Supporting Information for

Synthesis of biphenyl based ligand: Application in copper mediated chemoselective Michael reaction

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Experimental

Reagents were purchased from Sigma-Aldrich Chemicals Limited, SD Fine, Qualigens Limited etc. Thin Layer Chromatography was performed on Merck 60 F₂₅₄ Aluminium coated plates. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography using silica gel (60-120 mesh). All the products were characterized by H-NMR, IR, Mass spectroscopy and by comparison of m.p. with the reported values. ¹H NMR spectra were recorded on Bruker Avance 400 Spectrometer and were run in CDCl₃. Mass spectra were recorded on Thermo-Fischer DSQ II GCMS instrument. IR spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pallets. Melting points were recorded in Thiele's tube using paraffin oil and are uncorrected.

Reaction of diol **3** under different conditions was studied (Scheme i). In some cases the cyclization was observed to give compound **X**. For details see Table-ii.

Scheme i: Conditions for conversion of diol **3** to dibromo **4**.

Table ii: Conditions for Scheme i.

No	Reaction Conditions	Isolated Yield/% ^a		Yield/ % ^b
		4	X	
1	PPh ₃ (2.1 eq.), Br ₂ (2.2 eq.), MeCN, r.t., 18 h.	88	--	88
2	48% aq. HBr (2.5 eq.), dioxane, 60 °C, 24 h.	26	38	64
3	NaBr (2.5 eq.), conc. H ₂ SO ₄ (0.1 eq.), TBAB (0.1 eq.), dioxane, 60 °C, 24 h.	9	42	51
4	NaBr (2.5 eq.), conc. H ₂ SO ₄ (2.2 eq.), TBAB (0.1 eq.), dioxane, 60 °C, 24 h.	50	39	89
5	Conc. H ₂ SO ₄ (0.1 eq.), dioxane, 60 °C, 24 h.	--	90	90

^aIsolated. ^bCombined isolated yield.**6,7-Dihydro-5H-dibenz[*c,e*]oxepine (X):**

M. p. = 68 - 70 °C (Lit. 71.5 – 72.0 °C).

IR (KBr): ν 3066, 3018, 2965, 2913, 2855, 1483, 1458, 1442, 1377, 1198, 1073, 1044, 991, 902, 890, 786, 757, 602, 501 cm.⁻¹¹H NMR (400 MHz, CDCl₃): δ 7.60-7.58 (m, 2H), 7.55-7.51 (m, 2H), 7.48-7.42 (m, 4H), 4.39 (s, 4H).Mass (EI⁺) m/z (%) 196 (28), 195 (27), 167 (26), 166 (16), 164 (44), 152 (13), 148 (11), 121 (10), 94 (20), 83 (12), 80 (53), 71 (12), 68 (100), 68 (15), 66 (22), 56 (20), 54 (19).**4-Acetyl-1-(4-bromophenyl)-3-phenylhexane-1,5-dione (10) [Table 2, entry 2].**

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluoromethanesulfonate (12.5 mg, 0.035 mmol, 10.0 mol %) and the Ligand **1** (8.1 mg, 0.019 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate 4-acetyl-1-(4-bromophenyl)-3-phenylhexane-1,5-dione (0.10 g, 0.35 mmol, 1.0 eq.), acetyl acetone (0.05 g, 0.52 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as

monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**10**) (0.07 g, 54%).

M. p. = 136-138 °C (Lit.^[1] 129 °C).

IR (KBr): ν 3062, 2949, 1692, 1586, 1495, 1454, 1399, 1357, 1260, 1242, 1208, 1154, 1073, 1009, 981, 816, 760, 772, 703 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 7.70-7.67 (m, 2H), 7.57-7.52 (m, 2H), 7.26-7.23 (m, 2H), 7.21-7.17 (m, 3H), 4.32-4.29 (d, J = 10.8 Hz, 1H), 4.21-4.15 (m, 1H), 3.28-3.22 (dd, J = 16.4 and 8.8 Hz, 1H), 3.19-3.15 (dd, J = 16.4 and 4.4 Hz, 1H), 2.28 (s, 3H), 1.89 (s, 3H).

