Supporting Materials

DDQ-Mediated Direct Cross-Dehydrogenative-Coupling (CDC) between Benzyl Ethers and Simple Ketones

Yuhua Zhang¹ and Chao-Jun Li^{1,2*}

¹ *Department of Chemistry, Tulane University, New Orleans, Louisiana 70118, and* ² *Department of Chemistry, McGill University, 801 Sherbrooke St. West, Montreal, Quebec H3A 2K6, Canada*

Email: cj.li@mcgill.ca

Contents

- 1) Experimental details and characterization data for all new compounds;
- 2) PDF file of copies of ¹H NMR and ¹³C NMR spectra for all new compounds.

1) Experimental details and characterization data for all new compounds

General information: ^1H NMR spectra were recorded on 400 MHz spectrometer in CDCl_3 solution and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublet; ddd, doublet of doublet of doublet; dddd, doublet of doublet of doublet of doublet; dq, doublet of quartet; m, multiplet; q, quartet. The coupling constants, J , are reported in Hertz (Hz). ^{13}C NMR spectra were obtained at 75 MHz and referenced to the internal solvent signals (central peak is 77.00 ppm). MS data were obtained by Agilent 6890N Network GC System/Agilent 5973 Mass Selective Detector. HRMS were made by McGill University. IR spectra were recorded by an ABB Bomem MB100 instrument. Flash column chromatography was performed over SORBENT silica gel 30-60 μm . Thin layer chromatography was performed using Sorbent Silica Gel 60 F_{254} TLC plates and visualized with ultraviolet light. All reagents were weighed and handled in air, and backfilled under an inert atmosphere of nitrogen at room temperature. All reagents were purchased from Aldrich and Acros and used without further purification. 3-Methylisochroman (**2a**) was prepared by the literature method.^[1]

General procedure: To a mixture of DDQ (56 mg, 0.24 mmol) and acetophenone (71 μL , 0.6 mmol), isochroman (27mg, 0.2 mmol) was added dropwise under nitrogen at room temperature. Then the reaction mixture was stirred at 100°C immediately. During this course, it was readily noticeable that DDQ was dissolved and the reaction mixture became a liquid very soon; and then, white solids appeared in several minutes. After 2hrs, the resulting mixture was diluted with diethyl ether and filtered through a short silica gel in a pipette eluting with diethyl ether. The solvent was evaporated and the residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 5:1); and the fraction with an R_f = 0.4 was collected and concentrated to give the desired product **1c**.

2-(Isochroman-1-yl)-1-phenylethanone (1c). CA Registry Number [100008-34-2]. Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (liquid): $\nu_{\max}$ 1685, 1596, 1580, 1493, 1449, 1427, 1399, 1366, 1340, 1282, 1202, 1181, 1160, 1107, 1073, 1039, 1022, 1013, 1001, 927 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 8.03-8.00(m, 2H), 7.59-7.55(m, 1H), 7.49-7.45(m, 2H), 7.22-7.18(m, 2H), 7.16-7.10(m, 2H), 5.51(dd, J = 8.4, 3.2 Hz, 1H), 4.12(ddd, J = 10.8, 5.6, 3.6 Hz, 1H), 3.82(ddd, J = 3.6, 9.6, 11.2 Hz, 1H), 3.63(dd, J = 8.8, 16.6 Hz, 1H), 3.33(dd, J = 3.6, 16 Hz, 1H), 3.03(ddd, J = 5.6, 9.6, 15.6 Hz, 1H), 2.73(ddd, J = 3.6, 3.6, 16.4 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 198.3, 137.8, 137.4, 134.3, 133.4, 129.3, 128.8, 128.6, 126.8, 126.5, 124.8, 73.0, 63.8, 45.9, 29.3; MS (EI) m/z (%) 252, 175, 146, 133(100), 120, 105, 91, 77.

2-(Isochroman-1-yl)-1-phenylpropan-1-one (2c). CA Registry Number [100008-35-3]. The ratio of the two diastereoisomers is 1:1. Isolated by flash column chromatography (hexane/ethyl acetate = 4:1, R_f = 0.5). IR (liquid) of the mixture: $\nu_{\max}$: 1722, 1685, 1596, 1579, 1492, 1449, 1426, 1373, 1350, 1282, 1242, 1220, 1160, 1132, 1114, 1100, 1093, 1074 cm^{-1} ; ^1H NMR (400 MHz, ppm) of the mixture δ 8.00-7.97(m, 2H), 7.95-7.92(m, 2H), 7.58-7.41(m, 6H), 7.21-7.02(m, 8H), 5.30(d, J = 3.6 Hz, 1H), 5.24(d, J = 5.2 Hz, 1H), 4.15-4.10(m, 2H), 4.07-3.96(m, 2H), 3.69-3.57(m, 2H), 3.06-2.89(m, 2H), 2.67-2.57(m, 2H), 1.23(d, J = 6.8 Hz, 3H), 1.12(d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, ppm) of the mixture δ 202.7, 201.9, 137.5, 137.0, 136.4, 135.7, 135.2, 135.1, 132.9(two peaks), 129.3, 129.0, 128.9, 128.7,

