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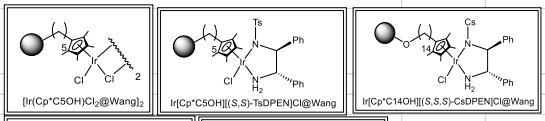
1 General

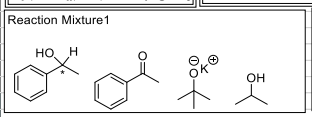
1a, and **2a** were prepared according to the literature method.[1, 2] The Wang resin, with particle sizes of 100-200 mesh, 1% cross linking of divinylbenzene and a 1.4 mmol/g loading, was purchased from Fluorochem Ltd. All reaction solvents employed were of HPLC grade. All other reagents are commercially available and were used as received.
All manipulations involving the synthesis of **3a**, **3b**, **3c, 3d, 4a, 4b, 4c** and **4d**, were conducted using standard Schlenk line techniques under an inert atmosphere.
^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AV3-400 (400/100 MHz) spectrometer and were referenced to $CHCl_3$. The values of chemical shifts are reported in parts per million (ppm) with the multiplicities of the spectra reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br), values for coupling constants (J) are assigned in Hz. Gas chromatography (GC) analyses were performed on a Hewlett Packard HP 6890 Series GC System. HPLC measurements were performed on an Agilent Technologies 1100 series system. Mass spectrometry analysis was carried out using a Bruker MaXis Impact spectrometer with Ultimate 3000 UPLC (HRMS). Electron microscopy was carried out using: Nova NanoSEM450 scanning electron microscope; FEI Tecnai TF20: FEGTEM Field emission gun TEM/STEM fitted with HAADF detector, Oxford Instruments INCA 350 EDX system/80mm X-Max SDD detector and Gatan Orius SC600A CCD camera.

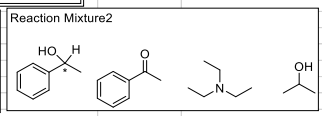
1.1 Iridium ICP MS analysis was performed by Adrian Cunliffe at the University of Leeds using Perkin Elmer Elan DRCe. Each sample was prepared by the following procedure[3]:
The overall iridium content of the continuous flow eluent was determined by combining all reaction volumes, taking 1 g of this and adding 2 mL trace-metal free concentrated hydrochloric acid HCl made up to 100 mL with ultra-pure water in a volumetric flask, mixed well and transferred to ICP sample tubes for analysis.
The iridium content of solid supported catalysts were determined by accurately weighing between 10 – 30 mg of each sample into a microwave tube. 1.5 ml trace-metal free concentrated sulfuric acid, 10 ml trace-metal free concentrated nitric acid and 3.0 ml trace-metal free concentrated hydrochloric acid were added slowly to each vessel. After stirring 20 min under room temperature, the tube was sealed and microwave heating was applied at 120 °C for 20 minutes. The samples were allowed to cool to room temperature then transferred to 100 ml volumetric flasks and made up to volume with ultra-pure water. 2.0 ml of each supernatant sample was then pipetted into 10 ml volumetric flasks. The samples were made up to volume with 2 wt% hydrochloric acid, mixed well and transferred to ICP sample tubes for analysis.

immobilized catalyst

sample	Lot No.	Ir concentration (mmol/g, as monomer)	comment
[Ir(Cp*C5OH)Cl$_2$@Wang]$_2$	MRC2066	0.70	
Ir(Cp*C5OH)(TsDPEN)Cl@Wang	YKK022-2	0.33	Tf_2O 1.1eq. DTBP 4.0eq.
	YKK022-3	0.22	Tf_2O 4.0eq. DTBP 1.1+1.5eq.
	YKK025-1	0.35	Tf_2O 2.05eq. DTBP 4.0eq.
	YKK025-1	0.31	Repeat
	YKK025-2	0.59	Tf_2O 2.05eq. DTBP 4.0eq. Without HCl wash
	MRC2082	0.32	Tf2O 4.1eq. DTBP 8.0eq.
	YKK030-2(25-1)	0.16	spent catalyst
Ir(Cp*C14OH)(TsDPEN)Cl@Wang	YKK017	0.15	
Ir(Cp*C5OH)(CsDPEN)Cl@Wang	YKK031	0.22	1st batch
	YKK038	0.14	2nd batch
	YKK044(038)	0.08	spent catalyst
	YKK061-1	0.14	n=1
	YKK061-1	0.12	n=2
Ir(Cp*C14OH)(CsDPEN)Cl@Wang	YKK027-2	0.04	-
	YKK061-2	0.066	







reaction mixture

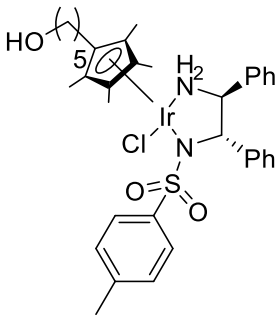
sample	Lot No.	total leaching Ir amount (mg)	used catalyst lot no.	reaction condition operation time(1RV=39min)
Reaction Mixture1 (KO*t*Bu)	YKK034-1	0.058	YKK031	CsDPEN, 60oC, 0.3M/AP, KOtBu0.02eq., 213RV
	YKK026-4	0.013	YKK022-2	TsDPEN, 80oC, 0.3M/AP, KOtBu0.05eq., 3.7RV
	YKK030-3,4	0.165	YKK027-1	CsDPEN, 70°C, 0.3M/AP, KOtBu0.05eq., 10RV
	YKK036-1	0.147	YKK031	CsDPEN, 60°C, 1.0M/AP, KOtBu0.005eq, 75RV
Reaction Mixture2 (Et_3N)	YKK040-1	0.286	YKK038	CsDPEN, 60°C, 0.3M/AP, Et3N3.0eq.,154RV
	YKK046-1	0.259	YKK038	CsDPEN, 60°C, 0.3M/AP, Et3N3.0eq.,187RV, add ligand
	YKK044	0.080	YKK038	CsDPEN, 60oC+50oC, 0.3M/AP, Et3N0.2eq.178RV(71RV/60oC+107/50oC)

standard

sample	comment
blank (2wt%HClaq.)	matrix blank
wang resin+Ir 1ppm	matrix matched standard1
wang resin+Ir 10ppm	matrix matched standard2

2 Preparation of the immobilized catalysts

Ir(Cp*$C_5H_{10}OH$){(*S,S*)-TsDPEN}Cl (**3a**)