Mass (EI⁺) m/z (%) 345 (22), 344 (21), 342 (41), 327 (26), 326 (25), 188 (5), 184 (100), 182 (94), 157 (5), 156 (14), 154 (20), 146 (20), 144 (6), 130 (7), 104 (5), 102 (7), 75 (7).

3-(Benzylthio)-1,3-diphenylpropan-1-one (**11**), [Table 2, entry 3]

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluoromethanesulfonate (17.4 mg, 0.048 mmol, 10.0 mol %) and the Ligand **1** (11.1 mg, 0.026 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.48 mmol, 1.0 eq.), benzyl mercaptan (0.089 g, 0.72 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a white solid (**11**) (0.142 g, 89%).

M. p. = 68-70 °C (Lit.^[2] 70-72 °C).

IR (KBr): ν 3058, 3021, 2891, 1680, 1595, 1491, 1447, 1369, 1343, 1225, 1074, 980, 922, 725 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 7.86-7.84 (m, 2H), 7.55-7.53 (m, 1H), 7.43-7.37 (m, 4H), 7.33-7.20 (m, 8H), 4.47-4.45 (dd, J = 7.6 Hz, 1H), 3.58-3.44 (m, 4H).

Mass (EI⁺) m/z (%) 331 (10), 242 (12), 241 (64), 240 (60), 209 (100), 120 (12), 105 (60), 90 (60), 77 (69).

4-Acetyl-3-(4-chlorophenyl)-1-phenylhexane-1,5-dione (**13**) (Table 2, entry 4):

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (14.9 mg, 0.041 mmol, 10.0 mol %) and the Ligand **1** (9.5 mg, 0.023 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate (E)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (0.10 g, 0.41 mmol, 1.0 eq.), acetyl acetone (0.06 g, 0.62 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**13**) (0.09 g, 65%).

M. p. = 138-140 °C (Lit.^[1] 141 °C)

IR (KBr): ν 3069, 2909, 1693, 1581, 1493, 1449, 1413, 1363, 1242, 1209, 1192, 1149, 1092, 1013, 953, 919, 823, 789, 750, 687, 594, 532 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 7.84-7.81 (m, 2H), 7.57-7.52 (tt, J =7.2 and 1.2 Hz, 1H), 7.44-7.41 (m, 2H), 7.23-7.21 (m, 2H), 7.19-7.16 (m, 2H), 4.29-4.27 (d, J = 11.2 Hz, 1H), 4.25-4.19 (m, 1H), 3.33-3.26 (dd, J = 16.4 and 8.8 Hz, 1H), 3.21-3.16 (dd, J = 16.4 and 3.6 Hz, 1H), 2.28 (s, 3H), 1.92 (s, 3H).

Mass (EI⁺) m/z (%) 301 (5), 300 (7), 299 (17), 298 (11), 283 (5), 282 (7), 280 (25), 18 (5), 119 (5), 106 (5), 104 (100), 78 (3), 76 (34).

3-(naphthalen-2-ylthio)-1,3-diphenylpropan-1-one (**14**) [Table 2, entry 5]

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (17.4 mg, 0.048 mmol, 10.0 mol %) and the Ligand **1** (11.1 mg, 0.026 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.48 mmol, 1.0 eq.), 2-naphthalithiol (0.115 g, 0.72 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 90:10) as eluent to obtain a solid (**14**) (0.07 g, 40%).

M. p. = 46-48 °C (Lit.^[2])

IR (KBr): ν 3054, 3024, 1673, 1593, 1497, 1448, 1362, 1335, 1228, 1077, 983, 864, 817, 746, 713, 690 cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 7.89-7.86 (m, 2H), 7.79-7.76 (m, 2H), 7.72-7.68 (m, 2H), 7.55-7.51 (m, 1H), 7.46-7.37 (m, 7H) 7.28-7.24 (m, 2H) 7.21-7.19 (m, 1H) 5.10-5.07 (dd, $J = 6$ Hz, 1H) 3.73-3.65 (d, $J = 17.2$ and 8 Hz, 1H), 3.65-3.59 (d, $J = 17.2$ and 6.4 Hz, 1H).

Mass (EI^+) m/z (%) 369 (29), 368 (43), 367 (100), 208 (69), 158 (46), 114 (71), 104 (67), 76 (52).

