Supplementary Information

Hydrogen peroxide mediated efficient amidation and esterification of aldehydes: Scope and selectivity

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Contents

1. General details

Reagents were obtained from commercial suppliers, and used without further purification. Column chromatographic purification of products was performed on silica gel (60-120 mesh). ^{1}H NMR spectra were recorded on a Bruker AVANCE II 400 MHz. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane and were reported as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Mass spectra were obtained from Agilent 5975C GC-MS and elemental analysis was performed on Elementar vario MICRO cube CHNS analyser.

2. Experimental procedure

2.1 General experimental procedure for preparation of amides-

6.5 mmol of amine was added to aldehyde (5.0 mmol) and mixed thoroughly. To this hydrogen peroxide (7.5 mmol) was added slowly with gentle sirring. The reaction mixture was heated at 70-75°C and monitored by GC for its progress. In case of 4-Isopropyl-benzaldehyde (Entry 2) which required more reaction time an additional amount of hydrogen peroxide (2.5 mmol) was added after an interval of every 2 hours. On completion of the reaction contents were cooled and neutralized with 5% sodium bicarbonate solution. An oil gets separated which was extracted with ethyl

acetate. Solvent removal under vacuum yielded the crude amide. Further purification was done by column chromatography.

2.2 General experimental procedure for preparation of esters-

7.5 mmol of alcohol (in case of methanol and ethanol 12.5 mmol of alcohol was used) and 5 mmol of aldehyde was taken in a round bottom flask fitted with a condensor. To this hydrogen peroxide (7.5 mmol) was added slowly with gentle sirring. The reaction mixture was heated at 70-75°C (in case of methanol and ethanol temperature was kept at 55-60 °C) and monitored by GC for its progress. After every 2 hours an additional amount of hydrogen peroxide (2.5 mmol) was added till the reaction is complete. On completion of the reaction contents were cooled and neutralized with 5% sodium bicarbonate solution. Organic phase gets separated which was extracted with ethyl acetate. Solvent removal under vacuum yielded the ester which was further purified by column chromatography if required.

3. Spectroscopic characterization data

(4-Isopropyl-phenyl)-piperidin-1-yl-methanone (2): Solid, m.p. 59-61°C (Lit[1] 60-61°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, 2H, *J*=8.0 Hz), 7.23 (d, 2H, *J*=8.0 Hz), 3.69 (br, s, 2H), 3.37 (br, s, 2H), 2.95-2.88 (m, 1H), 1.66-1.52 (m, 6H), 1.25-1.23 (d, 6H, *J*=7.2 Hz); EIMS: m/z 231 [M^+], 230, 216, 147, 132, 119, 91, 84, 77, 65, 55; Anal. Calcd for $C_{15}H_{21}NO$. C, 77.88; H, 9.15; N, 6.05. Found C, 78.01; H, 9.23; N, 5.83.

(4-Chloro-phenyl)-piperidin-1-yl-methanone (3): Solid, m.p. 80-82°C (Lit[2] 80-82°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.32 (m, 4H), 3.69 (br, s, 2H), 3.33 (br, s, 2H), 1.68-1.52 (m, 6H); EIMS: m/z 225 [M^++2], 223 [M^+], 222, 139, 111, 104, 84, 75, 57, 51; Anal. Calcd for $C_{12}H_{14}ClNO$. C, 64.43; H, 6.31; N, 6.26. Found C, 64.59; H, 6.22; N, 6.17.

(4-Nitro-phenyl)-piperidin-1-yl-methanone (4): Crystalline yellow solid, m.p. 121-122°C (Lit[2] 122-125°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28-8.25 (m, 2H), 7.56-7.54 (m, 2H), 3.73 (br, s, 2H), 3.28 (br, s, 2H), 1.70-1.53 (m, 6H); EIMS: m/z 234 [M^+], 233, 217, 187, 150, 120, 104, 92, 84, 76, 50; Anal. Calcd for $C_{12}H_{14}N_2O_3$. C, 61.53; H, 6.02; N, 11.96. Found C, 61.44; H, 6.14; N, 11.91.