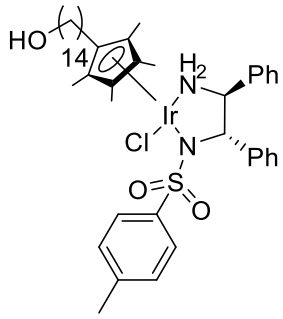
(*S,S*)-TsDPEN (1.69 g, 4.56 mmol, 2.0 equiv.), [Ir{η5-$C_5(CH_3)_4C_5H_{10}OH$}Cl_2]$_2$ (2.14 g, 2.28 mmol, 1.0 equiv.) and triethylamine (1.33 ml, 9.58 mmol, 4.2 equiv.) were added to dichloromethane (30 ml). After stirring for 24 hours under room temperature, the solution was washed with water (20 ml) three times, brine (10 ml), dried over $MgSO_4$ and the solvent evaporated. The resulting residue dried under vacuum to yield a deep purple solid (3.49 g, 4.37 mmol, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) 7.55-6.76 (m, 12H), 6.65 (d, *J* = 8.0 Hz, 2H), 4.49 (brt, 1H, N*H*), 4.30 (d, *J* = 8.0 Hz, 1H, C*H*-NTs), 4.06 (brd, 1H, N*H*), 3.73-3.60 (m, 3H, CH_2OH and C*H*-NH_2), 2.34 (s, 2H, CH_2Cp*), 2.23 (s, 3H, SO_2CH_3), 2.04-1.75 (m, 12H, $C_5(CH_3)_4$), 1.73-1.45 (m, 4H, 2 × CH_2), 1.35-1.20 (m, 2H, CH_2).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K) 147.6, 143.1, 139.3, 139.2, 128.4, 128.0, 128.0, 127.7, 127.3, 127.1, 126.7, 126.3, 86.1, 85.5, 84.9, 74.9, 69.9, 64.2, 33.9, 29.0, 26.1, 24.2, 21.1, 9.7, 9.4.

LC/MS (ESI) m/z: [M-H]$^-$ 799.2.

Ir(Cp*$C_{14}H_{28}OH$){(*S,S*)-TsDPEN}Cl (**3c**)



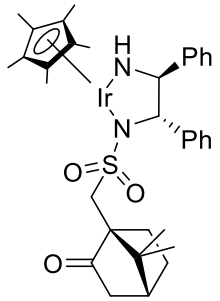
(*S,S*)-TsDPEN (869 mg, 2.34 mmol, 2.0 equiv.), [Ir{η5-$C_5(CH_3)_4C_{14}H_{28}OH$}$Cl_2$]$_2$ (1.40 g, 1.17 mmol, 1.0 equiv.) and triethylamine (0.69 ml, 4.93 mmol, 4.2 equiv.) were added to dichloromethane (15 ml). After stirring for 24 hours under room temperature, the solution was washed with water (10 ml) three times, brine (10 ml), dried over $MgSO_4$ and the solvent evaporated. The resulting residue dried under vacuum to yield a deep purple solid (2.10 g, 2.27 mmol, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) 7.55-6.75 (m, 12H), 6.67 (d, *J* = 8.0 Hz, 2H), 4.49 (brt, 1H, N*H*), 4.31 (d, *J* = 12.0 Hz, 1H, C*H*-NTs), 4.07 (brd, 1H, N*H*), 3.74-3.57 (m, 3H, CH_2OH and C*H*-NH_2), 2.28 (t, *J* = 6.0 Hz, 2H, CH_2Cp*), 2.23 (s, 3H, SO_2CH_3), 1.96-1.77 (m, 12H, $C_5(CH_3)_4$), 1.60-1.51 (m, 4H, 2 × CH_2), 1.37-1.22 (m, 20H, 10 × CH_2).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K) 140.6, 139.4, 138.8, 138.7, 129.1, 128.7, 128.5, 128.4, 127.8, 127.6, 127.1, 126.4, 87.5, 86.4, 86.0, 85.7, 85.3, 74.0, 69.5, 62.8, 32.7, 29.8, 29.6, 29.5, 29.5, 29.5, 29.4, 28.4, 25.8, 24.4, 21.2, 9.6, 9.6.

LC/MS (ESI) m/z: $[M-H]^-$ 925.4.

Ir(Cp*){(*S,S,S*)-CsDPEN}



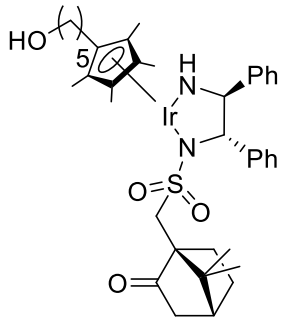
(*S,S,S*)-CsDPEN (236 mg, 0.55 mmol, 2.2 equiv.), [Ir{η5-$C_5(CH_3)_5$}Cl_2]$_2$ (200 mg, 0.25 mmol, 1.0 equiv.) and triethylamine (0.147 ml, 1.05 mmol, 4.2 equiv.) were added to dichloromethane (8 ml). After stirring for 18 hours under room temperature, the solution was washed with water (5 ml) three times, brine (5 ml), dried over $MgSO_4$ and the solvent evaporated. The resulting deep purple residue was dissolved in diethylether, precipitated with hexane, yielded a deep purple solid (282 mg, 0.37 mmol, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) 7.60 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 4.0 Hz, 2H), 7.33-7.24 (m, 2H), 7.21-7.11 (m, 4H), 5.37 (brs, 1H, N*H*), 4.44 (s, 1H, C*H*-NCs), 4.25 (s, 1H, C*H*-NH), 3.06 (d, *J* = 16 Hz, 1H, SO_2CH), 2.63 (dt, *J* = 4, 16 Hz, 1H, SO_2CH), 2.23 (dt, *J* = 4, 20 Hz, 1H, COC*H*), 1.98 (s, 15H, CH_3 of Cp*), 1.93-1.83 (m, 4H, CH_2+C*H* of cyclohexyl ring+COC*H*), 1.66 (d, *J* = 16 Hz, 1H, C*H* of cyclohexyl ring), 1.50 (dt, *J* = 4, 12 Hz, 1H, C*H* of cyclohexyl ring), 0.84 (s, 3H, CCH_3CH_3), 0.40 (s, 3H, CCH_3CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) 216.6, 147.2, 146.5, 128.1, 127.7, 127.2, 126.8, 126.6, 126.3, 85.4, 79.7, 75.2, 58.6, 48.9, 47.6, 42.9, 42.5, 27.0, 24.8, 20.1, 19.6, 10.1.

LC/MS (ESI) m/z: $[M+H]^+$ 753.2.