128.5(two peaks), 126.8, 126.7, 126.6, 126.1(two peaks), 124.7, 77.8, 76.9, 64.3, 63.7, 47.7, 47.2, 29.7, 29.3, 14.1, 10.4; MS (EI) m/z (%) 266, 251, 133(100), 105, 91, 77.

2-(Isochroman-1-yl)-1-p-tolyloethanone (3c). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (liquid): $\nu_{\max}$ 1682, 1606, 1572, 1492, 1452, 1426, 1406, 1365, 1283, 1199, 1181, 1107, 1038, 1014, 982, 843 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.92(d, J = 8.4 Hz, 2H), 7.27(d, J = 8.4 Hz, 2H), 7.21-7.10(m, 4H), 5.50(dd, J = 3.2, 8.8 Hz, 1H), 4.12(ddd, J = 4.4, 4.4, 10.8 Hz, 1H), 3.82(ddd, J = 3.6, 9.2, 10.4 Hz, 1H), 3.60(dd, J = 8.4, 16 Hz, 1H), 3.31(dd, J = 3.6, 16 Hz, 1H), 3.03(ddd, J = 5.2, 9.6, 16.4 Hz, 1H), 2.73(ddd, J = 3.6, 3.6, 16.4 Hz, 1H), 2.43(s, 3H); ^{13}C NMR (75 MHz, ppm) δ 197.9, 144.2, 137.9, 135.0, 134.2, 129.5, 129.3, 128.7, 126.8, 126.5, 124.8, 73.1, 63.8, 45.8, 29.3, 22.1; MS (EI) m/z (%) 266, 249, 175, 146, 133(100), 119, 105, 91, 77; HRMS calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: 266.1307; found: 266.1310.

1-(4-Bromophenyl)-2-(isochroman-1-yl)ethanone (4c). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (KBr): $\nu_{\max}$ 1685, 1583, 1497, 1397, 1367, 1283, 1196, 1174, 1106, 1068, 1016, 990, 847, 807 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.87(d, J = 8.4 Hz, 2H), 7.60(d, J = 8.8 Hz, 2H), 7.21-7.18(m, 2H), 7.16-7.08(m, 2H), 5.47(dd, J = 2.8, 8.4 Hz, 1H), 4.11(ddd, J = 3.6, 5.2, 11.2 Hz, 1H), 3.80(ddd, J = 3.6, 10, 11.2 Hz, 1H), 3.57(dd, J = 8.8, 16 Hz, 1H), 3.28(dd, J = 3.2, 16 Hz, 1H), 3.03(ddd, J = 5.6, 10, 15.6 Hz, 1H), 2.71(ddd, J = 3.2, 3.2, 16.4 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 197.4, 137.5, 136.2, 134.2, 132.1, 130.1, 129.3, 128.6, 126.9, 126.6, 124.7, 73.1, 63.9, 45.8, 29.3; MS (EI)

m/z (%) 330, 251, 198, 183, 157, 146, 133(100), 105, 91, 77; HRMS calcd for $C_{17}H_{15}O_2Br$: 330.0255; found: 330.0259.

2-(Isochroman-1-yl)-1-(4-methoxyphenyl)ethanone (5c). Isolated by flash column chromatography (hexane/ethyl acetate = 2:1, R_f = 0.5). IR (liquid): $\nu_{\max}$ 1676, 1600, 1575, 1510, 1452, 1420, 1366, 1259, 1167, 1106, 1027, 986, 915, 846 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 8.00(d, J = 8.8 Hz, 2H), 7.20-7.17(m, 2H), 7.15-7.10(m, 2H), 6.94(d, J = 8.8 Hz, 2H), 5.49(dd, J = 3.6, 8.8 Hz, 1H), 4.12(ddd, J = 3.6, 5.6, 12.4 Hz, 1H), 3.87(s, 3H), 3.81(ddd, J = 3.6, 9.6, 11.2 Hz, 1H), 3.58(dd, J = 8.8, 15.6 Hz, 1H), 3.27(dd, J = 3.6, 16 Hz, 1H), 3.03(ddd, J = 5, 10, 15.6 Hz, 1H), 2.72(ddd, J = 3.6, 3.6, 15.6 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 196.7, 163.7, 138.0, 134.2, 130.9, 130.6, 129.3, 126.8, 126.5, 124.8, 114.0, 73.2, 63.8, 55.8, 45.5, 29.3; MS (EI) m/z (%) 282, 264, 253, 150, 146, 135(100), 133, 105, 92, 77; HRMS calcd for $C_{18}H_{18}O_3$: 282.1256; found: 282.1255.

