Supporting Information

Formation of C-O bond via cross-dehydrogenative coupling (CDC) under metal-free oxidation condition between isochroman and oxime

Hua-Feng He, Kai Wang, Bo Xing, Guorong Sheng, Tingxuan Ma and Weiliang Bao*
*Department of Chemistry, Xi Xi Campus, Zhejiang University, Hangzhou, Zhejiang 310028, P. R. China, Fax: (+86)-571-88273814; E-mail: wlbao@css.zju.edu.cn

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(I) General Information

All the starting materials were commercially available. DMF were distilled from 4Å molecular sieves under reduced pressure; THF and toluene were distilled from sodium. The Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel plates (GF 254), visualized with a UV254 lamp. Column chromatography was performed on silica gel 60 (200-300 mesh) with petrol and ethyl acetate as eluents. All products were confirmed by 1H NMR, 13C NMR, MS and IR. Unknown compounds were additionally confirmed by High resolution mass spectrometry (HRMS). NMR spectra were recorded for 1H NMR at 400 MHz and for 13C NMR at 100 MHz. Chemical shifts (δ, ppm) were determined with TMS as internal standard. Coupling constants are reported in Hertz (Hz). Mass spectra were obtained using EI ionization. Melting points were uncorrected.

(II) General Experimental Procedures for the Synthesis of Starting Material

A) Synthesis of isochroman [1]
To a 250ml round bottom flasks, add 25.5g formaldehyde solution, 5.88g (3.2ml, 59.9mmol) concentrated sulfuric acid and 20.0g (163.7mmol) benzyl ethanol orderly. Stirred at 65°C for 12h, and then heated to 95°C in 3h and keep reflux for 10h. The reaction was monitored by TLC. After the reaction finished, cooled to room temperature, extracted by EtOAc, washed with brine, dried by Na2SO4, and then remove the solvent under vacuum. The isochroman was collected under reduced pressure distillation.

B) Synthesis of oximes [2]
30ml ethanol was added into a 100ml round bottom flasks, then added aldehyde 10mmol and 10mmol hydroxylamine hydrochloride. 20ml 1N sodium acetate solution was dropped slowly by funnel. The reaction was detected by TLC. After finished, removed the solvent and filtrated. Washed the white solid with water and dried under vacuum. The solid could be purified by column
(III) Representative Procedures for the Synthesis of product 3a-3p

120mg (0.6mmol) DDQ was added to an oven-dired Schlenk tube charged with a magnetic stir bar. Equipped with a constant pressure funnel, the Schlenk tube was evacuated and backfilled with N2 for 3 times. Then 1ml DCM was added as solvent. 2ml DCM solution of 0.5mmol isochroman and 0.5mmol oxime was added into the funnel through syringe, and dropped into the Schlenk tube in 2h. The reaction was conducted at 30°C for 24h, monitored by TLC. After finished, the reaction was filtrated and washed with EtOAc. Then removed the solvent, the crude was purified through column chromatography, PE: EtOAc= 30:1~ 40:1 as the eluent. The product was obtained as colorless oil.

(IV) Characterization of the Products

![Compound 3a](image)

**Compound 3a;** Colorless oil; Yield: 85%; IR (neat) ν 2939, 1740, 1492, 1316, 1208, 1096, 928, 748cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.15 (s, 1H), 7.58 (d, J = 8.0Hz, 2H), 7.34 (d, J = 8.0Hz, 3H), 7.31-7.25 (m, 2H), 7.17 (d, J = 8.0Hz, 1H), 6.36 (s, 1H), 4.18 (td, J₁ = 11.8Hz, J₂ = 3.2Hz, 1H), 4.03-3.98 (m, 1H), 3.12-3.03 (m, 1H), 2.65 (dd, J₁ = 16.4Hz, J₂ = 2.0Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 150.64, 134.82, 131.81, 131.74, 130.09, 128.58, 128.48, 127.87, 127.35, 126.34, 99.10, 58.36, 27.75. HRMS (EI): [M]⁺ calculated for C₁₆H₁₅NO₂: 253.1103, Found: 253.1105.

