Supporting Informations for Palladium Catalysed Hydroamidation of Alkenes

General Information

^{1}H NMR Spectra were recorded on Bruker DPX 250 and DPX 500 spectrometers in deuterochloroform, unless stated otherwise, operating at 250 and 500 MHz respectively. ^{13}C NMR Spectra were recorded on a Bruker DPX 250 spectrometer operating at 62.5 MHz. Chemical shifts are quoted relative to residual solvent (7.25 ppm for ^{1}H and 77.0 ppm for ^{13}C of $CDCl_3$) and coupling constants (*J*) are given in Hz. For convenience, the following abbreviations are used to indicate the multiplicity of the signals: s singlet; d doublet; t triplet; q quartet; qu quintet; dd doublet of doublets; m multiplet; br broad. The temperature of acquisition of the NMR spectra was 298 ± 3 K. High resolution mass spectral (HRMS) analyses were measured on a Kratos 890 spectrometer by means of EI, FAB, FIB or ES techniques. All anhydrous solvents were dried by standard techniques and freshly distilled before use or purchased in anhydrous form from Fluka. All flash chromatography was carried out using dry-packed Merck 9385 Kieselgel 60 silica gel. Reactions were monitored by thin layer chromatography (TLC), carried out on Kieselgel 60 PF_{254} (Merck) 0.2 mM plates. All chemicals were purchased from The Aldrich Chemical Company, Fluka, Lancaster or Avocado and distilled or recrystallised before use, where possible. All reactions were carried out under argon unless stated otherwise.

General Procedure for Palladium Catalysed Hydroamidation of Alkenes

Method A: For carbamate : enone ratio 1.5:1. The enone and benzyl carbamate (1.5 eq.), in dichloromethane (1 mL per mmol of enone), were added to a stirred solution of bis(acetonitrile)palladium (II) chloride (0.1 eq.) in dichloromethane (1 mL per mmol of enone). The reaction was stirred at room temperature for 14-24 hours. The reaction mixture filtered through a pad of silica to remove the catalyst (eluted with diethyl ether) and the solvent was removed from the resulting filtrate under reduced pressure. Purification by flash silica gel chromatography (diethyl ether-hexane 1:3) afforded the ketone.

Method B: For carbamate : enone ratio 1:2/3. The enone (2 eq.) and benzyl carbamate (1 eq.), in dichloromethane (1 mL per mmol of carbamate), were added to a stirred solution of bis(acetonitrile)palladium (II) chloride (0.1 eq.) in dichloromethane (1 mL per mmol of carbamate). The reaction was stirred at room temperature for 9 hours. The reaction mixture filtered through a pad of silica to remove the catalyst (eluted with diethyl ether)

and the solvent was removed from the resulting filtrate under reduced pressure. Purification by flash silica gel chromatography (ethyl acetate-hexane 1:3) afforded the ketone.

Amidation Reactions by *Method A*

Amidation of Methyl vinyl ketone 1a

4-*N*-(Benzyloxycarbonyl)-butan-2-one 2a. 1 mmol scale, 14 hrs., gave 186 mg, 88 %, white solid, R_f = 0.18 in diethyl ether-hexane 1:3 . ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5 H), 5.27 (br, 1 H), 5.07 (s, 2 H), 3.42-3.35 (q, 2 H, J = 6.0 Hz), 2.67-2.63 (t, 2 H, J = 5.9 Hz), 2.11 (s, 3 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 208.1, 156.4, 136.6, 128.6, 128.2, 128.1, 66.7, 43.3, 35.7, 30.1.

Amidation of 4-Hexen-2-one 1a

5-*N*-(Benzyloxycarbonyl)-hexan-3-one 2b. 1 mmol scale, 24 hrs., gave 210 mg, 84 %, R_f = 0.20 in diethyl ether-hexane 1:3, white solid. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.37-7.24 (m, 5 H), 5.22 (br, 1 H), 5.10-5.05 (d, 1 H, *J* = 12.2 Hz), 5.05-5.01 (d, 1 H, *J* = 12.2 Hz), 4.11-3.97 (m, 1 H), 2.72-7.63 (dd, 1 H, *J* = 16.6, 5.1 Hz), 2.58-2.49 (dd, 1 H, *J* = 16.6, 6.1 Hz), 2.42-2.34 (br, 2 H), 1.21-1.82 (d, 3 H, *J* = 6.8 Hz), 1.04-0.98 (t, 3 H, *J* = 7.3 Hz); ^{13}C NMR (250 MHz, $CDCl_3$) δ 210.1, 155.6, 136.6, 128.5, 128.2, 128.0, 66.5, 47.8, 43.9, 36.6, 20.6, 7.6; HRMS (+ESI) *m*/*z* calcd. for $[C_{14}H_{19}NO_3Na]^+$ 272.1263, found for $[M]^+$ 272.1261.