1-(2-Bromophenyl)-2-(isochroman-1-yl)ethanone (6c). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (KBr): $\nu_{\max}$ 1699, 1587, 1491, 1465, 1427, 1339, 1286, 1200, 1106, 1023, 987, 961 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.59(dd, J = 1.2, 7.6 Hz, 1H), 7.48(dd, J = 1.6, 8 Hz, 1H), 7.37(ddd, J = 1.2, 7.2, 7.6 Hz, 1H), 7.28(ddd, J = 1.6, 7.2, 8 Hz, 1H), 7.19-7.16(m, 2H), 7.13-7.10(m, 2H), 5.35(dd, J = 4, 8.8 Hz, 1H), 4.09(ddd, J = 4, 5.6, 11.2 Hz, 1H), 3.78(ddd, J = 4, 9.2, 11.2 Hz, 1H), 3.50(dd, J = 4, 16 Hz, 1H), 3.44(dd, J = 9.2, 16 Hz, 1H), 2.97(ddd, J = 5.6, 8.8, 16.4 Hz, 1H), 2.71(ddd, J = 4, 4, 16 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 202.4, 141.9, 137.1, 134.1, 133.6, 131.8, 129.3(possibly

overlapped), 127.7, 126.9, 126.5, 124.8, 118.8, 73.2, 63.5, 49.8, 29.2; MS (EI) m/z (%) 330, 251, 183, 155, 146, 133(100), 105, 91, 77; HRMS calcd for $C_{17}H_{15}O_2Br$: 330.0255; found: 330.0260.

1-(2-Hydroxyphenyl)-2-(isochroman-1-yl)ethanone (7c). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (KBr): $\nu_{\max}$ 3246, 1639, 1614, 1579, 1488, 1446, 1374, 1304, 1255, 1197, 1156, 1106, 1035, 1013, 988 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 12.33(s, 1H), 7.79(dd, J = 1.6, 8Hz, 1H), 7.48(ddd, J = 1.6, 7.2, 8.6 Hz, 1H), 7.22-7.19(m, 2H), 7.17-7.10(m, 2H), 7.01(dd, J = 1.2, 8.4 Hz, 1H), 6.90(ddd, J = 1.2, 8.4, 8.4 Hz, 1H), 5.49(dd, J = 2.8, 9.2 Hz, 1H), 4.13(ddd, J = 4, 5.2, 11.2 Hz, 1H), 3.82(ddd, J = 4, 10, 11.8 Hz, 1H), 3.63(dd, J = 8.8, 16 Hz, 1H), 3.35(dd, J = 3.6, 16 Hz, 1H), 3.03(ddd, J = 5.6, 10, 15.6 Hz, 1H), 2.74(ddd, J = 3.6, 3.6, 16.4 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 204.2, 162.8, 137.3, 136.8, 134.3, 130.5, 129.4, 127.0, 126.6, 124.7, 120.1, 119.2, 118.8, 72.8, 63.8, 45.4, 29.3; MS (EI) m/z (%) 268, 250, 146, 133(100), 121, 105, 91, 77; HRMS calcd for $C_{17}H_{16}O_3$: 268.1099; found: 268.1104.

1-(Furan-2-yl)-2-(isochroman-1-yl)ethanone (8c). Isolated by flash column chromatography (hexane/ethyl acetate = 2:1, R_f = 0.5). IR (liquid): $\nu_{\max}$ 1676, 1567, 1492, 1467, 1426, 1393, 1340, 1292, 1242, 1161, 1106, 1027, 988, 883 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.59(s, 1H), 7.24(d, J = 3.2 Hz, 1H), 7.21-7.17(m, 2H), 7.15-7.09(m, 2H), 6.55-6.54(m, 1H), 5.45(dd, J = 3.2, 9.2 Hz, 1H), 4.11(ddd, J = 4.8, 4.8, 11.2 Hz, 1H), 3.80(ddd, J = 3.6, 9.2, 11.2 Hz, 1H), 3.45(dd, J = 9.6, 15.6 Hz, 1H), 3.20(dd, J = 3.2, 15.6 Hz, 1H),

3.00(ddd, $J = 5.2, 9.6, 16.2$ Hz, 1H), 2.72(ddd, $J = 4, 4, 16.4$ Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 187.1, 153.2, 146.8, 137.5, 134.2, 129.3, 126.9, 126.5, 124.8, 118.0, 112.6, 73.0, 63.6, 45.7, 29.2; MS (EI) m/z (%) 242, 173, 165, 153, 146, 139, 133(100), 110, 105, 95, 91, 77, 65; HRMS calcd for $\text{C}_{15}\text{H}_{14}\text{O}_3$: 242.0943; found: 242.0945.