(E)-3-Acetyl-4,8-diphenyloct-7-ene-2,6-dione (**16**) [Table 2, entry 6]

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (15.5 mg, 0.043 mmol, 10.0 mol %) and the Ligand **1** (9.87 mg, 0.024 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate (1E,4E)-1,5-diphenylpenta-1,4-dien-3-one (0.10 g, 0.43 mmol, 1.0 eq.), acetyl acetone (0.064 g, 0.64 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**16**) (0.115 g, 81%).

M. p. = 138-140 $^{\circ}\text{C}$ (Lit.^[3] 139-141 $^{\circ}\text{C}$).

IR (KBr): ν 3031, 2891, 1693, 1655, 1495, 1450, 1356, 1261, 1201, 1085, 975, 748, 703 cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 7.48-7.46 (m, 2H), 7.44-7.40 (d, $J = 16.4$ Hz, 1H), 7.39-7.37 (m, 3H), 7.25-7.22 (m, 4H), 7.21-7.16 (m, 1H), 6.58-6.54 (d, $J = 16.4$ Hz, 1H), 4.32-4.29 (d, $J = 11.2$ Hz, 1H), 4.17-4.11 (m, 1H), 3.03-2.96 (dd, $J = 15.6$ and 9.2 Hz, 1H), 2.92-2.87 (dd, $J = 15.6$ and 4 Hz, 1H), 2.29 (s, 3H). 1.89 (s, 3H)..

Mass (EI^+) m/z (%) 315 (25), 290 (86), 273 (35), 272 (90), 144 (42), 131 (58), 130 (64), 102 (100).

3-(2,4-Dioxopentan-3-yl)cyclohexanone (**18**) [Table 2, entry 7].

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10 g, 1.04

mmol, 1.0 eq.), acetyl acetone (0.17 g, 1.56 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a yellow solid (**18**) (0.167 g, 82%).

M. p. = 52-54 °C (Lit.^[4] 53-54 °C)

IR (KBr): ν 2956, 2873, 2848, 1711, 1427, 1361, 1327, 1264, 1218, 1154, 1063, 1041, 975, 947, 906, 868, 832, 778, 757, 674, 627, 600, 565, 505 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 3.66-3.63 (d, J = 10 Hz, 1H), 2.74-2.64 (m, 1H), 2.4-2.39 (m, 1H), 2.34-2.22 (m, 2H), 2.19 (s, 3H), 2.17 (s, 3H), 2.09-2.01 (m, 2H), 1.81 (m, 1H), 1.77-1.66 (m, 1H), 1.43-1.33 (m, 1H).

Mass (EI⁺) m/z (%) 152 (53), 111 (18), 110 (16), 107 (10), 99 (7), 96 (100), 95 (10), 84 (15), 83 (11), 82 (13), 68 (18), 67 (13), 66 (7), 54 (17).

Ethyl 3-oxo-2-(3-oxocyclohexyl)butanoate (**19**) [Table 2, entry 8]

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluoromethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10 g, 1.04 mmol, 1.0 eq.), ethyl aceto acetate (0.203 g, 1.56 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a colorless oil (**19**)^[5] (0.198 g, 83%).

IR (KBr): ν 2942, 2870, 1734, 1714, 1448, 1424, 1360, 1252, 1227, 1156, 1097, 1024, 869 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 4.25-4.18 (m, 3H, CH₂-CH₃ and CH-CO protons merged) 3.76-3.75 (d, J = 6.4 Hz, 1H), 3.46-3.38 (m, 2H), 2.61-2.58 (m, 2H), 2.43-2.35 (m, 4H), 2.31-2.22 (m, 8H), 2.19-1.26 (m, 15H).

Mass (EI⁺) m/z (%) 226 (M⁺) (5), 182 (16), 152 (29), 129 (39), 109 (14), 96 (100), 95 (38), 80 (32).

3-(Naphthalen-3-ylthio)cyclohexanone (**21**) [Scheme 2]:

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), naphthalene-2-thiol (0.20 g, 1.25 mmol, 1.2 eq.) and piperidine (0.11 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a white solid (**21**) (0.158 g, 59 %).