Piperidin-1-yl-thiophen-2-yl-methanone (5): Solid, m.p. 64-67°C (Lit[3] 66.5-68°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (m, 1H), 7.27-7.25 (dd, 1H, J_1=0.8 Hz, J_2=3.6 Hz), 7.03-7.01 (dd, 1H, J_1=3.6 Hz, J_2=4.8 Hz), 3.66 (t, 4H, *J*=5.6 Hz), 1.72-1.67 (m, 2H), 1.65-1.59 (m, 4H); EIMS: 195 [M^+], 167, 162, 140, 111, 84, 69, 56, 51.; Anal calc. for $C_{10}H_{13}NOS$. C, 61.50; H, 6.71; N, 7.17; S, 16.42. Found C, 61.58; H, 6.58; N, 7.28; S, 16.34.

(4-Fluoro-phenyl)-piperidin-1-yl-methanone (6): Colorless oil (Lit[4]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.37 (m, 2H), 7.10-7.05 (m, 2H), 3.67 (br, s, 2H), 3.36 (br, s, 2H), 1.68-1.59 (m, 6H); EIMS: m/z 207 [M^+], 206, 178, 164, 140, 123, 95, 84, 75, 56; Anal. Calcd for $C_{12}H_{14}FNO$. C, 69.55; H, 6.81; N, 6.76. Found C, 69.67; H, 6.71; N, 6.72.

Phenyl-morpholin-4-yl-methanone (7): Solid, m.p. 74-75°C (Lit[5] 73-74°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.20 (m, 5H), 3.70-3.46 (m, 8H); EIMS: m/z 191 [M^+], 190, 176, 160, 148, 105, 86, 77, 56, 51; Anal. Calcd for $C_{11}H_{13}NO_2$. C, 69.09; H, 6.85; N, 7.32. Found C, 69.17; H, 6.91; N, 7.17.

(4-Chloro-phenyl)-morpholin-4-yl-methanone (8): White solid, m.p. 76-77°C (Lit[4] 76°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.27 (m, 4H), 3.87-3.45 (m, 8H); EIMS: 227 [M^++2], 225 [M^+], 210, 194, 139, 111, 86, 75, 56; Anal calc. for $C_{11}H_{12}ClNO_2$. C, 58.54; H, 5.36; N, 6.21. Found C, 58.67; H, 5.28; N, 6.14.

(4-Nitro-phenyl)-morpholin-4-yl-methanone (9): Crystalline yellow solid, m.p. 101-102°C (Lit[6] 101-103°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.28 (dd, 2H, J_1=1.6 Hz, J_2=6.0 Hz), 7.59-7.57 (dd, 2H, J_1=2.0 Hz, J_2=6.8 Hz), 3.80-3.38 (m, 8H); EIMS: m/z 236 [M^+], 235, 221, 205, 189, 150, 120, 104, 86, 76, 56; Anal. Calcd for $C_{11}H_{12}N_2O_4$. C, 55.93; H, 5.12; N, 11.86. Found C, 56.02; H, 5.20; N, 11.68.

Morpholin-4-yl-thiophen-2-yl-methanone (10): Yellow oil (Lit[7]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.45 (m, 1H), 7.29-7.28 (m, 1H), 7.06-7.04 (dd, 1H, J_1=3.6 Hz, J_2=4.8 Hz), 3.77-3.75 (m, 4H), 3.73-3.71 (m, 4H); EIMS: m/z 197 [M^+], 182, 164, 111, 98, 86, 70, 56, 50; Anal. Calcd for $C_9H_{11}NO_2S$. C, 54.80; H, 5.62; N, 7.10; S, 16.26. Found C, 54.88; H, 5.72; N, 7.02; S,16.15.

