Supporting Information

Ruthenium Hydride/Nitrogen Tridentate Ligand-Catalyzed \( \alpha \)-Alkylation of Acetamides with Primary Alcohols.

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General Information. \(^1^H\) NMR spectra are recorded with a JEOL ECS-400 (400 MHz) spectrometers in CDCl\(_3\) and referenced at 0.0 ppm for TMS in CDCl\(_3\). \(^{13}\)C NMR spectra were recorded with JEOL ECS-400 (100 MHz) spectrometers in CDCl\(_3\) and are referenced at 77.16 ppm for CDCl\(_3\). Chemical shifts are reported in parts per million (δ). Splitting patterns are indicated as follows: br, broad; brs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet. Infrared spectra were obtained on a JASCO FT/IR-4100 spectrometer; absorptions were reported in reciprocal centimeters. Both conventional and high resolution mass spectra were recorded with a JEOL MS-700 spectrometer. Melting point was measured by BÜCHI Melting Point B-540. The products were purified by flash column chromatography on silica gel (Kanto Chem. Co. Silica Gel 60N (spherical, neutral, 40-50 µm)) and/or preparative HPLC (Japan Analytical Industry Co., Ltd., LC-908) with GPC columns using CHCl\(_3\) as an eluent. RuHCl(CO)(PPh\(_3\))\(_3\) was purchased from Wako Pure Chemical Industries, Ltd. Other reagents were commercially available and used without further purification. L1 was prepared with procedure according to the procedure. \(^1\)

Typical Procedure for the Ruthenium Hydride-Catalyzed α-Alkylation of Acetamides with Primary Alcohols:

<Method A>
Table 2, entry 2.
RuHCl(CO)(PPh\(_3\))\(_3\) (14.6 mg, 0.015 mmol), \(p\)-tert butyl benzylalcohol (2b, 84.2 mg, 0.51 mmol), KO’Bu (70.3 mg, 0.63 mmol), 2,2’-bipyridine (8.1 mg, 0.052 mmol) and \(N,\text{N}\)-dimethylacetamide (DMA; 1a) (2 mL) were placed in a screw capped test tube. The test tube was purged with nitrogen and sealed. The mixture was stirred at 140 °C for 18 h. When the reaction was finished, the reaction mixture was cooled to room temperature and then quenched with water (5 mL). Organic layer was extracted with Et\(_2\)O (10 mL) three times, washed by brine (30 mL), and then dried over MgSO\(_4\). After concentration under reduced pressure, the residue was purified by flash chromatography on silica gel (eluent: Et\(_2\)O) to give the corresponding amide 3b (73.2 mg, 61%).

<Method B>
Table 2, entry 1
RuHCl(CO)(PPh\(_3\))\(_3\) (14.6 mg, 0.015 mmol), benzylalcohol (2a, 54.7 mg, 0.51 mmol), KO’Bu (73.1 mg, 0.65 mmol), L1 (8.3 mg, 0.034 mmol) and \(N,\text{N}\)-dimethylacetamide (DMA; 1a) (2 mL) were placed in a screw capped test tube. The test tube was purged with nitrogen and sealed. The mixture was stirred at 140 °C for 18 h. When the reaction was finished, the reaction mixture was cooled to room temperature and then quenched with water (5 mL). Organic layer was extracted with Et\(_2\)O (10 mL) three times, washed by brine (30 mL), and then dried over MgSO\(_4\). After concentration under reduced pressure, the residue was purified by flash chromatography on silica

gel (eluent: Et₂O) to give the corresponding amide 3a (66.4 mg, 74%).

**N,N-Dimethyl-3-phenylpropanamide (3a)**

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 2.60-2.64 (m, 2H), 2.93-2.99 (m, 8H), 7.18-7.31 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 31.50, 35.47, 35.57, 37.29, 126.22 (2×CH), 128.57 (2×CH), 141.64, 172.32.

**3-(4-(tert-Butyl)phenyl)-N,N-dimethylpropanamide (3b)**

Brown solid; m.p. 68-69 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.31 (s, 9H), 2.59-2.63 (m, 2H), 2.92-2.96 (m, 8H), 7.16 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 30.91, 31.53 (3×CH₃), 34.51, 35.49, 35.57, 37.29, 125.49 (2×CH), 128.20 (2×CH), 138.54, 149.05, 172.48; IR (KBr) 1639 cm⁻¹; EIMS m/z (relative intensity) 233 (M⁺, 89), 219 (14), 218 (86), 161 (15), 160 (22), 147 (17), 146 (18), 145 (100), 132 (14), 131 (31), 117 (38), 115 (16), 105 (12), 91 (23), 72 (25); HRMS (EI) m/z calcd for C₁₅H₂₃NO: 233.1780, found: 233.1786.