Amidation of (*E*)-1-Phenyl-2-penten-1-one, 1c

3-*N*-(Benzyloxycarbonyl)-1-phenyl-pentan-1-one 2c. 1 mmol scale, 24 hrs., gave 310 mg, 99 %, R_f = 0.22 in ethyl acetate-hexane 1:3, pale yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.95-7.92 (m, 2 H), 7.58-7.41 (m, 3 H), 7.34-7.24 (m, 5 H), 5.42-5.39 (br, 1 H, *J* = 7.7 Hz), 5.12-5.08 (d, 1 H, *J* = 12.7 Hz), 5.08-5.03 (d, 1 H, *J* = 12.7 Hz), 4.13-3.98 (m, 1 H), 3.37-3.27 (dd, 1 H, *J* = 16.7, 4.4 Hz), 3.14-3.05 (dd, 1 H, 16.7, 5.9 Hz), 1.72-1.60 (m, 2 H), 0.97-0.91 (t, 3 H, *J* = 7.4 Hz); ^{13}C NMR (250 MHz, $CDCl_3$) δ 198.9, 156.1, 137.0, 136.7, 133.3, 128.7, 128.5, 128.5, 128.1, 128.0, 66.5, 50.0, 27.3, 10.8; HRMS (+ES) *m*/*z* calcd. for $[C_{19}H_{21}NO_3Na]^+$ 334.14191, found for $[M]^+$ 334.14130.

Amidation of 2-cyclohexan-1-one 1e

3-*N*-(Benzyloxycarbonyl)-cyclohexanone 2e. 1 mmol scale, 20 hrs., gave 160 mg, 65 %, R_f = 0.11 in ethyl acetate-hexane 1:3, off-white solid. ^{1}H NMR (250 MHz, $CDCl_3$) δ

7.33-7.29 (m, 5 H), 5.07 (br, 2 H), 4.95-4.93 (br, 1 H, J = 5.8 Hz), 3.98-3.92 (br, 1 H), 2.72-2.64 (dd, 1 H, J = 14.1. 4.7 Hz), 2.38-2.17 (m, 3 H), 2.09-1.87 (m, 2 H), 1.68-1.66 (m, 2 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 208.7, 155.3, 136.3, 128.6, 128.3, 128.1, 66.8, 50.2, 48.0, 40.8, 31.1, 21.9.

Amidation Reactions by *Method B*

Amidation of 2-cyclohexan-1-one 1e

3-*N*-(Benzyloxycarbonyl)-cyclohexanone 2e. 1 mmol scale, **2** eq. enone, 9 hrs., gave 198 mg, 80 %, off-white solid, R_f = 0.11 in 1:3 ethyl acetate:hexane.

3-*N*-(Benzyloxycarbonyl)-cyclohexanone 2e. 1 mmol scale, **3** eq. enone, 9 hrs., gave 200 mg, 81 %, off-white solid, R_f = 0.11 in 1:3 ethyl acetate:hexane.

Amidation of tri-substituted alkenes

General procedure

Method A. The enone and benzyl carbamate (1.5 eq.), in dichloromethane (1 mL per mmol of enone), were added to a stirred solution of bis(acetonitrile)palladium (II) chloride (0.1 eq.) in dichloromethane (1 mL per mmol of enone). The reaction was stirred at room temperature for the appropriate time. The reaction mixture filtered through a pad of silica to remove the catalyst (eluted with diethyl ether) and the solvent was removed from the resulting filtrate under reduced pressure. Purification by flash silica gel chromatography (diethyl ether-hexane 1:3) afforded the ketone.

Amidation of Mesityl Oxide 1f

4-*N*-(Benzyloxycarbonyl)-4-methyl-pentan-2-one 2f 1 mmol scale, 8 hrs., gave 181 mg, 73 %, R_f = 0.28 in ethyl acetate-hexane 1:3, off-white solid. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.37-7.30 (m, 5 H), 5.19 (br, 1 H), 5.03 (s, 2 H), 2.86 (s, 2 H), 2.08 (s, 3 H), 1.36 (s, 6 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 207.8, 154.9, 136.7, 128.5, 128.0, 127.9, 66.1, 51.5, 51.4, 31.8, 27.5; HRMS (EI) *m*/*z* calcd. for $[C_{14}H_{19}NO_3]^+$ 249.13649, found for $[M]^+$ 249.13755.

Amidation of 1-Acetyl-Cyclohexene 1h

1-Acetyl-3-*N*-(Benzyloxycarbonyl)-cyclohexane 2h. 1 mmol scale, 36 hrs., gave 151 mg, 55 %, off-white solid, R_f = 0.19 in 1:3 ethyl acetate-hexane. ^{1}H NMR (250 MHz, $CDCl_3$)

δ 7.36-7.32 (m, 5 H), 5.10-5.05 (d, 1 H, *J* = 12.6 Hz), 5.04-4.99 (d, 1 H, *J* = 12.6 Hz), 4.76-4.73 (br, 1 H), 3.81-3.67 (m, 1 H, J = 11.0, 4.1 Hz), 2.41-2.27 (dt, 1H, *J* = 11.0, 3.4 Hz), 2.12 (s, 3 H), 2.06-2.00 (m, 1 H), 1.84-1.81 (m, 1 H), 1.77-1.71 (m, 2 H), 1.52-1.35 (m, 2 H), 1.30-1.11 (m, 2 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 210.8, 155.5, 136.5, 128.5, 128.1, 128.0, 66.7, 57.8, 51.3, 32.9, 28.7, 27.5, 24.8, 24.6; HRMS (+ESI) *m*/*z* calcd. for $[C_{16}H_{21}NO_3Na]^+$ 298.1419, found for $[M]^+$ 298.1428.