![Compound 3b](image)

**Compound 3b;** Colorless oil; Yield: 93%; IR (neat) ν 2933, 1608, 1456, 1315, 1206, 1056, 927, 747cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.17 (s, 1H), 7.55 (d, J = 8.0Hz, 2H), 7.36 (dd, J₁ = 8.0Hz, J₂ = 0.8Hz, 1H), 7.31-7.24 (m, 2H), 7.20-7.17 (m, 3H), 6.36 (s, 1H), 4.20 (td, J₁ = 11.8Hz, J₂ = 3.6Hz, 1H), 4.03-3.98 (m, 1H), 3.13-3.04 (m, 1H), 2.66 (dd, J₁ = 16.8Hz, J₂ = 2.0Hz, 1H), 2.37 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 150.73, 134.82, 131.81, 131.74, 130.09, 128.58, 128.48, 127.87, 127.35, 126.34, 99.10, 58.38, 27.75. HRMS (EI): [M]⁺ calculated for C₁₇H₁₇NO₂: 267.1259, Found: 267.1257.
Compound 3c; Colorless oil; Yield: 66%; IR (neat) ν 2936, 1740, 1512, 1250, 1094, 925, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.16 (s, 1H), 7.60 (d, J = 8.0Hz, 2H), 7.36 (d, J = 8.0Hz, 1H), 7.31-7.24 (m, 2H), 7.17 (d, J = 8.0Hz, 1H), 6.90 (d, J = 8.0Hz, 2H), 6.35 (s, 1H), 4.20 (td, J₁ = 12.0Hz, J₂ = 3.2Hz, 1H), 4.03-3.99 (m, 1H), 3.82 (s, 3H), 3.12-3.04 (m, 1H), 2.65 (d, J = 16Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 161.12, 150.33, 134.82, 131.84, 128.89, 128.55, 128.49, 127.89, 126.33, 124.38, 114.04, 98.91, 58.29, 55.25, 27.77. HRMS (EI): [M]⁺ calculated for C₁₇H₁₇NO₃: 283.1208, Found: 283.1205.

Compound 3d; Yellow oil; Yield: 82%; IR (neat) ν 2939, 1712, 1490, 1318, 1206, 1093, 929, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (s, 1H), 7.66-7.64 (m, 2H), 7.38-7.34 (m, 4H), 7.31-7.23 (m, 2H), 7.16 (d, J = 6.8Hz, 1H), 6.38 (s, 1H), 4.20 (td, J₁ = 11.8Hz, J₂ = 3.0Hz, 1H), 4.02-3.98 (m, 1H), 3.12-3.03 (m, 1H), 2.64 (dd, J₁ = 16.4Hz, J₂ = 2.0Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.40, 135.95, 134.81, 131.54, 130.35, 128.87, 128.64, 128.52, 127.85, 126.35, 99.22, 58.42, 27.72. HRMS (EI): [M]⁺ calculated for C₁₆H₁₄ClNO₂: 287.0713, Found: 287.0711.

Compound 3e; Yellow oil; Yield: 85%; IR (neat) ν 2937, 1710, 1488, 1318, 1096, 1068, 928, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.13 (s, 1H), 7.52-7.48 (m, 4H), 7.35-7.23 (m, 3H), 7.16 (d, J = 8.0Hz, 1H), 6.36 (s, 1H), 4.17 (td, J₁ = 11.8Hz, J₂ = 3.0Hz, 1H), 4.02-3.98 (m, 1H), 3.11-3.02 (m, 1H), 2.64 (dd, J₁ = 16.4Hz, J₂ = 2.0Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.44, 134.76, 131.77, 131.46, 130.72, 128.70, 128.61, 128.46, 127.81, 126.31, 124.26, 99.18, 58.37, 27.66. HRMS (EI): [M]⁺ calculated for C₁₆H₁₄BrNO₂: 331.0208, Found: 331.0206.
Compound 3f; Yellow oil; Yield: 92%; IR (neat) ν 2937, 1710, 1559, 1317, 1205, 1096, 931, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.12 (s, 1H), 7.85 (t, J = 1.6 Hz, 1H), 7.54-7.48 (m, 2H), 7.33 (td, J₁ = 6.2 Hz, J₂ = 2.0 Hz, 1H), 7.30-7.21 (m, 3H), 7.17 (d, J = 8.0 Hz, 1H), 6.36 (s, 1H), 4.17 (td, J₁ = 11.7 Hz, J₂ = 3.2 Hz, 1H), 4.03-3.98 (m, 1H), 3.12-3.03 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.09, 134.79, 133.85, 132.94, 131.43, 130.09, 129.86, 128.67, 128.50, 127.84, 126.36, 126.07, 122.76, 99.29, 58.42, 27.68. HRMS (EI): [M]⁺ calculated for C₁₆H₁₄BrNO₂: 331.0208, Found: 331.0207.

Compound 3g; Yellow oil; Yield: 74%; IR (neat) ν 2938, 1711, 1430, 1317, 1097, 996, 930, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.62 (s, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.32-7.26 (m, 3H), 7.24-7.17 (m, 2H), 6.39 (s, 1H), 4.21 (td, J₁ = 11.6 Hz, J₂ = 3.1 Hz, 1H), 4.04-4.00 (m, 1H), 3.13-3.04 (m, 1H), 2.65 (d, J = 16.0 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.96, 134.76, 132.98, 131.39, 131.30, 131.06, 128.67, 128.50, 127.83, 127.77, 127.43, 126.36, 123.99, 99.27, 58.40, 27.66. HRMS (EI): [M]⁺ calculated for C₁₆H₁₄BrNO₂: 331.0208, Found: 331.0209.