**3-[(1,1'-Biphenyl)-4-yl]-N,N-dimethylpropanamide (3c)**

White solid; m.p. 72-73 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.64-2.68 (m, 2H), 2.96 (s, 3H), 2.97 (s, 3H), 3.00-3.04 (m, 2H), 7.29-7.35 (m, 3H), 7.41-7.45 (m, 2H), 7.52-7.61 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 31.09, 35.39, 35.60, 37.32, 127.12 (2×CH), 127.22, 127.34 (2×CH), 128.88 (2×CH), 129.01 (2×CH), 139.22, 140.78, 141.12, 172.27; IR (neat) 1636 cm⁻¹; EIMS m/z (relative intensity) 253 (M⁺, 7), 180 (11), 119 (35), 117 (61), 115 (59), 72 (13), 70 (19), 65 (34), 63 (100); HRMS (EI) m/z calcd for C₁₇H₁₉NO: 253.1467, found: 253.1460.

**3-(2-Methoxyphenyl)-N,N-dimethylpropanamide (3d)**

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 2.57-2.61 (m, 2H), 2.92-2.96 (m, 8H), 3.83 (s, 3H), 6.84-6.90 (m, 2H), 7.17-7.22 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 26.82, 33.87, 35.51, 37.30, 55.33, 110.31, 120.66, 127.60, 129.80, 130.33, 157.61, 173.01.

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3-(3-Methoxyphenyl)-N,N-dimethylpropanamide (3e)

Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.61-2.63 (m, 2H), 2.93-2.97 (m, 8H), 3.80 (s, 3H), 6.74-6.83 (m, 3H), 7.19-7.23 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 31.56, 35.39, 35.60, 37.32, 55.32, 111.51, 114.32, 120.92, 129.60, 143.29, 159.82, 172.31; IR (neat) 1651 cm$^{-1}$; EIMS m/z (relative intensity) 207 (M$^+$, 27), 206 (100), 135 (12), 134 (13), 72 (13); HRMS (EI) m/z calcd for C$_{12}$H$_7$NO: 207.1259, found: 207.1256.

3-(4-Methoxyphenyl)-N,N-dimethylpropanamide (3f)$^2$

Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.58-2.60 (m, 2H), 2.89-2.95 (m, 8H), 3.79 (s, 3H), 6.83 (d, $J = 8.3$ Hz, 2H), 7.14 (d, $J = 8.3$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 30.63, 35.57, 35.71, 37.32, 55.40, 113.99 (2×CH), 129.49 (2×CH), 133.67, 158.08, 172.44.

N,N-Dimethyl-3-(3-(trifluoromethyl)phenyl)propanamide (3g)

Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.61-2.65 (m, 2H), 2.95 (brs, 6H), 3.02-3.06 (m, 2H), 7.40-7.47 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 31.14, 34.94, 35.57, 37.24, 123.09 (d, $J_{CF} = 3.8$ Hz), 124.30 (q, $J_{CF} = 271.7$ Hz), 125.18 (d, $J_{CF} = 3.9$ Hz), 128.99, 130.80 (q, $J_{CF} = 31.8$ Hz), 132.16, 142.55, 171.67; IR (neat) 1652 cm$^{-1}$; EIMS m/z (relative intensity) 245 (M$^+$, 100), 226 (13), 173 (35), 172 (26), 159 (54), 153 (25), 151 (18), 133 (33), 127 (15), 119 (17), 117 (31), 115 (30), 109 (17), 103 (12), 86 (14), 73 (12), 72 (34), 65 (12), 63 (38); HRMS (EI) m/z calcd for C$_{12}$H$_4$F$_3$NO: 245.1027, found: 245.1206.