M. p. = 46-48 °C. (lit.^[2] 48 °C)

IR (KBr): ν 3050, 2934, 2912, 1712, 1595, 1496, 1444, 1313, 1278, 1218, 969, 864, 817, 747 cm^{-1}

¹H NMR (400 MHz, CDCl₃): δ 7.92-7.91 (d, J = 1.2 Hz, 1H), 7.83-7.78 (m, 3H), 7.53-7.47 (m, 3H), 3.55-3.54 (m, 1H), 2.76-2.71 (m, 1H), 2.46-2.42 (m, 1H), 2.39-2.26 (m, 2H), 2.24-2.13 (m, 2H), 1.80-1.73 (m, 2H).

Mass (EI⁺) m/z (%) 258 (12), 257 (42), 256 (43), 255. (73), 255 (71), 162 (10), 161 (25), 160 (40), 159 (73), 159 (70), 157 (22), 148 (10), 128 (17), 127 (15), 125 (13), 116 (11), 114 (100), 96 (57), 68 (97), 54 (23).

3-(Benzylthio)cyclohexanone (**24**) [Scheme 3]:

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), naphthalene-2-thiol (0.20 g, 1.25 mmol, 1.2 eq.) and benzyl mercaptan (0.16 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the

completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a yellow liquid (**24**)^[2] (0.127 g, 56.2 %) and a white solid (**21**) (0.06 g, 22.5 %).

Spectral data for **24**:

IR (Neat): ν 3060, 3027, 2942, 2867, 1712, 1601, 1494, 1452, 1421, 1341, 1314, 1283, 1222, 1175, 1069, 1030, 972, 879, 766, 704 cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 7.34-7.29 (m, 4H), 7.29-7.2 (m, 1H), 3.76-3.74 (ab, q, $J = 13.6$ Hz, and 2 Hz), 2.96-2.89 (m, 1H), 2.70-2.66 (m, 1H), 2.41-2.29 (m, 3H), 2.10 (m, 2H), 1.72-1.65 (m, 2H).

Mass (EI^+) m/z (%) 219 (48), 129 (17), 127 (30), 124 (12), 122 (100), 100 (13), 98 (10), 97 (46), 96 (47), 95 (9), 92 (23), 91 (58), 90 (39), 88 (9), 76 (9), 68 (38), 66 (13), 64 (30), 54 (15).

3-(2-Hydroxyethylthio)cyclohexanone (**26**) [Scheme 4]:

In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2-dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), 2-mercapto ethanol (0.08 g, 1.04 mmol, 1 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 60:40) as eluent to obtain a pale yellow oil (**26**)^[6] (0.08 g, 44 %).

IR (Neat): ν 3407, 2943, 2869, 1706, 1446, 1418, 1343, 1315, 1283, 1223, 1175, 1046, 1013, 972, 879 cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 3.76-3.73 (t, $J = 6$ Hz, and 2 Hz), 3.11 (m, 1H), 2.78 (t, $J = 6$ Hz, and 2 Hz), 2.73 (m, 1H), 2.43-2.34 (m, 3H), 2.15 (m, 3H), 1.74 (m, 2H).

Mass (EI^+) m/z (%) 173 (18), 155 (16), 143 (100), 98 (11), 97 (98), 96 (42), 95 (85), 78 (11), 73 (10), 69 (59), 68 (80), 67 (29), 54 (67).

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Spectral Data

^1H -NMR Spectrum of Compound 1 in CDCl_3 (400 MHz)

^{13}C -NMR Spectrum of Compound 1 in CDCl_3 (100 MHz)

¹H-NMR Spectrum of Compound 3 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 4 in CDCl₃ (400 MHz)

^1H -NMR Spectrum of Compound 5 in CDCl_3 (400 MHz)

^1H -NMR Spectrum of Compound X in CDCl_3 (400 MHz)

¹H-NMR Spectrum of Compound 8 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 10 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 11 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 13 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 14 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 16 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 18 in CDCl₃ (400 MHz)

¹H-NMR Spectrum of Compound 19 in CDCl₃ (400 MHz)

^1H -NMR Spectrum of Compound 21 in CDCl_3 (400 MHz)

^1H -NMR Spectrum of Compound 24 in CDCl_3 (400 MHz)

¹H-NMR Spectrum of Compound 26 in CDCl₃ (400 MHz)

Mass Spectrum of complex of ligand 1 and Cu(OTf)₂