1-Cyclohexenyl-2-(isochroman-1-yl)ethanone (9c). Isolated by flash column chromatography (hexane/ethyl ether = 5:1, $R_f = 0.5$). IR (liquid): ν_{max} 1721, 1664, 1635, 1492, 1452, 1428, 1379, 1342, 1288, 1190, 1164, 1106, 1029, 992, 923 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.19-7.16(m, 2H), 7.13-7.10(m, 1H), 7.06-7.02(m, 1H), 6.94-9.92(m, 1H), 5.38(dd, $J = 3.2, 8.8$ Hz, 1H), 4.11(ddd, $J = 4, 5.6, 11.2$ Hz, 1H), 3.80(ddd, $J = 4, 10, 11.6$ Hz, 1H), 3.32(dd, $J = 9.2, 16.4$ Hz, 1H), 3.00(ddd, $J = 5.2, 9.2, 16$ Hz, 1H), 2.95(dd, $J = 3.6, 16$ Hz, 1H), 2.71(ddd, $J = 4, 3.2, 16$ Hz, 1H), 2.35-2.23(m, 4H), 1.70-1.59(m, 4H); ^{13}C NMR (75 MHz, ppm) δ 198.9, 141.0, 140.0, 138.1, 134.2, 129.2, 126.7, 126.4, 124.8, 73.2, 63.7, 44.2, 29.4, 26.6, 23.6, 22.3, 21.9; MS (EI) m/z (%) 256, 238, 227, 199, 187, 173, 146, 133(100), 124, 109, 105, 91, 81, 79, 77; HRMS calcd for $\text{C}_{17}\text{H}_{20}\text{O}_2$: 256.1463; found: 256.1466.

2-(Isochroman-1-yl)pentan-3-one (10c). The ratio of two diastereoisomers is 1:1. Isolated by flash column chromatography (hexane/ethyl acetate = 4:1, $R_f = 0.5$). IR (liquid) of the mixture: ν_{max} 1713, 1605, 1492, 1454, 1426, 1374, 1342, 1283, 1262, 1184, 1099, 1076, 979, 942, 919 cm^{-1} ; ^1H NMR (400 MHz, ppm) of the mixture δ 7.20-7.02(m, 8H), 5.30(d, $J = 2.8$ Hz, 1H), 4.98(d, $J = 4.8$ Hz, 1H), 4.20-4.10(m, 2H), 3.74-3.65(m, 2H), 3.14-2.95(m, 4H), 2.69-2.56(m, 4H), 2.41-2.25(m, 2H), 1.22(d, $J = 7.2$ Hz, 3H), 1.11(t, $J = 7.2$ Hz, 3H), 0.97(t,

$J = 7.2$ Hz, 3H), 0.96(d, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, ppm) of the mixture δ 212.7, 212.6, 136.2(two peaks), 135.2, 134.6, 129.2(possibly overlapped), 126.9, 126.6(two peaks), 126.3, 125.6, 124.6, 78.2, 77.1, 64.3, 64.0, 52.2, 52.0, 35.4, 34.3, 29.4(two peaks), 14.3, 9.6, 8.3, 8.1; MS (EI) m/z (%) 218, 203, 189, 159, 143, 133(100), 128, 115, 105, 91, 85, 77; HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$: 218.1293; found: 218.1290.