Ir(Cp*C_5H_{10}OH){(*S,S,S*)-CsDPEN} (**3b**)



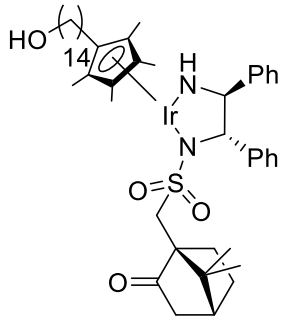
(*S,S,S*)-CsDPEN (998 mg, 2.34 mmol, 2.0 equiv.), [Ir{η5-$C_5(CH_3)_4C_5H_{10}OH$}Cl_2]$_2$ (1.10 g, 1.17 mmol, 1.0 equiv.) and triethylamine (0.68 ml, 4.91 mmol, 4.2 equiv.) were added to dichloromethane (15 ml). After stirring for 18 hours under room temperature, the solution was washed with water (10 ml) three times, brine (15 ml), dried over $MgSO_4$ and the solvent evaporated. The resulting residue dried under vacuum to yield a deep purple solid (1.96 g, 1.17 mmol, quant.).

^{1}H NMR (400 MHz, $CDCl_3$) 7.58 (brd, 2H), 7.48-7.08 (m, 8H), 5.40 (brs, 1H, N*H*), 4.44 (s, 1H, C*H*-NCs), 4.25 (s, 1H, C*H*-NH), 3.66 (t, *J* = 6 Hz, 2H, C*H*$_2$OH), 3.06 (d, *J* = 16 Hz, 1H, SO_2C*H*), 2.69-2.57 (m, 1H, SO_2C*H*), 2.34 (t, *J* = 6.0 Hz, 2H, C*H*$_2$Cp*), 2.27-2.18 (m, 1H, COC*H*), 1.99 (s, 12H, C*H*$_3$ of Cp*), 1.93-1.85 (m, 4H, C*H*$_2$+C*H* of cyclohexyl ring+COC*H*), 1.54-1.42 (m, 6H, 2 × CH_2, C*H*$_2$ of cyclohexyl ring), 1.33-1.20 (m, 2H, CH_2), 0.84 (s, 3H, CCH_3CH_3), 0.40 (s, 3H, CCH_3CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) 216.7, 147.2, 146.5, 129.0, 128.7, 128.1, 127.7, 126.8, 126.6, 88.6, 86.1, 85.0, 75.2, 71.0, 62.5, 58.6, 48.9, 47.6, 44.5, 42.8, 32.5, 27.0, 26.0, 20.0, 19.6, 10.3, 10.1.

LC/MS (ESI) m/z: $[M+H]^+$ 825.3.

Ir(Cp*$C_{14}H_{28}OH$){(*S,S,S*)-CsDPEN}Cl (**3d**)



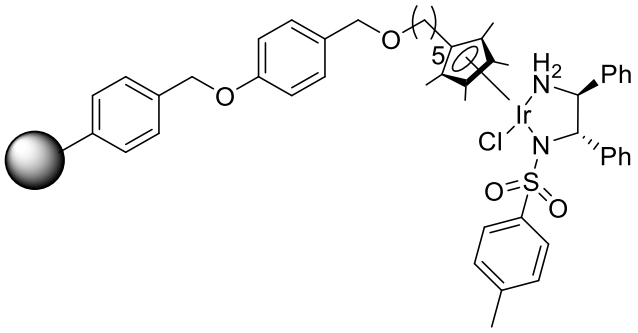
(*S,S,S*)-CsDPEN (998 mg, 2.34 mmol, 2.0 equiv.), [Ir{η5-$C_5(CH_3)_4C_{14}H_{28}OH$}$Cl_2$]$_2$ (1.40 g, 1.17 mmol, 1.0 equiv.) and triethylamine (0.68 ml, 4.91 mmol, 4.2 equiv.) were added to dichloromethane (15 ml). After stirring for 20 hours under room temperature, the solution was washed with water (10 ml) three times, brine (15 ml), dried over $MgSO_4$ and the solvent evaporated. The resulting residue dried under vacuum to yield a deep purple solid (1.96 g, 1.17 mmol, 99.1%).

^{1}H NMR (400 MHz, $CDCl_3$) 7.58 (brd, 2H), 7.44 (d, *J* = 4.0 Hz, 2H), 7.32-6.95 (m, 6H), 5.38 (brs, 1H, N*H*), 4.44 (s, 1H, C*H*-NCs), 4.24 (s, 1H, C*H*-NH), 3.63 (t, *J* = 6.0 Hz, 2H, C*H*$_2$OH), 3.07 (d, *J* = 12 Hz, 1H, SO_2C*H*), 2.72-2.57 (m, 1H, SO_2C*H*), 2.41 (t, *J* = 8.0 Hz, 2H, C*H*$_2$Cp*), 2.29-2.18 (m, 1H, COC*H*), 2.07-1.93 (m, 12H, $C_5(CH_3)_4$), 1.93-1.83 (m, 4H, C*H*$_2$+C*H* of cyclohexyl ring+COC*H*),1.65-1.42 (m, 6H, C*H2* of cyclohexyl ring and 2 × CH_2), 1.42-1.18 (m, 20H, 10 × CH_2), 0.85 (s, 3H, CCH_3CH_3), 0.41 (s, 3H, CCH_3CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) 216.1, 139.8, 138.2, 128.4, 128.3, 128.0, 127.7, 127.0, 126.8, 88.3, 85.8, 84.3, 76.0, 70.8, 62.5, 51.2, 47.9, 44.4, 42.5, 32.6, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 27.3, 25.7, 24.9, 24.3, 20.4, 19.7, 9.4, 9.3.

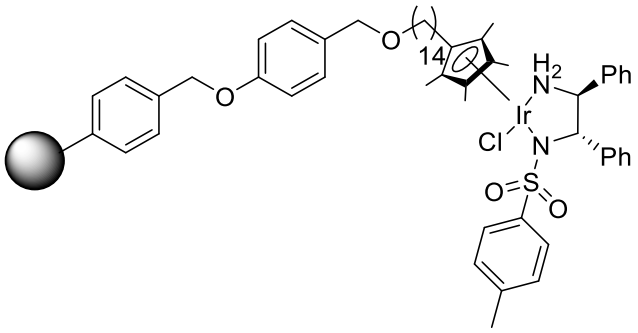
LC/MS (ESI) m/z: $[M+H]^+$ 951.4.

