Convenient and improved protocols for the hydrogenation of esters at near-ambient temperatures using Ru catalysts derived from (P,P), (P,N,N) and (P,N,O) ligands.

Ian Carpenter,[a] Susan C. Eckelmann,[b] Michael T. Kuntz,[b] José A. Fuentes,[a] Marcia B. France,[b] and Matthew L. Clarke[a]*

Supporting information:

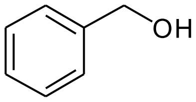
General information: All reactions were carried out under an inert atmosphere using Schlenk techniques. Commercially available starting materials and reagents were used without further purification, unless otherwise stated. Methyl benzoate, methyl 4-methylbenzoate, methyl 4-fluorobenzoate, methyl 4-chlorobenzoate, methyl 4-bromobenzoate, methyl 2-naphthoate and methyl nicotinate were all obtained from Sigma-Aldrich. Methyl 4-bromobenzoate was obtained from Alfa Aesar. $[RuCl_2(NBD)(Py)_2]$ and the $[RuCl_2(PNX)(DMSO)]$ complexes were prepared using literature procedures[4,5]. ^1H, ^{13}C and ^{19}F were performed on either a Bruker 400 Avance or a Bruker 300 Avance spectrometer. Chemical shifts are quoted as ppm and referenced to residual solvent protons. Proton multiplicity are given using the following abbreviations; singlet (s), doublet (d), triplet (t), q (quartet), multiplet (m), broad (br) and coupling constants (*J*) are quoted as Hz. High and low resolution mass spectra were recorded on a Waters Micromas LCT.

General procedure for the hydrogenation of ester using *in situ* formed $[RuCl_2(diamine)(diphosphine)]$ complexes using microwave heating (A): Under a nitrogen atmosphere, $[RuCl_2(NBD)(Py)_2]$ (4.0 µmol, 0.5 mol%) and diphosphine (4.0 µmol, 0.5 mol%) were dissolved in 2-methyltetrahydrofuran (3ml) in a microwave vial equipped with a stirring bead, the mixture was heated to 120°C for 5 mins using a microwave. The diamine (4.0 µmol, 0.5 mol%) was then added and heated for a further 5 mins at 120°C in the microwave. The substrate (0.8 mmol) and KO*t*-Bu (0.2 mmol, 25 mol%) were added. The vial was then transferred to a steel autoclave, with the needle used as a nitrogen inlet left open and pressurised with hydrogen gas (50 bar). The autoclave was heated to the required temperature using an oil bath and left to stir. After the required amount of time the autoclave was cooled and depressurised. The solvent was then removed and the resulting residue was purified using column chromatography (Silica; ethyl acetate/ hexane), solvents were removed carefully at room temperature for more volatile substrates.

General procedure for the hydrogenation of ester using *in situ* formed $[RuCl_2(diamine)(diphosphine)]$ complexes (B): Under a nitrogen atmosphere, $[RuCl_2(NBD)(Py)_2]$ (4.0 µmol, 0.5 mol%) and diphosphine (4.0 µmol, 0.5 mol%) were dissolved in 2-methyltetrahydrofuran (3ml) in a microwave vial equipped with a stirring bead, the mixture was refluxed for 10 mins. The diamine (4.0 µmol, 0.5 mol%) was then added and refluxed for a further 10 mins. The substrate (0.8 mmol) and KO*t*-Bu (0.20 mmol, 25 mol%) were added. The vial was then transferred to a steel autoclave, with the needle used as a nitrogen inlet left open and pressurised with hydrogen gas (50 bar). The autoclave was heated to the required temperature using an oil bath and left to stir. After the required amount of time the autoclave was cooled and depressurised. The solvent was then removed and the resulting residue was purified using column chromatography (Silica; ethyl acetate/ hexane), solvents were removed carefully at room temperature for more volatile substrates.

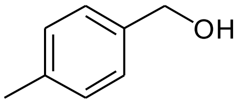
General procedure for the hydrogenation of esters using $[RuCl_2(PNX)(DMSO)]$ complexes (C): Under a nitrogen atmosphere, the substrate (0.8 mmol) and $[RuCl_2(PNX)(DMSO)]$ (4.0 µmol, 0.5 mol%) were dissolved in methyltetrahydrofuran (3ml) in a microwave vial equipped with a stirring bead, KO*t*-Bu (0.2 mmol, 25 mol%) was added. The vial was then transferred to a steel autoclave, with the needle used as a nitrogen inlet left open and pressurised with hydrogen gas. The autoclave was heated to the required temperature using an oil bath and left to stir. After the required amount of time the autoclave was cooled and depressurised. The solvent was then removed and the resulting residue was purified using column chromatography (Silica; ethyl acetate/ hexane), solvents were removed carefully at room temperature for more volatile substrates.