4-(Isochroman-1-yl)nonan-5-one (11c). The ratio of the diastereoisomers is 1:1. Isolated by flash column chromatography (hexane/ethyl acetate = 10:1, $R_f = 0.5$). IR (liquid) of the mixture: ν_{max} 1712, 1492, 1464, 1453, 1377, 1279, 1190, 1116, 1102, 1093, 1062, 1041, 999, 965 cm^{-1} ; ^1H NMR (400 MHz, ppm) of the mixture δ 7.23-7.03(m, 8H), 5.11(d, $J = 3.6$ Hz, 1H), 4.92(d, $J = 4.4$ Hz, 1H), 4.20(ddd, $J = 2.8, 5.6, 11.2$ Hz, 1H), 4.12(ddd, $J = 2.8, 5.6, 11.2$ Hz, 1H), 3.72-3.65(m, 2H), 3.05-2.94(m, 4H), 2.67-2.58(m, 2H), 2.55-2.50(m, 2H), 2.31-2.16(m, 2H), 1.92-1.82(m, 2H), 1.66-1.54(m, 3H), 1.44-1.09(m, 11H), 0.96-0.91(m, 6H), 0.82-0.78(m, 6H); ^{13}C NMR (75 MHz, ppm) of the mixture δ 212.2, 212.1, 136.4(possibly overlapped), 135.0, 134.5, 129.3, 129.2, 126.9, 126.7, 126.5, 126.3, 125.6, 124.8, 77.1(two peaks), 64.2, 64.1, 58.2, 58.0, 42.7, 42.2, 31.4, 29.4, 29.3, 27.5, 26.2, 25.8, 22.7, 22.6, 21.8, 21.4, 14.6(two peaks), 14.4, 14.3; MS (EI) m/z (%) 274, 245, 231, 217, 189, 171, 159, 133(100), 115, 105, 91, 77; HRMS calcd for $\text{C}_{18}\text{H}_{25}\text{O}_2$: 273.1855($\text{M}^+ - \text{H}$); found: 273.1857.

Ethyl 3-(isochroman-1-yl)-2-oxopropanoate (12c). Isolated by flash column chromatography (hexane/ethyl acetate = 2:1, $R_f = 0.6$). IR (liquid): ν_{max} 1726, 1666, 1606, 1493, 1453, 1427, 1372, 1306, 1281, 1248, 1207, 1108, 1037, 920 cm^{-1} ; ^1H NMR (400 MHz,

ppm) δ 7.12-7.08(m, 2H), 7.05-7.02(m, 1H), 6.97-6.94(m, 1H), 5.27(dd, J = 3.6, 9.2 Hz, 1H), 4.25(q, J = 7.2 Hz, 2H), 4.01(ddd, J = 4.8, 4.8, 10.8 Hz, 1H), 3.70(ddd, J = 4, 9.2, 11.6 Hz, 1H), 3.31(dd, J = 9.2, 15.6 Hz, 1H), 3.18(dd, J = 3.6, 15.6 Hz, 1H), 2.88(ddd, J = 5.2, 8.8, 15.2 Hz, 1H), 2.64(ddd, J = 4.4, 4.4, 16.4 Hz, 1H), 1.30(t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 192.6, 161.1, 136.6, 134.0, 129.3, 127.0, 126.6, 124.7, 72.5, 63.4, 62.8, 46.2, 29.0, 14.4.

2-(3-Methylisochroman-1-yl)pentan-3-one (13c). The ratio of four diastereoisomers is 1:1:0.8:1.2. Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (liquid) of the mixture of four isomers: $\nu_{\max}$ 1712, 1606, 1491, 1455, 1383, 1366, 1266, 1183, 1147, 1120, 1079, 1065, 1037, 973 cm^{-1} ; Isomer 1: ^1H NMR (400 MHz, ppm) δ 5.24(s, 1H), Isomer 2: ^1H NMR (400 MHz, ppm) δ 5.06(d, J = 6.8 Hz, 1H), Isomer 3: ^1H NMR (400 MHz, ppm) δ 4.96(d, J = 3.2 Hz, 1H), Isomer 4: ^1H NMR (400 MHz, ppm) δ 4.86(d, J = 9.2 Hz, 1H) Other overlapped peaks: ^1H NMR (400 MHz, ppm) δ 7.11-6.81(m), 4.15-4.06(m), 4.04-3.96(m), 3.70-3.60(m), 3.09-2.94(m), 2.88-2.83(m), 2.80-2.71(m), 2.61-2.14(m), 1.24-1.10(m), 1.04-0.94(m), 0.89-0.95(m); ^{13}C NMR (75 MHz, ppm) of the mixture of four isomers δ 213.7, 213.3, 213.2, 212.8, 136.5, 136.2, 136.1, 135.5, 135.3, 135.1, 133.7, 133.4, 129.4, 129.3, 129.0(two peaks), 127.2, 126.9, 126.8, 126.6, 126.5, 126.4(two peaks), 126.2, 125.6, 125.1(two peaks), 124.4, 78.6, 77.8, 77.0, 74.7, 70.7, 70.3, 65.6, 65.1, 52.8, 52.2, 51.7(two peaks), 37.1, 36.9, 36.6, 35.9, 35.6, 35.2, 34.7, 33.9, 22.2, 22.0, 21.8, 21.1, 15.2, 13.8, 13.1, 9.4, 8.3, 8.2, 8.1, 8.0; MS (EI) m/z (%) 232, 217, 203, 189, 175, 159, 147(100), 142, 131, 129, 115, 97, 91, 85, 77, 71, 57; HRMS calcd for $\text{C}_{15}\text{H}_{19}\text{O}_2$: 231.1385($\text{M}^+ - \text{H}$); found: 231.1389.