Phenyl-pyrrolidin-1-yl-methanone (11): Solid, m.p. 46-47°C (Lit[8] 46-47°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.37 (m, 5H), 3.65 (t, 2H, *J*=6.8 Hz), 3.42 (t, 2H, *J*=6.4 Hz), 2.04-1.85 (m, 4H); EIMS: m/z 175 [M^+], 146, 105, 77, 70, 51; Anal. Calcd for $C_{11}H_{13}NO$. C, 75.40; H, 7.48; N, 7.99. Found C, 75.53; H, 7.42; N, 7.91.

(4-Nitro-phenyl)-pyrrolidin-1-yl-methanone (12): Crystalline yellow solid, m.p. 75°C (Lit[4] 74-75°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29-8.25 (m, 2H), 7.69-7.66 (m, 2H), 3.67 (t, 2H, *J*=6.8 Hz), 3.38 (t, 2H, *J*=6.4 Hz), 2.01-1.91 (m, 4H); EIMS: 220 [M^+], 203, 175, 150, 120, 104, 92, 76, 64, 56; Anal calc. for $C_{11}H_{12}N_2O_3$. C, 59.99; H, 5.49; N, 12.72. Found C, 60.08; H, 5.56; N, 12.54.

(4-Chloro-phenyl)-pyrrolidin-1-yl-methanone (13): Solid, m.p. 76-78°C (Lit[9] 74-76°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-7.45 (m, 2H), 7.38-7.35 (m, 2H), 3.63 (t, 2H, *J*=6.8 Hz), 3.41 (t, 2H, *J*=6.4 Hz), 1.98-1.86 (m, 4H); EIMS: 211 [M^++2], 209 [M^+], 180, 146, 139, 111, 75, 56. Anal calc. for $C_{11}H_{12}ClNO$. C, 63.01; H, 5.77; N, 6.68. Found C, 62.88; H, 5.85; N, 6.72.

Pyrrolidin-1-yl-4-tolyl-methanone (14): Brown solid, m.p. 90-91°C (Lit[4] 90.2-90.6); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (d, 2H, *J*=8.0 Hz),7.20-7.18 (d, 2H, *J*=8.0 Hz), 3.63 (t, 2H, *J*=6.8 Hz), 3.43 (t, 2H, *J*=6.4 Hz), 2.37 (s, 3H), 1.96-1.82 (m, 4H); EIMS: 189 [M^+], 160, 146, 119, 91, 77, 65, 51. Anal calc. for $C_{12}H_{15}NO$. C, 76.16; H, 7.99; N, 7.40. Found C, 76.23; H, 8.07; N 7.24.

(4-Methoxy-phenyl)-pyrrolidin-1-yl-methanone (15): White solid, m.p. 78-79°C (Lit[4] 78.4-78.8°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.50 (dd, 2H, J_1=2.0 Hz, J_2=6.8 Hz), 6.90-6.88 (dd, 2H, J_1=2.0 Hz, J_2=7.2 Hz), 3.83 (s, 3H), 3.63 (t, 2H, *J*=6.8 Hz), 3.50-3.45 (t, 2H, *J*=3.2 Hz), 2.04-1.85 (m, 4H); EIMS: 205 [M^+], 135, 107, 92, 77, 64, 50. Anal calc. for $C_{12}H_{15}NO_2$. C, 70.22; H, 7.37; N, 6.82. Found C, 70.30; H, 7.32; N, 6.77.

1-(4-Benzoyl-piperazin-1-yl)-ethanone (16): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.40 (m, 5H), 3.61-3.51 (m, 8H), 2.12 (s, 3H); EIMS: 232 [M^+], 207, 189, 173, 164, 148, 134, 127, 105, 85, 77, 69, 56. Anal calc. for $C_{13}H_{16}N_2O_2$. C, 67.22; H, 6.94; N, 12.06. Found C, 67.31; H, 6.86; N, 12.03.