Benzyl alcohol[1]:



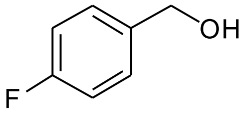
Prepared using general procedure **B**. Methyl benzoate (124 µl, 0.84 mmol), $[RuCl_2(NBD)(Py)_2]$ (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A yellow oil was obtained after chromatography (88 mg, 97% yield). δ_H (400 MHz, $CDCl_3$) 2.14 (br s, 1H, O***H***), 4.67 (s, 2H, C***H***$_2$), 7.27-7.34 (m, 1H, Ar***H***), 7.34-7.38 (m, 4H, 4xAr***H***). δ_C (75 MHz, $CDCl_3$) 65.3 (***C***H$_2$), 127.0 (2xAr***C***H), 127.7 (Ar***C***H), 128.6 (2xAr***C***H), 140.9 (Ar***C***). m/z (GCMS) 108 (M+).

4- Methylbenzyl alcohol[1]:



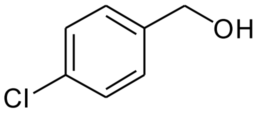
Prepared using general procedure **B**. Methyl 4-methylbenzoate (123.4 mg, 0.82 mmol), $[RuCl_2(NBD)(Py)_2]$ (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A white solid was obtained after chromatography (96 mg, 96% yield). δ_H (400 MHz, $CDCl_3$) 1.87 (br s, 1H, O***H***),2.26 (s,3H, C**H$_3$**), 4.53 (s, 2H, C***H***$_2$), 7.15 (dd, J_1= 7.8, J_2= 26.7, 4H, 4xAr***H***). δ_C (75 MHz, $CDCl_3$) 21.2 (***C***H$_3$) 65.2 (***C***H$_2$), 127.1 (2xAr***C***H), 129.2 (2xAr***C***H), 137.4 (Ar***C***), 137.9 (Ar***C***). m/z (ES+) 145.01 (M+Na$^+$).

4-Fluorobenzyl alcohol[2]:



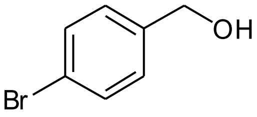
Prepared using general procedure **B**. Methyl 4-fluorobenzoate (156 µl, 0.85 mmol), $[RuCl_2(NBD)(Py)_2]$ (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A yellow oil was obtained after chromatography (103 mg, 96% yield). δ_H (400 MHz, $CDCl_3$) 2.02 (br s, 1H, O***H***), 4.63 (s, 2H, C***H***$_2$), 6.99-7.09 (m, 2H, 2xArC***H***) 7.28-7.36 (m, 2H, 2xArC***H***). δ_C (75 MHz, $CDCl_3$) 64.6 (***C***H$_2$), 115.3 (Ar***C***H), 115.5 (Ar***C***H), 128.7 (Ar***C***H), 128.8 (Ar***C***H),136.6 (***C***CH$_2$OH), 161.1 (**C**F). Δ_F (377 MHz, $CDCl_3$) 115.4. m/z (GCMS) 126 (M+).

4-Chlorobenzyl alcohol[1]:



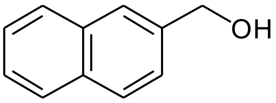
Prepared using general procedure **B**. Methyl 4-Chlorobenzoate (143.4mg, 0.84 mmol), $[RuCl_2(NBD)(Py)_2]$ (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A white solid was obtained after chromatography (117 mg, 98% yield). δ_H (400 MHz, $CDCl_3$) 1.96 (br s, 1H, O***H***), 4.64 (s, 2H, C***H***$_2$), 7.31 (dd, J_1= 8.8, J_2= 12.1, 4H, 4xArC***H***). δ_C (75 MHz, $CDCl_3$) 64.5 (***C***H$_2$), 128.3 (2xAr***C***H), 128.7 (2xAr***C***H),133.3 (***C***CH$_2$OH), 139.3 (**C**Cl). m/z (GCMS) 142 (M+).

4-**Bromobenzyl alcohol**[1]:



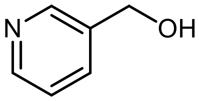
Prepared using general procedure **B**. Methyl 4-bromobenzoate (180.6 mg, 0.84 mmol), [RuCl$_2$(NBD)(Py)$_2$] (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A white solid was obtained after chromatography (149 mg, 95% yield). δ_H (400 MHz, CDCl$_3$) 2.28 (br s, 1H, O***H***), 4.60 (s, 2H, C***H***$_2$), 7.20 (d, *J*= 8.6, 2H, 2xArC***H***) 7.45 (d, *J* = 8.6, 2H, 2xArC***H***). δ_C (75 MHz, CDCl$_3$) 64.5 (***C***H$_2$), 121.5 (***C***CH$_2$OH), 128.6 (2xAr***C***H), 131.6 (2xAr***C***H), 139.8 (**C**Br). m/z (GCMS) 186 (M+).