Ir(Cp*$C_5H_{10}OH$){(*S,S*)-TsDPEN}Cl immobilized on Wang resin (**4a**)



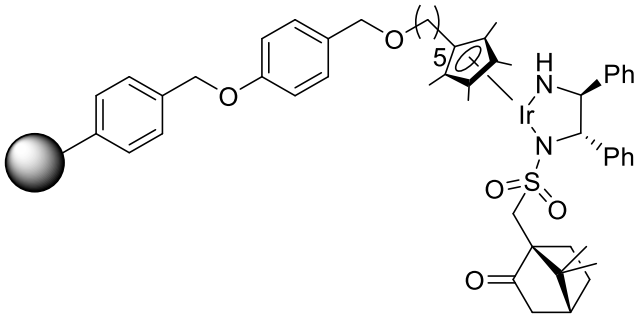
A solution of 2,6-di-*tert*-butylpyridine (2.55 ml, 11.5 mmol, 4.0 equiv.) in dichloromethane (12 ml) was added to trifluoromethanesulfonic anhydride (0.99 ml, 5.88 mmol, 2.05 equiv.) in dichloromethane (12 ml) at -10 °C. A solution of **3a** (2.29 g, 2.87 mmol, 1.0 equiv.) in dichloromethane (12 ml) was slowly added over 30 minutes. After stirring for 1 hour, the resulting solution was evaporated to dryness to remove excess trifluoromethanesulfonic anhydride, the residue was dissolved in dichloromethane (24 ml) and Wang resin (2.05 g, 2.87 mmol, 1.0 equiv.) was added. After stirring for 20 hours, the suspension was filtered and washed with dichloromethane until the filtrate was colourless. The residue was added to H_2O (120 ml) and the slurry filtered. This was repeated with 1M HCl (40 ml), H_2O (120 ml / until pH was 6-7), methanol (60 ml), and the resulting dark red resin was repeatedly washed with isopropanol (120 ml) at 60 °C for 1 hour until no colour was seen in solution, filtered and dried under vacuum (2.49 g, 0.35 mmol Ir/g, 0.87 mmol Ir, 30%).

Ir(Cp*$C_{14}H_{28}$OH){(*S,S*)-TsDPEN}Cl immobilized on Wang resin (**4c**)



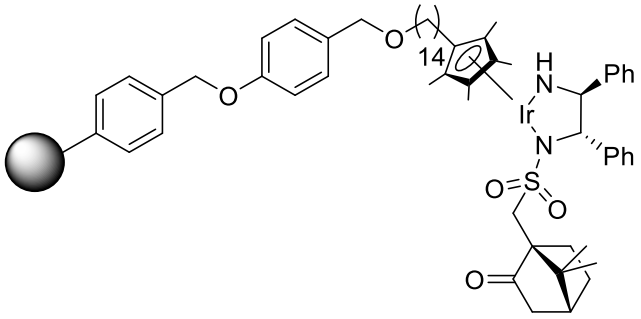
A solution of 2,6-di-*tert*-butylpyridine (3.71 ml, 16.7 mmol, 8.0 equiv.) in dichloromethane (8.2 ml) was added to trifluoromethanesulfonic anhydride (1.43 ml, 8.56 mmol, 4.1 equiv.) in dichloromethane (8.2 ml) at -10 °C. A solution of **3c** (1.93 g, 2.09 mmol, 1.0 equiv.) in dichloromethane (10 ml) was slowly added over 30 minutes. After stirring for 1 hour, the resulting solution was evaporated to dryness to remove excess trifluoromethanesulfonic anhydride, the residue was dissolved in dichloromethane (17 ml) and Wang resin (1.49 g, 2.09 mmol, 1.0 equiv.) was added. After stirring for 17 hours, the suspension was filtered and washed with dichloromethane until the filtrate was colourless. The residue was added to H_2O (90 ml) and the slurry filtered. This was repeated with 1M HCl (30 ml), H_2O (100 ml / until pH was 6-7), methanol (45 ml), and the resulting dark red resin was repeatedly washed with isopropanol (38 ml) at 60 °C for 1 hour until no colour was seen in solution, filtered and dried under vacuum (1.88 g, 0.15 mmol Ir/g, 0.28 mmol Ir, 14%).

Ir(Cp*C_5H_{10}OH){(*S,S,S*)-CsDPEN}Cl immobilized on Wang resin (**4b**)



A solution of 2,6-di-*tert*-butylpyridine (3.16 ml, 14.2 mmol, 4.0 equiv.) in dichloromethane (15 ml) was added to trifluoromethanesulfonic anhydride (1.22 ml, 7.28 mmol, 2.05 equiv.) in dichloromethane (15 ml) at -10 °C. A solution of **3a** (3.00 g, 3.55 mmol, 1.03 equiv.) in dichloromethane (22.5 ml) was slowly added over 30 minutes. After stirring for 1 hour, the resulting solution was evaporated to dryness to remove excess trifluoromethanesulfonic anhydride, the residue was dissolved in dichloromethane (30 ml) and Wang resin (2.54 g, 3.55 mmol, 1.0 equiv.) was added. After stirring for 22 hours, the suspension was filtered and washed with dichloromethane until the filtrate was colourless. The residue was added to H_2O (150 ml) and the slurry filtered. This was repeated with 1M HCl (60 ml), H_2O (270 ml / until pH was 6-7), methanol (75 ml), and the resulting dark red resin was repeatedly washed with isopropanol (150 ml) at 60 °C for 1 hour until no colour was seen in solution, filtered and dried under vacuum (3.25 g, 0.22 mmol Ir/g, 0.72 mmol Ir, 20%).

Ir(Cp*$C_{14}H_{28}$OH){(*S,S,S*)-CsDPEN}Cl immobilized on Wang resin (**4d**)



A solution of 2,6-di-*tert*-butylpyridine (1.76 ml, 7.91 mmol, 4.0 equiv.) in dichloromethane (10 ml) was added to trifluoromethanesulfonic anhydride (0.68 ml, 4.06 mmol, 2.05 equiv.) in dichloromethane (10 ml) at -10 °C. A solution of **3d** (1.92 g, 2.02 mmol, 1.02 equiv.) in dichloromethane (15 ml) was slowly added over 30 minutes. After stirring for 1 hour, the resulting solution was evaporated to dryness to remove excess trifluoromethanesulfonic anhydride, the residue was dissolved in dichloromethane (19 ml) and Wang resin (1.41 g, 1.98 mmol, 1.0 equiv.) was added. After stirring for 21 hours, the suspension was filtered and washed with dichloromethane until the filtrate was colourless. The residue was added to H_2O (96 ml) and the slurry filtered. This was repeated with 1M HCl (38 ml), H_2O (170 ml / until pH was 6-7), methanol (48 ml), and the resulting dark red resin was repeatedly washed with isopropanol (96 ml) at 60 °C for 1 hour until no colour was seen in solution, filtered and dried under vacuum (1.20 g, 0.066 mmol Ir/g, 0.0792 mmol Ir, 4.0%).