Compound 3h; White solid; Yield: 57%; Melting point: 127~129°C; IR (neat) ν 3370, 2938, 1704, 1959, 1515, 1342, 1096, 934, 749 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.26-8.23 (m, 3H), 7.83 (d, J = 8.0 Hz, 2H), 7.36-7.28 (m, 3H), 7.20 (d, J = 8.0 Hz, 1H), 6.41 (s, 1H), 4.19 (td, J₁ = 11.8 Hz, J₂ = 2.8 Hz, 1H), 4.06-4.02 (m, 1H), 3.14-3.06 (m, 1H), 2.68 (dd, J₁ = 16.6 Hz, J₂ = 1.4 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 148.48, 148.37, 137.98, 134.83, 131.10, 128.85, 128.58, 127.96, 127.83, 126.44, 123.90, 99.72, 58.63, 27.66. HRMS (EI): [M]⁺ calculated for C₁₆H₁₄N₂O₄: 298.0954, Found: 298.0958.
Compound 3i; Blue oil; Yield: 77%; IR (neat) v 2935, 1711, 1493, 1274, 1095, 984, 922, 746 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.74-7.72 (m, 2H), 7.37-7.35 (m, 4H), 7.30-7.23 (m, 2H), 7.17 (d, \(J = 8.0\) Hz, 1H), 6.40 (s, 1H), 4.18 (td, \(J_1 = 11.7\)Hz, \(J_2 = 3.5\)Hz, 1H), 4.02-3.98 (m, 1H), 3.11-3.03 (m, 1H), 2.65 (d, \(J = 16.0\)Hz, 1H), 2.25 (s, 3H); \(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 156.48, 136.22, 134.86, 132.23, 129.21, 128.36, 128.25, 128.03, 126.27, 126.18, 98.98, 58.43, 27.85, 13.20. HRMS (EI): [M]\(^+\) calculated for C\(_{17}\)H\(_{17}\)NO\(_2\): 267.1259, Found: 267.1257.

Compound 3j; White solid; Yield: 56%; IR (neat) v 2881, 1657, 1562, 1449, 1275, 1088, 958, 739, 697 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.55 (d, \(J = 8.0\)Hz, 2H), 7.39-7.29 (m, 9H), 7.23-7.31 (m, 2H), 7.11 (d, \(J = 8.0\)Hz, 1H), 6.42 (s, 1H), 4.03-4.00 (m, 2H), 3.08-2.99 (m, 1H), 2.57 (d, \(J = 16.0\)Hz, 1H); \(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 158.56, 136.35, 134.88, 133.41, 132.07, 129.48, 129.14, 128.62, 128.29, 128.23, 128.14, 128.09, 127.92, 126.15, 99.60, 58.75, 27.87. HRMS (EI): [M]\(^+\) calculated for C\(_{22}\)H\(_{19}\)NO\(_2\): 329.1416, Found: 329.1413.

Compound 3k; Colorless oil; Yield: 51%; IR (neat) v 2932, 1608, 1457, 1326, 1271, 1093, 922, 747 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.32-7.22 (m, 3H), 7.16 (d, \(J = 7.2\)Hz, 1H), 6.22 (s, 1H), 4.14 (td, \(J_1 = 11.4\)Hz, \(J_2 = 1.4\)Hz, 1H), 4.00-3.96 (m, 1H), 3.10-3.01 (m, 1H), 2.64 (d, \(J = 16.0\)Hz, 1H), 1.97 (s, 3H), 1.89 (s, 3H); \(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 157.19, 134.87, 132.35, 128.39, 128.30, 127.98, 126.16, 98.26, 58.26, 27.88, 22.11, 16.13. HRMS (EI): [M]\(^+\) calculated for C\(_{12}\)H\(_{15}\)NO\(_2\): 205.1103, Found: 205.1101.

Compound 3l; White solid; Yield: 62%; Melting point: 110-112°C; IR (neat) v 2923, 1727, 1459,
1372, 1294, 1117, 966, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.87-7.84 (m, 2H), 7.77-7.74 (m, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.37-7.31 (m, 2H), 7.20 (d, J = 8.0 Hz, 1H), 6.19 (s, 1H), 4.70 (td, J₁ = 12.4 Hz, J₂ = 2.5 Hz, 1H), 4.05-4.00 (m, 1H), 3.14-3.05 (m, 1H), 2.72 (dd, J₁ = 16.2 Hz, J₂ = 2.6 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 163.82, 134.78, 134.30, 129.50, 129.24, 129.08, 128.66, 128.40, 126.53, 123.41, 102.07, 59.52, 27.38. HRMS (EI): [M]⁺ calculated for C₁₇H₁₃NO₄: 295.0845, Found: 295.0844.