2-Naphthylmethanol[3]:



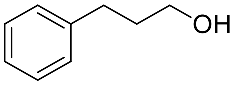
Prepared using general procedure **B**. Methyl 2-naphthoate (186.1 mg, 0.84 mmol), [RuCl$_2$(NBD)(Py)$_2$] (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A white solid was obtained after chromatography (121 mg, 91% yield). δ_H (400 MHz, CDCl$_3$) 2.50 (br s, 1H, O***H***), 4.81 (s, 2H, C***H***$_2$), 7.42-7.53 (m, 3H, 3xArC***H***) 7.77 (s, 1H ArC***H***) 7.80-7.86 (m, 3H, 3xArC***H***). δ_C (75 MHz, CDCl$_3$) 65.3 (***C***H$_2$), 125.2 (Ar***C***H), 125.4 (Ar***C***H), 125.9 (Ar***C***H), 126.2 (Ar***C***H), 127.8 (Ar***C***H), 127.9 (Ar***C***H), 128.3 (Ar***C***H), 132.9 (Ar***C***), 133.4 (Ar***C***), 138.4 (**C**CH$_2$OH). m/z (ES+) 180.94 (M+Na$^+$).

3-Pyridinemethanol[6]:



Prepared using general procedure **B**. Methyl nicotinate (114.2 mg, 0.83 mmol), [RuCl$_2$(NBD)(Py)$_2$] (1.8 mg, 4.27 µmol), 1,3-bis(diphenylphosphino)propane (1.8 mg, 4.37 µmol), 2-picolylamine (0.5 µl, 4.41 µmol). A colourless oil was obtained after chromatography (86 mg, 95% yield). δ_H (400 MHz, CDCl$_3$) 2.48 (br s, 1H, O***H***), 4.74 (s, 2H, C***H***$_2$), 7.30 (ddd, J_1 = 0.7, J_2 = 4.9, J_3 = 7.8, 1H, 1x ArC***H***), 7.71-7.76 (m, 1H, 1XArC***H***), 8.51 (dd, J_1 = 1.6, J_1 = 4.9, 1H, 1xArC***H***), 8.57 (d, J_1 = 1.7, 1H, ArC***H***). δ_C (75 MHz, CDCl$_3$) 62.7 (***C***H$_2$), 123.7 (Ar***C***H), 135.4 (Ar***C***H), 138.2 (Ar***C***), 148.2 (Ar***C***H), 148.5 (Ar***C***H). m/z (GCMS) 109 (M+).

Benzenepropanol[7]:



Prepared using general procedure **C**. Ethyl 3-phenylpropionate (71 µl, 0.40 mmol), Ru precursor **1** (1.2 mg, 2.05 µmol). A colourless oil was obtained after chromatography (42 mg, 78% yield). δ_H (400 MHz, CDCl$_3$) 1.50 (br s, 1H, O***H***), 1.75-1.87 (m, 2H, CH$_2$C***H***$_2$CH$_2$OH), 2.63 (t, *J*= 7.7, C***H***$_2$CH$_2$CH$_2$OH), 3.60 (t, *J*= 6.4, CH$_2$CH$_2$C***H***$_2$OH), 7.10-71.5 (m, 3H, 3xArC***H***), 7.18-7.25 (m, 2H, 2xArC***H***). δ_C (125 MHz, CDCl$_3$) 32.1 (***C***H$_2$), 34.3 (***C***H$_2$), 62.3 (***C***H$_2$OH), 125.9 (Ar***C***H), 128.4 (2xAr***C***H), 128.5 (2xAr***C***H), 141.8 (Ar***C***).

1. F. Jiang, D. Bézier, J. Sortais, and C. Darcel, *Advanced Synthesis & Catalysis.*, 2011, **353**, 239-244.
2. P. Tang, T. Furuya, and T. Ritter, *J. Am. Chem. Soc.*, 2011, **132**, 12150-12154.
3. S. Chakraborty, J. A. Krause, and H. Guan, *Organometallics.*, 2011, **28**, 582-586.
4. C. Leong, O.Akotsi, M. Ferguson, and S. Bergens, *Chem. Commun*., 2003, 750–751.
5. M. Diaz-Valenzuela, S. Phillips, M. France, M. Gunn, and M. Clarke, *Chem. Eur. J.*, 2009, **15**, 1227-1232.
6. A. Dieskau, J. Begouin, and B. Plietker, *Eur. J. Org. Chem.,* 2011, **27**, 5291–5296.
7. G. Chen, C. Fu, and S. Ma, *Tetrahedron*., 2006, 62, 18, 4444–4452.