Furan-2-yl-piperidin-1-yl-methanone (17): Solid, m.p. 65-68 °C (Lit[10] 67-69 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42 (dd, 1H, J_1=0.8 Hz, J_2=1.8 Hz), 6.80 (dd, 1H, J_1=0.8 Hz, J_2=3.6 Hz), 6.37 (dd, 1H, J_1=2.0 Hz, J_2=3.8 Hz), 3.62 (s, br, 4H), 1.53 (s, br, 6H); EIMS: 179 [M^+], 150, 95, 84. Anal Calc. for $C_{10}H_{13}NO_2$. C, 67.02; H, 7.31; N, 7.82. Found C, 67.16; H, 7.25; N, 7.72.

Naphthalen-2-yl-piperidin-1-yl-methanone (18): Solid, m.p. 110-112 °C (Lit[11] 110-111 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90-7.83 (m, 4H), 7.51-7.42 (m, 3H), 3.74 (s, br, 2H), 3.38 (s, br, 2H), 1.67 (s, br, 4H), 1.54 (s, br, 2H); EIMS: 239 [M^+], 238,

207, 155, 127, 101, 77. Anal Calc. for $C_{16}H_{17}NO$. C, 80.30; H, 7.16; N, 5.85. Found C, 80.44; H, 7.07; N, 5.78.

Naphthalen-2-yl-pyrrolidin-1-yl-methanone (19): Solid, m.p. 76-77 °C (Lit[12] 75.5-76.5 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92-7.79 (m, 3H), 7.56-7.40 (m, 4H), 3.80 (t, 2H, *J*=6.8 Hz), 3.00 (t, 2H, *J*=6.8 Hz), 2.08-1.89 (m, 2H), 1.88-1.73 (m, 2H); EIMS: 225 [M^+], 155, 127, 101, 77. Anal Calc. for $C_{15}H_{15}NO$. C, 79.97; H, 6.71; N, 6.22. Found C, 80.08; H, 6.85; N, 5.97.

Benzoic acid methyl ester (20): Colorless liquid, b.p. 198-200°C (Lit[13] 199.5°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04-8.02 (dd, 2H, J_1=1.6 Hz, J_2=3.6 Hz), 7.56-7.52 (m, 1H), 7.44-7.41 (m, 2H), 3.91(s, 3H); EIMS: 136 [M^+], 105, 77, 51. Anal calc. for $C_8H_8O_2$. C, 70.57; H, 5.92. Found C, 70.70; H, 5.77.

4-Nitro-benzoic acid ethyl ester (21): Light yellow solid, m.p. 56-57°C (Lit[14] 57 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29-8.27 (dd, 2H, J_1=2.0 Hz, J_2=7.2 Hz), 8.22-8.20 (m, 2H), 4.46-4.41 (q, 2H), 1.43 (t, 3H, *J*=7.2 Hz); EIMS: 195 [M^+], 178, 167, 150, 120, 104, 92, 76, 65, 51. Anal calc. for $C_9H_9NO_4$. C, 55.39; H, 4.65; N, 7.18. Found C, 55.50; H, 4.63; N, 7.07.

4-Nitro-benzoic acid *n*-propyl ester (22): Yellow solid, m.p. 33-34°C (Lit[15] 34°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.28 (m, 2H), 8.22-8.20 (m, 2H), 4.34 (t, 2H, *J*=6.8 Hz), 1.85-1.80 (m, 2H), 1.05 (t, 3H, *J*=7.6 Hz); EIMS: 209 [M^+], 192, 168, 150, 120, 104, 92, 76, 65, 51. Anal calc. for $C_{10}H_{11}NO_4$. C, 57.41; H, 5.30; N, 6.70. Found C, 57.53; H, 5.36; N, 6.51.