N,N-Dimethyl-3-(naphthalen-1-yl)propanamide (3h)

Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.72-2.76 (m, 2H), 2.86 (s, 3H), 2.97 (s, 3H), 3.43-3.47 (m, 2H) 7.34-7.42 (m, 2H), 7.47-7.54 (m, 2H) 7.73 (d, $J = 7.8$ Hz, 1H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.06 (d, $J = 8.3$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 28.62, 34.67, 35.57, 37.23, 123.71, 125.68, 125.75, 126.15, 126.29, 127.04, 128.97, 131.81, 133.97, 137.73, 172.40; IR (neat) 1651 cm$^{-1}$; EIMS m/z (relative intensity) 227 (M$^+$, 91), 226 (14), 181 (13), 175 (14), 155 (46), 154 (100), 153 (73), 152 (42), 151 (12), 142 (12), 141 (79), 139 (18), 128 (23), 127 (18), 115 (39), 72 (28); HRMS (EI) m/z calcd for C$_{13}$H$_7$NO: 227.1310, found: 227.1308.

3-(Furan-2-yl)-N,N-dimethylpropanamide (3i)

Brown solid; m.p. 43-44 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.64-2.68 (m, 2H), 2.96-3.01 (m, 8H), 6.03 (d, $J = 3.7$ Hz, 1H), 6.29 (d, $J = 1.8$ Hz, 1H), 7.30 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 23.81, 31.91, 35.55, 37.19, 105.33, 110.36, 141.11, 155.13, 171.78; IR (neat) 1654 cm$^{-1}$; EIMS m/z (relative intensity) 167 (M$^+$, 100), 95 (13), 94 (25), 81 (26), 72 (26);
HRMS (EI) m/z calcd for C₉H₁₃NO₂: 167.0946, found: 167.0941.

1-Morpholino-3-phenylpropan-1-one (3j)

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 2.60-2.64 (m, 2H), 2.96-3.00 (m, 2H), 3.35-3.37 (m, 2H), 3.50-3.52 (m, 2H), 3.58-3.65 (m, 4H) 7.21-7.31 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 31.60, 34.95, 42.06, 46.09, 66.59, 66.98, 126.41, 128.59 (2×CH), 128.68 (2×CH), 141.18, 171.00; IR (neat) 1644 cm⁻¹; EIMS m/z (relative intensity) 219 (98), 133 (15), 128 (31), 105 (83), 104 (45), 103 (18), 91 (100), 88 (28), 79 (12), 78 (15), 77 (27), 65 (12), 63 (28), 57 (28), 56 (16), 51 (10); HRMS (EI) m/z calcd for C₁₃H₁₇NO₂: 219.1259, found: 219.1267.

N,N-Dimethyloctanamide (3k)

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, J = 6.8 Hz, 3H), 1.28-1.32 (m, 8H), 1.61-1.65 (m, 2H), 2.29-2.32 (m, 2H), 2.94 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 14.22, 22.75, 25.32, 29.25, 29.61, 31.85, 33.56, 35.47, 37.43, 173.41; IR (neat) 1659 cm⁻¹; EIMS m/z (relative intensity) 171 (M⁺, 10), 100 (25), 87 (100), 85 (41), 83 (62), 72 (32), 57 (11); HRMS (EI) m/z calcd for C₁₀H₂₁NO: 171.1623, found: 171.1630.

3-Cyclohexyl-N,N-dimethylpropanamide (3l)

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 0.86-0.95 (m, 5H), 1.19-1.24 (m, 4H), 1.50-1.57 (m, 2H), 1.60-1.74 (m, 5H), 2.30-2.34 (m, 2H), 2.94 (s, 3H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 26.41, 26.71 (2×CH₂), 31.07, 32.73, 33.28 (2×CH₂), 35.52, 37.44, 37.60, 173.70; IR (neat) 1652 cm⁻¹; EIMS m/z (relative intensity) 183 (M⁺, 8), 100 (36), 68 (100), 25 (36), 55 (17); HRMS (EI) m/z calcd for C₁₁H₂₃NO: 183.1623, found: 183.1623.

N,N-Dimethyl-5-methylhexanamide (3m)

Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 0.80-0.95 (m, 5H), 1.19-1.24 (m, 2H), 1.53-1.67 (m, 4H), 2.27-2.31 (m, 2H), 2.94 (s, 3H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 22.69 (2×CH₂), 23.19, 28.06, 33.79, 35.48, 37.43, 38.91, 173.39; IR (neat) 1651 cm⁻¹; EIMS m/z (relative intensity) 157 (M⁺, 16), 114 (19), 100 (17), 87 (100), 72 (44), 63 (16); HRMS (EI) m/z calcd for C₈H₁₀NO: 157.1467, found: 157.1460.