3 Typical procedure of ATH (Batch mode)

a) Homogenous catalyst

Under a nitrogen atmosphere, the Ir(Cp*C_5H_{10}OH){(*S,S*)-TsDPEN}Cl **3a** (16.0 mg, 0.02 mmol, 0.04 equiv.) and KO^{t}Bu (5.6 mg, 0.05 mmol, 0.10 equiv.) were added to 2-propanol (2.0 ml). Acetophenone (58 μl, 0.50 mmol, 1.0 equiv.) was added, followed by 2-propanol (0.50 ml). After stirring for 5 hours at 60°C, the reaction mixture was sampled and analysed by GC for conversion and enantioselectivity.

b) Immobilized catalyst

Under a nitrogen atmosphere, the immobilized C_5 tethered/CsDPEN catalyst **4b** (41.7 mg, 9.2 μmol, 0.22 mmol/g, 0.037 equiv.) and Et_3N (35 μl, 0.25 mmol, 1.0 equiv.) were added to 2-propanol (1.0 ml). Acetophenone (29 μl, 0.25 mmol, 1.0 equiv.) was added, followed by 2-propanol (0.25 ml). After stirring for 24 hours at 60°C, the reaction mixture was sampled and analysed by GC for conversion and enantioselectivity.

4 Typical procedure of ATH (Flow mode)

a) Two pump system

The immobilized C_5 tethered/TsDPEN catalyst **4a** (500 mg, 0.35 mmol/g, 0.18 mmol) and sand (low iron, 2.50 g) were mixed by shaking and placed in the steel column (length: 170 mm, inner diameter: 4.5 mm, volume: 2.7 ml) with filter. Two HPLC pumps (JASCO, PU-980) were connected to the T-shape mixer and packed column with heating block. After being filled with isopropanol (each flow rate: 0.2 ml/min, 30 min), heating block was heated and maintained at 50 °C.

Feed A: acetophenone (3.60 g, 30 mmol) was dissolved and make up to 100 ml by isopropanol at room temperature.

Feed B: KO^{t}Bu (168 mg, 1.5 mmol) was dissolved and make up to 100 ml by isopropanol at room temperature.

Each solution was fed into the packed column at each flow rate of 18 □l/min whilst maintaining the reaction temperature at 50 °C. For reaction monitoring, the reactor eluent was collected for 6 minutes each time and analysed by GC.

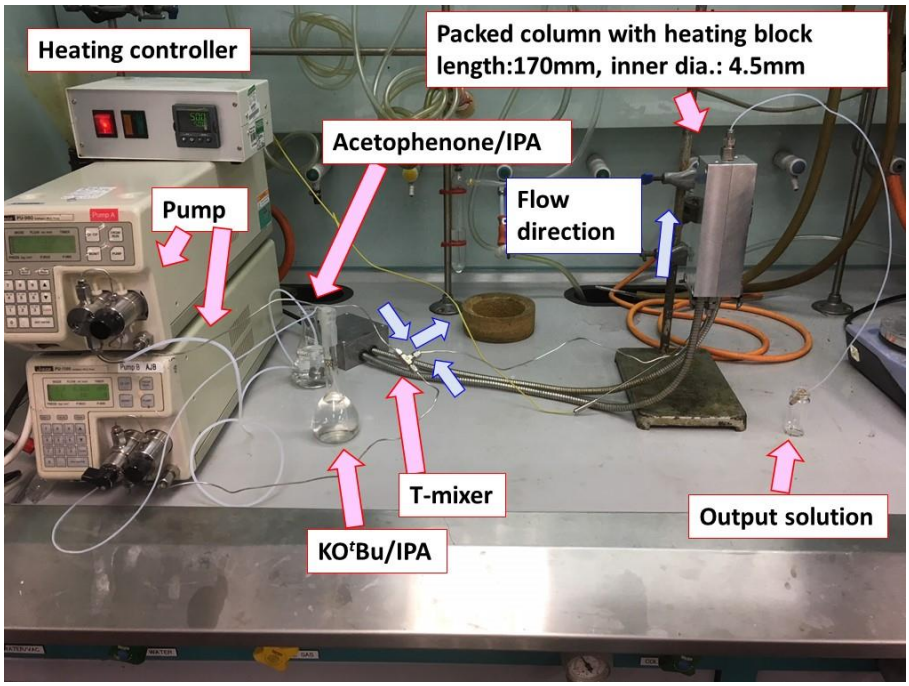


Figure S1. Configuration of the continuous flow system for ATH

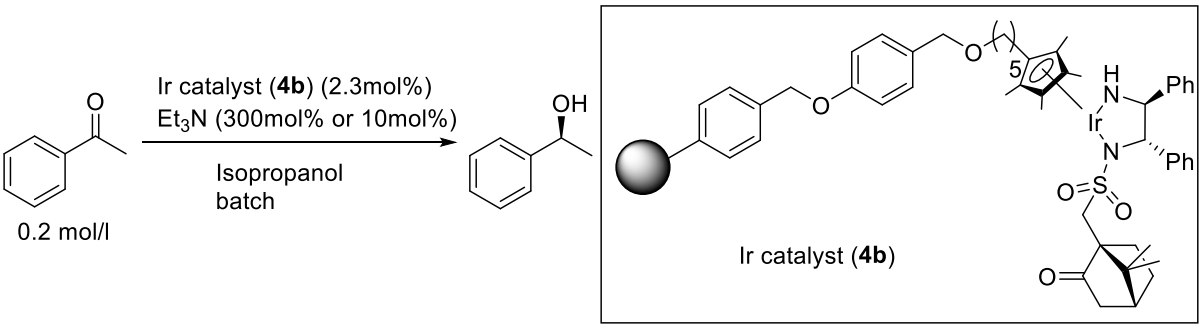
b) Single pump system

The immobilized C_5 tethered/CsDPEN catalyst **4b** (500 mg, 0.14 mmol/g, 0.07 mmol) and Sand (low iron, 2.50 g) were mixed by shaking and placed in the steel column (Length: 170 mm, Inner diameter: 4.5 mm, Volume: 2.7 ml) with filter. HPLC pump (JASCO, PU-980) was connected to the packed column with heating block. After being filled with isopropanol (0.3 ml/min, 30 min), heating block was heated and maintained at 60 °C. Acetophenone (3.60 g, 30 mmol), Et_3N (9.11 g, 90 mmol) and (*S,S,S*)-CsDPEN (621 mg, 0.15 mmol) were dissolved at 30-40°C in isopropanol and make up to 200 ml by isopropanol

at room temperature. The prepared mixture was fed into the packed column at the flow rate of 36 μl/min whilst maintaining the reaction temperature at 60°C. The reactor eluent was continuously collected in the flask at room temperature. Once the feed solution was nearly empty, the feed solution was prepared anew and was replaced with previous one.

For reaction monitoring, the reactor eluent was collected for 3 minutes each time and analysed by GC.

5 Temperature and concentration effect on ee with conversion



The temperature effect was investigated in batch condition. Lower temperature gave slower reaction rate, whilst excellent enantioselectivity was obtained at all the reaction temperature.