3-Methoxy-2-methyl-1,3-diphenylpropan-1-one (14c). CA Registry Number [167990-19-4]. The ratio of two diastereoisomers is 1:1. Isolated by flash column chromatography (hexane/ethyl acetate = 10:1, R_f = 0.4). IR (liquid) of the mixture: $\nu_{\max}$ 1680, 1596, 1579, 1492, 1453, 1372, 1300, 1259, 1220, 1182, 1096, 976, 949 cm^{-1} ; ^1H NMR (400 MHz, ppm) of the mixture δ 8.06-8.03(m, 2H), 7.76-7.71(m, 2H), 7.59-7.55(m, 1H), 7.50-7.44(m, 3H), 7.41-7.30(m, 9H), 7.26-7.22(m, 2H), 7.18-7.14(m, 1H), 4.50-4.47(m, 2H), 3.88-3.76(m, 2H), 3.22(s, 3H), 3.10(s, 3H), 1.37(d, J = 7.2 Hz, 3H), 0.87(d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, ppm) of the mixture δ 203.8, 202.6, 140.4, 139.9, 137.7, 137.0, 133.1, 132.9, 128.7(three peaks), 128.6, 128.4, 128.3(two peaks), 127.9(two peaks), 127.6, 86.7, 84.9, 57.3, 57.2, 48.9, 47.6, 15.3, 14.9; MS (EI) m/z (%) 254, 239, 222, 178, 149, 147, 131, 121(100), 105, 91, 77, 58.

1-Methoxy-2-methyl-1-phenylpentan-3-one (15c). CA register number [134810-62-1]. The ratio of two isomers is 1:2. Isolated by flash column chromatography (hexane/ethyl acetate = 10:1, R_f = 0.4). IR (liquid) of the mixture: $\nu_{\max}$ 1716, 1668, 1494, 1454, 1374, 1364, 1311, 1213, 1091, 1072, 1028, 949 cm^{-1} ; Major isomer: ^1H NMR (400 MHz, ppm) δ 4.20(d, J = 10.4 Hz, 1H), 3.09(s, 3H), 2.69-2.51(m, 2H), 1.10(t, J = 7.2 Hz, 3H), 0.74(d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 214.5, 86.7, 57.0, 52.6, 37.1, 14.3, 7.9; Minor isomer: ^1H NMR (400 MHz, ppm) δ 4.30(d, J = 7.6 Hz, 1H), 3.21(s, 3H), 2.30(dq, J = 7.2, 18 Hz, 1H), 1.97(dq, J = 7.2, 18 Hz, 1H), 1.20(d, J = 7.2 Hz, 3H), 0.83(t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 213.3, 84.8, 57.2, 53.9, 36.5, 13.5, 7.7; Other overlapped peaks: ^1H NMR (400 MHz, ppm) δ 7.39-7.23(m), 2.92-2.80(m); ^{13}C NMR (75 MHz, ppm) of the mixture δ 140.3, 140.0, 128.6,

128.5, 128.3, 128.0, 127.8, 127.3; MS (EI) m/z (%) 206, 191, 177, 174, 149, 121(100), 118, 105, 91, 86, 77, 57.

