 0.30. ¹H NMR (DMSO-d₆) δ = 10.41 (s, 1H), 7.22-7.12 (m, 5H), 6.96 (d, *J* = 2.2 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.64 (s, 1H), 2.52 (s, 6H); ¹³C NMR (DMSO-d₆) δ = 178.06, 140.80, 135.69, 130.26, 129.10, 128.22, 127.66, 125.96, 125.29, 124.68, 111.46, 77.34; HRMS calcd for C₁₄H₁₀NO₂³⁷Cl: *m/z* 259.0399, found: 259.0397.

Table 1, entry 4: 3-(4'-Methylphenyl)-3-hydroxyoxindole **3d**

Yield: 99%. mp 209.0°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) *R_f* = 0.27. ¹H NMR (DMSO-d₆) δ = 10.28 (s, 1H), 7.17 (dt, *J* = 7.7 Hz, *J* = 1.1 Hz, 1H), 7.10-7.00 (m, 4H), 6.89 (dt, *J* = 7.7 Hz, *J* = 1.1 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.46 (s, 1H), 2.19 (s, 3H); ¹³C NMR (DMSO-d₆) δ = 178.54, 141.89, 138.58, 136.54, 133.81, 129.12, 128.57, 125.35, 124.72, 121.96, 109.77, 77.13, 20.63; HRMS calcd for C₁₅H₁₃NO₂: *m/z* 239.0946, found: 239.0961.

Table 1, entry 5: 3-(3',5'-Dimethylphenyl)-3-hydroxyoxindole **3e**

Yield: 99%. mp 234.1°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) *R_f* = 0.39. ¹H NMR (DMSO-d₆) δ = 10.20 (s, 1H), 7.09 (dt, *J* = 7.7 Hz, *J* = 1.5 Hz, 1H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.75-6.71 (m, 4H), 6.37 (s, 1H), 2.07 (s, 6H); ¹³C NMR (DMSO-d₆) δ = 178.51, 141.89, 141.46, 136.94, 133.94, 129.10, 128.78, 124.68, 123.01, 121.96, 109.76, 77.19, 21.04; HRMS calcd for C₁₆H₁₅NO₂: *m/z* 253.11027, found: 253.1117.

Table 1, entry 6: 3-(2'-Methylphenyl)-3-hydroxyoxindole **3f**

Yield: 99%. mp 229.7°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) . R_f = 0.33. ¹H NMR (DMSO-d₆) δ = 10.40 (s, 1H), 7.73 (dt, J = 7.7 Hz, J = 1.1 Hz, 1H), 7.14 (t, J = 7.3 Hz, 1H), 7.10 (dt, J = 7.7 Hz, J = 0.7 Hz, 1H), 7.05 (dt, J = 7.3 Hz, J = 1.5 Hz, 1H), 6.90 (d, J = 7.3 Hz, 1H), 6.77 (d, J = 7.0 Hz, 1H), 6.75 (d, J = 7.7 Hz, 1H), 6.68 (d, J = 7.0 Hz, 1H), 6.45 (s, 1H), 1.65 (s, 3H); ¹³C NMR (DMSO-d₆) δ = 177.74, 142.53, 139.16, 134.28, 132.31, 130.86, 129.36, 127.42, 126.55, 125.39, 124.31, 121.96, 109.69, 76.61, 18.76; HRMS calcd for C₁₅H₁₃NO₂: m/z 239.0946, found: 239.0961.

Table 1, entry 7; 3-(4'-Methoxyphenyl)-3-hydroxyoxindole **3g**

Yield: 98%. mp 219.9°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 70/30) R_f = 0.39. ¹H NMR (DMSO-d₆) δ = 10.18 (s, 1H), 7.10 (t, J = 7.7 Hz, 1H), 7.06-7.02 (m, J = 8.8 Hz, 2H), 6.96 (d, J = 7.3 Hz, 1H), 6.32 (d, J = 7.3 Hz, 1H), 6.75-6.70 (m, 3H), 6.37 (s, 1H), 3.57 (s, 3H); ¹³C NMR (DMSO-d₆) δ = 178.62, 158.64, 141.86, 133.72, 133.45, 129.11, 126.79, 124.77, 121.95, 113.44, 109.77, 76.87, 55.08; HRMS calcd for C₁₅H₁₃NO₃: m/z 225.0895, found: 255.0885.