4-Nitro-benzoic acid *n*-butyl ester (23): Light yellow solid, m.p. 35-37°C (Lit[16] 34-36°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.27 (m, 2H), 8.22-8.20 (m, 2H), 4.38 (t, 2H, *J*=6.8 Hz), 1.80-1.76 (m, 2H), 1.52-1.46 (m, 2H), 0.99 (t, 3H, *J*=7.6 Hz); EIMS: 223 [M^+], 207, 193, 168, 150, 120, 104, 92, 76, 65, 51. Anal calc. for $C_{11}H_{13}NO_4$. C, 59.19; H, 5.87; N, 6.27. Found C, 59.31; H, 5.94; N, 6.07

4-Nitro-benzoic acid methyl ester (24): Light yellow solid, m.p. 95°C (Lit[17] 96°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.28 (m, 2H), 8.23-8.20 (m, 2H), 3.98 (s, 3H); EIMS: 181 [M^+], 164, 150, 120, 104, 92, 76, 65, 51. Anal calc. for $C_8H_7NO_4$. C, 53.04; H, 3.89; N, 7.73. Found C, 53.16; H, 3.97; N, 7.52.

4-Methyl-benzoic acid methyl ester (25): Solid, m.p. 35-36°C (Lit[18] 37°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.91 (d, 2H, *J*=8.4 Hz), 7.23-7.21 (d, 2H, *J*=8.0 Hz), 3.89 (s, 3H), 2.39 (s, 3H); EIMS: 150 [M^+], 119, 91, 65, 51. Anal calc. for $C_9H_{10}O_2$. C, 71.98; H, 6.71. Found C, 72.08; H, 6.60.

Benzoic acid benzyl ester (26): Colorless oil (Lit[19]); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08-8.06 (m, 2H), 7.55-7.21 (m, 8H), 5.35 (s, 2H); EIMS: 212 [M^+], 194, 167, 105, 91, 77, 65. Anal Calc. for $C_{14}H_{12}O_2$. C, 79.22; H, 5.70. Found C, 79.33; H, 5.58.

Benzoic acid octyl ester (27): Colorless liquid, b.p.148-151 °C/5 Torr (Lit[20] 180-182 °C/20 Torr); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05-7.97 (m, 2H), 7.55-7.30 (m, 3H), 4.26 (t, 2H, *J*=6.8 Hz), 1.78-1.61 (m, 2H), 1.39-1.18 (m, 10H), 0.82 (t, 3H, *J*=6.8 Hz);

EIMS: 234 [M^+], 123, 105, 77, 56. Anal Calc. for $C_{15}H_{22}O_2$. C, 76.88; H, 9.46. Found C, 76.97; H, 9.35.

Benzoic acid 3-methyl-butyl ester (28): Colorless liquid, b.p. 114-115 ^oC/6 Torr (Lit[21] 108-110 ^oC/3-4 torr); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18-8.02 (m, 2H), 7.64-7.42 (m, 3H), 4.5 (t, 2H, *J*=7.2 Hz), 1.98-1.81 (m, 3H), 0.98 (d, 6H, *J*=6.0 Hz); EIMS: 192 [M^+], 123, 105, 77, 70, 55. Anal Calc. for $C_{12}H_{16}O_2$. C, 74.97; H, 8.39. Found C, 75.09; H, 8.26.

Benzoic acid 2-methoxy-ethyl ester (29): Colorless oil (Lit[19]); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.02 (d, 2H, *J*=4.8 Hz), 7.52 (dd, 1H, *J*=8.0 Hz), 7.38 (dd, 2H, *J*=7.6 Hz), 4.44 (t, 2H, *J*=4.2 Hz), 3.69 (t, 2H, *J*=5.2 Hz), 3.40 (s, 3H); EIMS: 180 [M^+], 105, 77, 58. Anal Calc. for $C_{10}H_{12}O_3$. C, 66.65; H, 6.71. Found C, 66.75; H, 6.60.

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