1-(Isochroman-1-yl)pentan-2-one (16c) and 3-(Isochroman-1-yl)pentan-2-one (16d). The ratio of **16c** and **16d** is 1:1.5, the ratio of the two diastereoisomers of **16d** is 1:1. Isolated by flash column chromatography (hexane/ethyl acetate = 4:1, R_f = 0.5). IR(liquid) of the mixture of **16c** and **16d**: $\nu_{\max}$ 1713, 1604, 1492, 1463, 1453, 1427, 1375, 1363, 1280, 1252, 1215, 1176, 1109, 1093, 1061, 1040, 991 cm^{-1} ; Compound **16c**: ^1H NMR (400 MHz, ppm) δ 5.26(dd, J = 3.6, 9.2 Hz, 1H), 4.10(ddd, J = 3.6, 5.2, 10.8 Hz, 1H), 3.79(ddd, J = 3.6, 9.2, 11.2 Hz, 1H), 2.95(dd, J = 9.2, 16.6 Hz, 1H), 2.83(dd, J = 3.6, 16 Hz, 1H), 2.50(dt, J = 2.8, 7.2 Hz, 2H), 1.66(q, J = 7.2 Hz, 2H), 0.94(t, J = 7.2 Hz, 3H); MS (EI) m/z (%) 218, 189, 175(100), 147, 133(100), 128, 115, 105, 98, 91, 77, 71, 55; HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$: 218.1293; found: 218.1293; The mixture of two diastereoisomers of compound **16d**: ^1H NMR (400 MHz, ppm) δ 5.15(d, J = 3.6 Hz, 1H), 4.93(d, J = 4.4 Hz, 1H), 4.21(ddd, J = 2.8, 5.6, 10.8 Hz, 1H), 4.13(ddd, J = 2.8, 5.6, 11.2 Hz, 1H), 3.74-3.65(m, 2H), 2.28(s, 3H), 1.96(s, 3H), 1.94-1.80(m, 2H), 1.77-1.61(m, 2H), 0.97(t, J = 7.6 Hz, 3H), 0.80(t, J = 7.6 Hz, 3H); MS (EI) m/z (%) 217 ($\text{M}^+ - \text{H}$), 203, 189(50), 147, 133(100), 127, 115, 105, 91, 85, 77, 71, 55; HRMS calcd for $\text{C}_{14}\text{H}_{17}\text{O}_2$: 217.1229($\text{M}^+ - \text{H}$); found: 217.1231; Other overlapped peaks of compound **16c** and **16d**: ^1H NMR (400 MHz, ppm) δ 7.20-7.00(m), 3.05-2.90(m), 2.87-2.81(m), 2.73-2.59(m); ^{13}C NMR (75 MHz, ppm) of the mixture of **16c** and **16d** δ 210.5, 210.2, 209.2, 137.5, 136.3(possibly overlapped), 135.1, 134.4, 134.1, 129.3(possibly overlapped), 127.0, 126.8, 126.7, 126.6, 126.5, 126.4, 125.5, 124.7, 124.6, 77.2, 76.7, 73.0, 64.3, 64.2, 63.7, 60.8, 60.7, 49.7, 46.2, 30.1, 29.8, 29.3(two peaks), 29.2, 22.3, 18.4, 17.4, 14.1, 13.3, 12.7.

Reference:

[1] 3-Methylisochroman was prepared by the reaction of the corresponding homobenzylic alcohol with dimethoxymethane in the presence of BF_3 etherate or TMSOTf, see: DeNinno, M. P.; Perner, R. J.; Morton, H. E.; DiDomenico, S., Jr. *J. Org. Chem.* **1992**, *57*, 7115.

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
 Archive directory: /export/home/izhao/vnmrSYS/data
 Sample directory:
 File: zyhl1-11-17
 Pulse Sequence: szpul
 Solvent: CDCl3
 Temp. 25.0 C / 298.1 K
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.998 sec
 Width 6410.3 Hz
 32 repetitions
 OBSERVE H1, 400.1245662 MHz
 DATA PROCESSING
 FT size 32768
 Total time 1 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/izhao/vnmrSYS/data
 Sample directory:
 File: zyhl-11-17/carbon

Pulse Sequence: s2pul
 Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 1867.9 Hz
 2560 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610293 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
 Archive directory: /export/home/izhao/vnmrSYS/data
 Sample directory:
 File: zyhl1-11-18

Pulse Sequence: szpul
 Solvent: CDCl3
 Temp. 25.0 C / 298.1 K
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.998 sec
 Width 6410.3 Hz
 32 repetitions
 OBSERVE H1, 400.1245662 MHz
 DATA PROCESSING
 FT size 32768
 Total time 1 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/lzhao/vnmr-sys/data
 Sample directory:
 File: zyhl1-11-18carbon
 Pulse Sequence: szpul
 Solvent: CDCl3
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 2560 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 Continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
 Archive directory: /export/home/12hao/vnmr sys/data
 Sample directory:
 File: zyhl1-11-19
 Pulse Sequence: szpu1
 Solvent: CDCl3
 Temp. 25.0 C / 298.1 K
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.998 sec
 Width 6410.3 Hz
 32 repetitions
 OBSERVE H1, 400.1245662 MHz
 DATA PROCESSING
 FT size 32768
 Total time 1 min

¹³C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/1zhao/vnmr-sys/data
 Sample directory:
 File: zyhl1-11-19carbon

Pulse Sequence: szpu1
 Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 2368 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/1zhaq/vnmrSYS/data
 Sample directory:
 File: zyhl1-11-14carbon

Pulse Sequence: szpul

Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 2944 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
 Archive directory: /export/home/izhao/vnmrSYS/data
 Sample directory:
 file: zyhl1-11-12