Compound 3m; Colorless oil; Yield: 35%; IR (neat) ν 2937, 1619, 1477, 1330, 1097, 1001, 919, 745 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (s, 1H), 7.44 (s, 1H), 7.38-7.27 (m, 3H), 7.23-7.19 (m, 1H), 6.41 (t, J = 1.2 Hz, 1H), 4.13 (td, J₁ = 11.7 Hz, J₂ = 3.2 Hz, 1H), 4.03-3.99 (m, 1H), 3.15-3.06 (m, 1H), 2.67 (d, J = 16.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 144.58, 142.88, 137.27, 134.39, 131.06, 128.04, 127.91, 127.46, 125.80, 117.76, 111.70, 98.95, 58.14, 27.26. HRMS (EI): [M]⁺ calculated for C₁₄H₁₃NO₃: 243.0895, Found: 243.0892.

Compound 3m'; Colorless oil; Yield: 29%; IR (neat) ν 2937, 1622, 1483, 1311, 1272, 1096, 921, 744 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (s, 1H), 7.51 (s, 1H), 7.35-7.24 (m, 3H), 7.18 (d, J = 7.2 Hz, 1H), 6.70 (d, J = 3.2 Hz, 1H) 6.48 (t, J = 1.6 Hz, 1H), 6.37 (s, 1H), 4.18 (td, J₁ = 11.7 Hz, J₂ = 3.2 Hz, 1H), 4.03-3.99 (m, 1H), 3.13-3.04 (m, 1H), 2.66 (d, J = 16.4 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 146.26, 143.91, 140.30, 134.30, 130.96, 128.14, 127.98, 127.35, 125.84, 112.86, 111.11, 98.77, 57.82, 24.15. HRMS (EI): [M]⁺ calculated for C₁₄H₁₃NO₃: 243.0895, Found: 243.0892.

Compound 3n; Yellow oil; Yield: 59%; IR (neat) ν 2930, 1607, 1511, 1304, 1105, 982, 913, 813 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (s, 1H), 7.95 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.2 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.57-7.49 (m, 4H), 7.43 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 6.47 (s, 1H), 4.34 (td, J₁ = 11.6 Hz, J₂ = 3.6 Hz, 1H), 4.21-4.17 (m, 1H), 3.26-3.20 (m, 1H), 3.08 (dd, J₁ = 16.8 Hz, J₂ = 2.8 Hz, 1H), 2.36 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 150.79, 140.38, 133.24, 131.38, 131.14, 129.36, 128.98, 128.82, 128.56, 127.36, 126.66, 126.35, 126.29, 125.07, 123.04, 99.24, 58.13, 24.49, 21.46. HRMS (EI): [M]⁺ calculated for C₂₁H₁₃NO₃: 317.1416, Found: 317.1415.
Compound 3o; Yellow oil; Yield: 49%; IR (neat) \(\nu\) 2921, 1705, 1606, 1440, 1244, 1009, 922, 758 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.93 (s, 1H), 7.87-7.84 (m, 2H), 7.50-7.44 (m, 4H), 7.38 (t, \(J = 7.2\) Hz, 1H), 7.26 (t, \(J = 8.0\) Hz, 1H), 7.16-7.10 (m, 4H), 6.84 (s, 1H), 2.34 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 151.33, 150.58, 140.56, 130.02, 129.51, 129.37, 129.26, 128.72, 127.86, 127.74, 127.37, 127.17, 122.84, 122.33, 121.89, 121.06, 118.40, 99.67, 21.45. HRMS (EI): [M] \(^+\) calculated for C\(_{21}\)H\(_{17}\)NO\(_2\): 315.1259, Found: 315.1260.

Compound 3p; Yellow solid; Yield: 44%; IR (neat) \(\nu\) 2971, 1700, 1590, 1486, 1244, 1005, 918, 750 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.92 (s, 1H), 7.88 (t, \(J = 6.8\) Hz, 2H), 7.55-7.41 (m, 7H), 7.28 (t, \(J = 8.0\) Hz, 1H), 7.14-7.11 (m, 2H), 6.84 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 150.41, 150.13, 132.36, 131.87, 130.90, 130.45, 130.10, 129.53, 129.22, 128.76, 127.88, 127.45, 127.15, 124.52, 122.82, 122.40, 121.89, 120.94, 118.31, 99.80. HRMS (EI): [M] \(^+\) calculated for C\(_{20}\)H\(_{14}\)BrNO\(_2\): 379.0208, Found: 379.0206.

(V) Reference


(VI) \(^1\)H and \(^{13}\)C NMR Spectra