Table 1, entry 8: 3-Naphthyl-3-hydroxyoxindole **3h**

Yield: 87%. mp 223.2°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) R_f = 0.42. ¹H NMR (DMSO-d₆) δ = 10.34 (s, 1H), 7.77-7.71 (m, 3H), 7.69 (d, J = 7.7 Hz, 1H), 7.37 (s, 1H), 7.35 (d, J = 4.8 Hz, 1H), 7.18 (d, J = 9.9 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 6.99 (d, J = 7.0 Hz, 1H), 6.83 (t, J = 7.7 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 6.64 (s, 1H); ¹³C NMR (DMSO-d₆) δ = 178.38, 142.01, 139.01, 133.69, 132.53, 132.30, 129.35, 127.97, 127.76, 127.41, 126.27, 126.06, 124.83, 123.88, 123.75, 122.12, 109.95, 77.45; HRMS calcd for C₁₈H₁₃NO₂: m/z 275.0946, found: 275.0974.

Table 1, entry 9: 3-(3'-Nitrophenyl)-3-hydroxyoxindole **3i**

Yield: 66%. mp 205.3°C (dec). TLC conditions: (CH₂Cl₂/ethyl acetate: 80/20) R_f = 0.47. ¹H NMR (DMSO-d₆) δ = 10.52 (s, 1H), 8.13 (s, 1H), 8.10 (d, J = 7.7 Hz, 1H), 7.57 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 8.1 Hz, 1H), 7.25 (t, J = 7.7 Hz, 1H), 7.09 (d, J = 7.3 Hz, 1H), 6.98 (s, 1H), 6.95 (t, J = 7.3 Hz, 1H), 6.90 (d, J = 7.7 Hz, 1H); ¹³C NMR (DMSO-d₆) δ = 177.48, 147.73, 143.70, 142.04, 132.52, 132.19, 129.99, 129.88, 124.88, 122.64, 122.45, 120.12, 110.24, 76.84; HRMS calcd for C₁₄H₁₀N₂O₄: m/z 270.0640, found: 270.0648. Anal. calcd for C₁₄H₁₀O₄N₂: 62.2 (C), 3.73 (H), 10.37 (N), found: 61.8 (C), 3.96 (H), 9.88 (N).

Table 1, entry 10: 5-Chloro-3-(4'-carbethoxyphenyl)-3-hydroxyoxindole **3j**

Table 1, entry 11: 3-(2'-Fluorophenyl)-3-hydroxyoxindole **3k**

Table 1, entry 12: 3-Thienyl-3-hydroxyoxindole **3l**

Table 1, entry 13: 3-(β-Styryl)-3-hydroxyoxindole **3m**

Enantioselective Catalytic Addition Reaction

In a flame dried Schlenk tube flushed with nitrogen, 1.55 mg (6.0 μmol , 3 mol%) of $\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2$ and 8.0 mg (18.0 μmol , 9 mol%) of **L** were dissolved in 2 mL of dioxane. After stirring for 5 min at room temperature, 0.2 mmol of substrate **1a** and 0.4 mmol of arylboronic acid **2a** were added and the resulting mixture was stirred at 40°C. After 4 h the reaction mixture was cooled to RT and the solvent evaporated under reduced pressure. Product **3a** was purified by column chromatography using eluent conditions reported for TLC (*vide supra*). Yield: 99%. The ee was determined on a Chiralcel OD-H column with heptane : isopropanol = 90 : 10, flow = 0.5 mL/min. Retention times: 25.5 and 29.5 min. 55% ee. $[\alpha]_{\text{D}} = +16.5$ ($c = 1.06$, MeOH). Literature value for (R)-**3a**: $[\alpha]_{\text{D}} = -12.3$ ($c = 0.91$, MeOH).² After recrystallisation from 2-propanol the supernatant gave the enantioenriched product in 59% isolated yield and 94% ee.

References

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