Pulse Sequence: szpu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

8 repetitions

OBSERVE H1, 400.1245662 MHz

DATA PROCESSING

FI size 32768

Total time 0 min

¹³C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/rgunn/vnmrSYS/data
 Sample directory:
 File: CARBON

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 20.1 C / 293.2 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.815 sec

Width 18867.9 Hz

2304 repetitions

OBSERVE C13, 75.4500158 MHz

DECOUPLE H1, 300.0610299 MHz

Power 35 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

FT size 131072

Total time 80 hr, 54 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/izhao/vnmr-sys/data
 Sample directory:
 File: zyhl1-11-3carbon

Pulse Sequence: szpu1
 Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 2624 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

220 200 180 160 140 120 100 80 60 40 20 0 ppm

187.086

153.201

149.996

146.810

137.476

134.191

129.306

126.876

126.498

124.800

118.034

112.612

77.781

77.357

76.934

72.973

63.582

45.709

29.232

100

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13C OBSERVE

Data Collected On: m300-mercury300
 Archive directory: /export/home/1zhao/vnmr-sys/data
 Sample directory:
 File: zyhl1-11-9carbon

Pulse Sequence: szpul
 Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 1728 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 continuously ON
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
 Archive directory: /export/home/izhao/vnmr sys/data
 Sample directory:
 File: zyhl1-11-2

Pulse Sequence: szpu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

32 repetitions

OBSERVE H1, 400.1245662 MHz

DATA PROCESSING

FT size 32768

Total time 1 min

13C OBSERVE

Data Collected on: m300-mercury300
Archive directory: /export/home/lzhao/vnmrsys/data
Sample directory:
File: zyhl-11-2

Pulse Sequence: s2pu1

Solvent: CDCl3

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
1472 repetitions
OBSERVE C13, 75.4500158 MHz
DECOUPLE H1, 300.0610299 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury/400
 Archive directory: /export/home/lzhaq/vnmr/sys/data
 Sample directory:
 File: zym11-11-11

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

32 repetitions

OBSERVE H1, 400.1245662 MHz

DATA PROCESSING

FT size 32768

Total time 1 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/izhao/vnmrSYS/data
 Sample directory:
 File: zyhl1-11-11carbon

Pulse Sequence: szpu1

Solvent: CCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 2816 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 continuously ON
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT Size 131072
 Total time 80 hr, 54 min

137 135 133 131 129 127 ppm

Data Collected on: m400-mercury400
 Archive directory: /export/home/iznao/vnmr sys/data
 Sample directory:
 File: zyhl2-5-1

Pulse Sequence: szpul
 Solvent: CDCl3
 Temp: 25.0 C / 298.1 K
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.398 sec
 Width 6410.3 Hz
 8 repetitions
 OBSERVE H1, 400.1246011 MHz
 DATA PROCESSING
 FT size 32768
 Total time 0 min

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/lzhaq/vnmrsys/data
 Sample directory:
 File: CARBON

Pulse Sequence: szpu1

Solvent: CDCl3
 Temp. 21.6 C / 294.8 K

Relax. delay 1.000 sec
 Pulse 45.0 degrees

Acq. time 1.815 sec
 Width 18667.9 Hz

3776 repetitions

OBSERVE C13, 75.4500158 MHz

DECOUPLE H1, 300.0610299 MHz

Power 35 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

FT size 131072

Total time 80 hr, 54 min

STANDARD 1H OBSERVE

Data Collected on: m400-mercury400
Archive directory: /export/home/1zhao/vnmrSYS/data
Sample directory:
File: zyhl2-5-2

Pulse Sequence: szpul

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

Single scan

OBSERVE H1, 400.1246011 MHz

DATA PROCESSING

FT size 32768

Total time 0 min

13C OBSERVE

Data Collected on: m300-mercury300
Archive directory: /export/home/xyao/vnmrSYS/data
Sample directory:
File: CARBON

Pulse Sequence: s2pu1
Solvent: CDCl3

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
5056 repetitions
OBSERVE C13, 75.4500158 MHz
DECOUPLE H1, 300.0610299 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
FT size 131072
Total time 80 hr, 54 min

and

13C OBSERVE

Data Collected on: m300-mercury300
 Archive directory: /export/home/1zhao/vnmr/sys/data
 Sample directory:
 File: 11-11-1carbon

Pulse Sequence: szpul
 Solvent: CDCl3

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 18867.9 Hz
 4480 repetitions
 OBSERVE C13, 75.4500158 MHz
 DECOUPLE H1, 300.0610299 MHz
 Power 35 dB
 Continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 80 hr, 54 min

and