Table S1 Temperature effect for ATH

Base	Temperature (°C)		Reaction time (h)						
			0	0.5	1	2	4	6	24
Et_3N (10 mol%)	30	conversion	0	0.6	2	8.1	23	39	94
		%*ee*	0	100	100	88	92	94	96
Et_3N (300 mol%)	30	conversion	0	0.9	3.5	14	40	60	98
		%*ee*	0	100	100	95	97	97	97
	40	conversion	0	13	29	52	80	89	96
		%*ee*	0	92	95	96	97	97	96
	50	conversion	0	32	53	72	83	86	91
		%*ee*	0	95	96	96	96	95	94
	60	conversion	0	42	61	75	85	89	93
		%*ee*	0	95	95	95	95	94	94

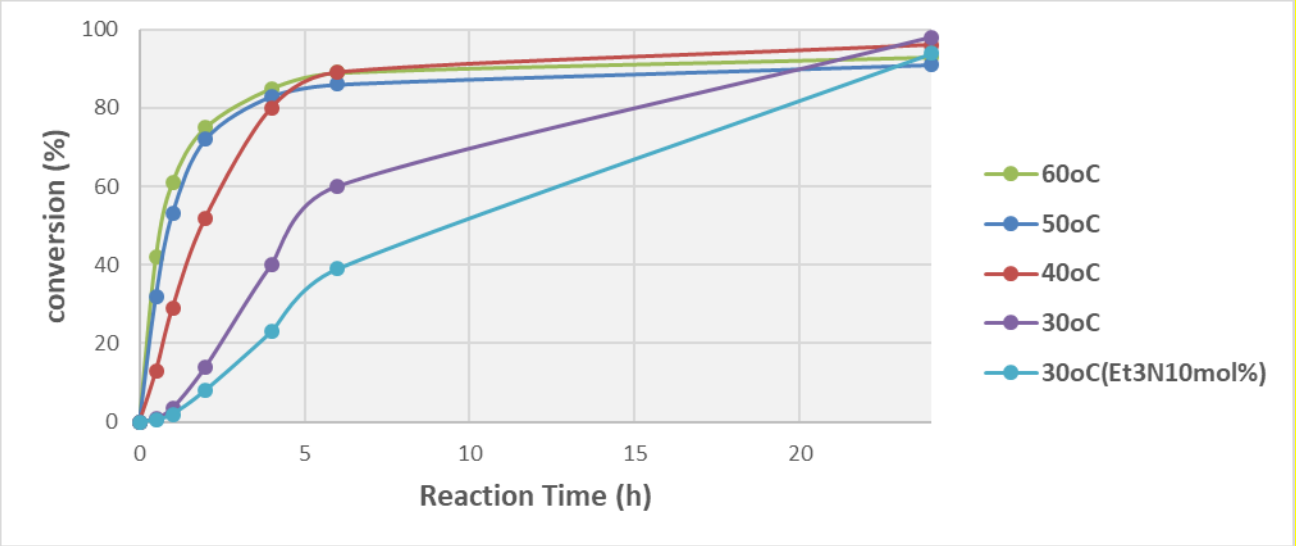


Figure S2. Temperature effect for ATH

Previous batch experiments have looked at the change in enantiomeric excess of 1-phenethyl alcohol with conversion of acetophenone in the isopropanol system using 0.1 mol% ClRhCp*(1*S*,2*R*)-1-aminoindan-2-ol at different concentrations and temperatures.[4] A higher concentration or higher temperature result predictably in a lower ee with conversion as a result of the reaction equilibrium.

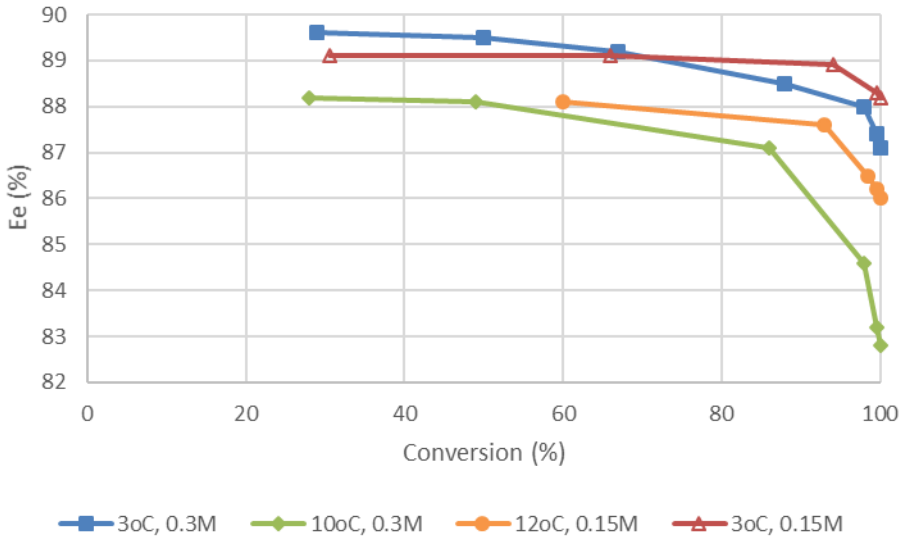


Figure S3. Change in selectivity with conversion

6 Calculation of TON

[Batch experiment]
For batch experiment, TON was evaluated as below.

TON = (Substrate / Catalyst mol ratio) * (Conversion / 100)
TON of catalyst (**3a**) = (100/4)*(60/100) = 15

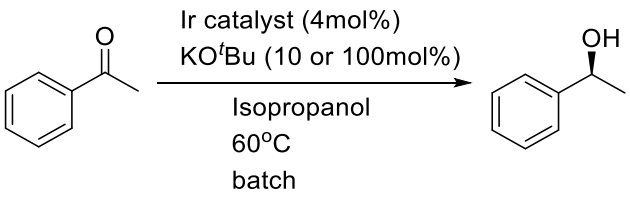


Table S2.

Entry	Substrate/ Catalyst/Base	Catalyst	Conversion (%)	TON
1	100/4/10	IrClCp*TsDPEN	59	15
2		IrClCp*CsDPEN	90	23
3		3a 5Ts	60	15
4		3b 5Cs	96	24
5		3c 14Ts	67	17
6		3d 14Cs	97	24
7	100/4/100	4a 5Ts	62	16
8		4b 5Cs	95	24
9		4c 14Ts	86	22
10		4d 14Cs	96	24

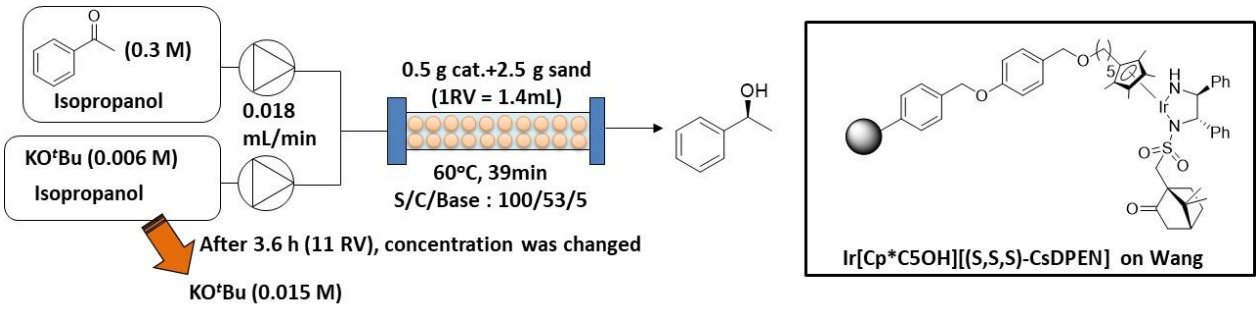


Figure S4. Flow experimental set-up

At 73 RV (Operation time was 47.5 h), conversion was 79%.
Theoretical yield = {Operation time (h)} * {60 (min/h)} * {Flow rate of substrate (ml/min)} *
{Concentration of substrate (mmol/ml)}
= 47.5*60*0.018*0.3 (mmol/ml)
= 15.4 mmol.
Packed catalyst amount = 0.5 (g)*0.22 (mmol/g)
= 0.11 mmol.
If conversion was constant,
TON = {Theoretical yield (mmol)} * {Conversion (%)} / {Catalyst amount (mmol)}
= 15.4*0.79/0.11
= 111.

[Flow experiment for long run]
After calculating the TON values for periods between two consequential samples, the total turnover TTN was calculated as a sum for each period.

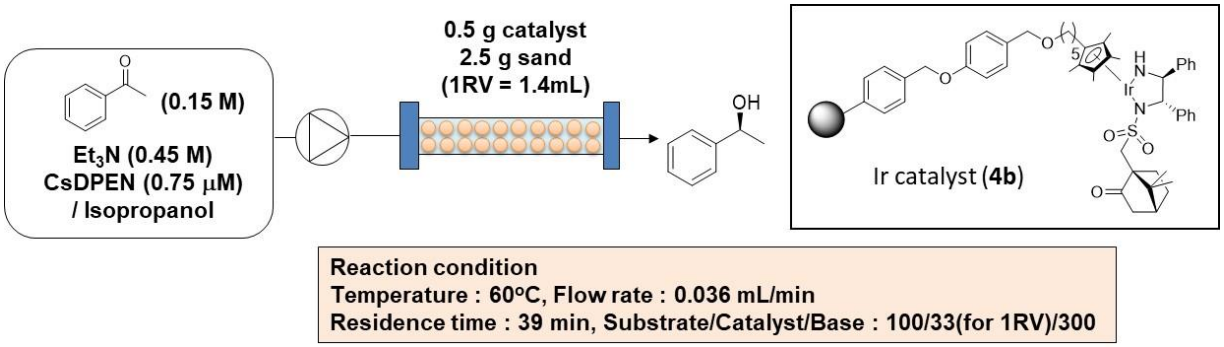


Table S3.

Substrate / Catalyst / Base = 100 / 33 / 300											
Time (h)	1.5	2.8	6.0	22	25	30	46	49	54	118	122
Enantioselectivity (%*ee*)	94	93	93	94	94	94	94	94	94	92	92
Conversion (%)	94	94	94	93	94	92	87	86	82	31	25
TON for each period	-	5.7	13.7	66.8	16.7	19.1	63.7	15.4	17.3	165	5.0
Summed TON	-	5.7	19.4	86.2	103	122	186	201	218	383	388
TOF for each period (h^{-1})	-	4.4	4.3	4.3	4.3	4.3	4.1	4.0	3.8	2.6	1.3

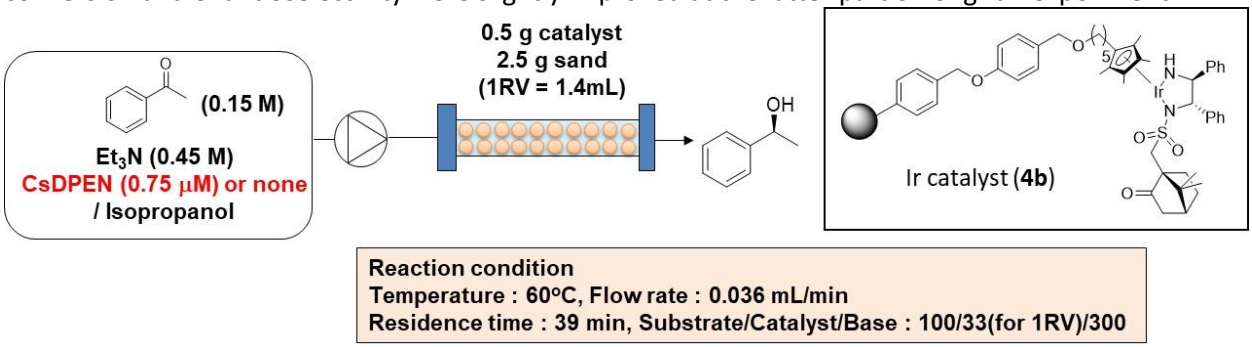
Each TON for each period and TOF (Turn over frequency) were calculated as below.

TON [From 1.5 h to 2.8 h]
= (Substrate / Catalyst ratio per 1RV) / {Residence time of 1 RV (min)}*
{Operation time of each term (h)}*{60 (min/h)}*{Average conversion of each term}
= (100/33)/39*(2.8–1.5)*60*{(94+94)/2/100}
= 5.7

TOF [from 1.5 h to 2.8 h]
= TON for each term / Operation time of each term (h)
= 5.7/(2.8-1.5)
= 4.4

7 Effect of ligand as additive

The effect of CsDPEN ligand as additive was confirmed. For adding 0.5 mol% of CsDPEN ligand, both conversion and enantioselectivity were slightly improved at the latter part of long run experiment.



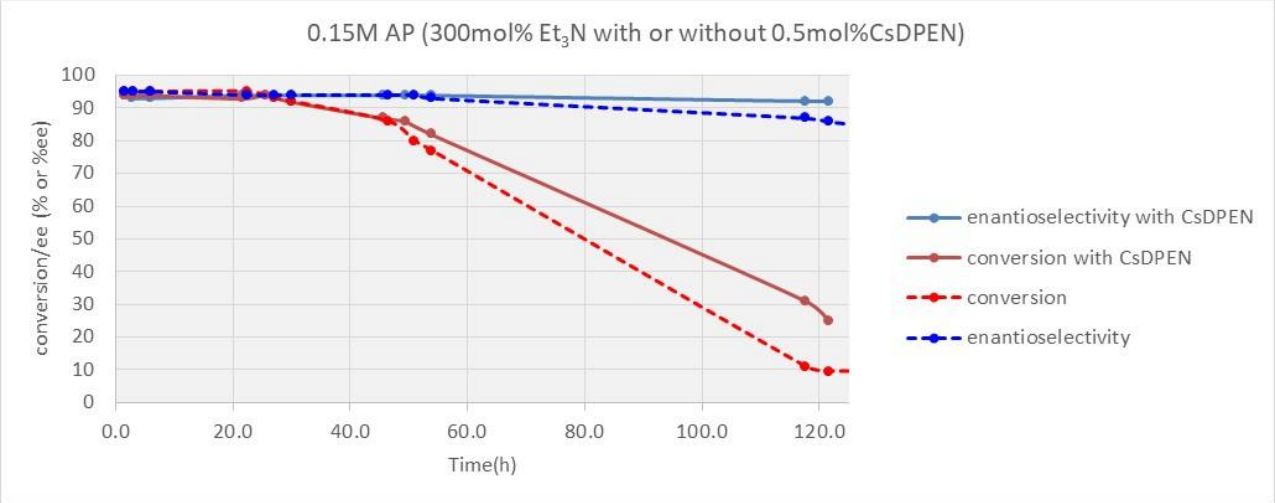
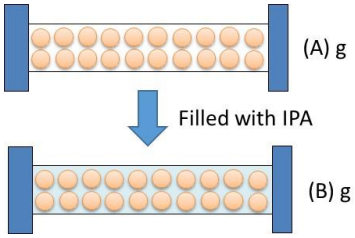


Figure S5. Effect of ligand as additive

8 Determination of the residence time for packed bed reactor

In order to determine the residence time for the flow reaction, the void space in the packed-column was calculated as shown below.

Calculation method based on volume of filled solvent

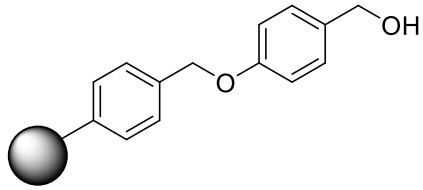


1. The weight of the column is measured (including sand and catalyst)
   (A) g = 45.5932 g
2. IPA is passed through the column
3. The weight of the column is measured (including sand, catalyst and IPA)
   (B) g = 46.6917 g
4. The volume of IPA (= void space) is calculated by using the density of IPA
   Void space = Volume of IPA = {(B g) – (A g)} / 0.786 g/cm^3 (density of IPA)
   = **1.40 cm^3**

Adopting 1.4 cm^3 as reaction volume for calculating residence time, residence time equals 39 min in the case of 0.036 ml/min as total flow rate.

9 SEM data of the immobilized catalyst

Wang resin and immobilized iridium catalyst was analysed by SEM. Both are fine particle and particle size is uniformed well. But after using this catalyst for TH in batch, all the particle was crushed by magnetic stirrer bar, which might be problematic to recycle the immobilized catalyst in batch mode, but not in flow mode.



Wang resin

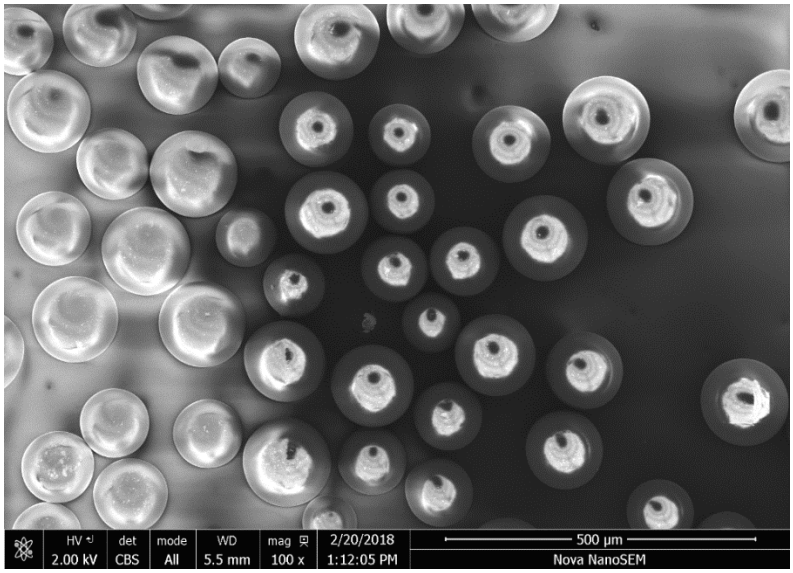
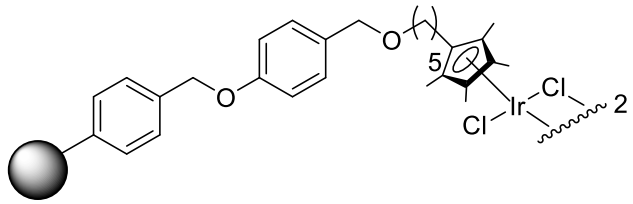


Figure S6. SEM image of Wang resin



$[Ir\{\eta5\text{-}C_5(CH_3)_4C_5H_{10}OH\}Cl_2]_2$ on Wang resin

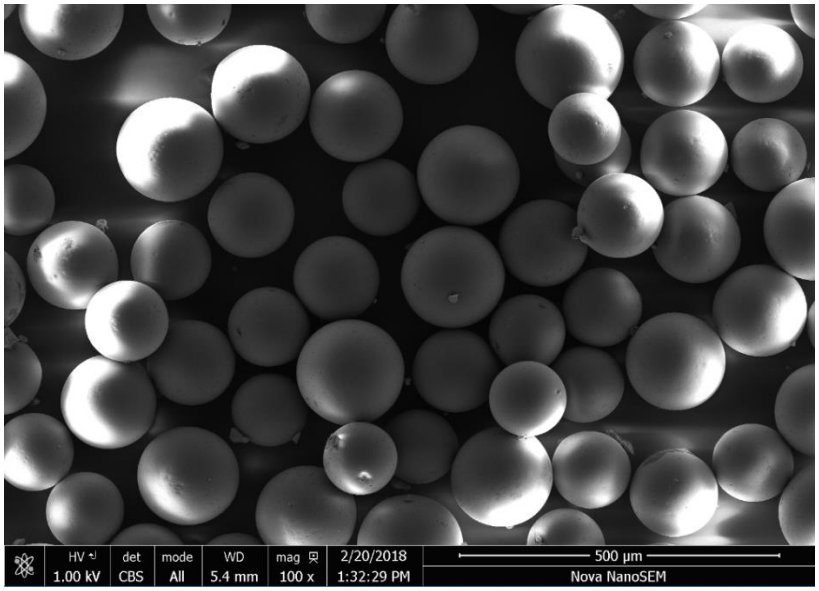


Figure S7. SEM Image of the fresh immobilized catalyst

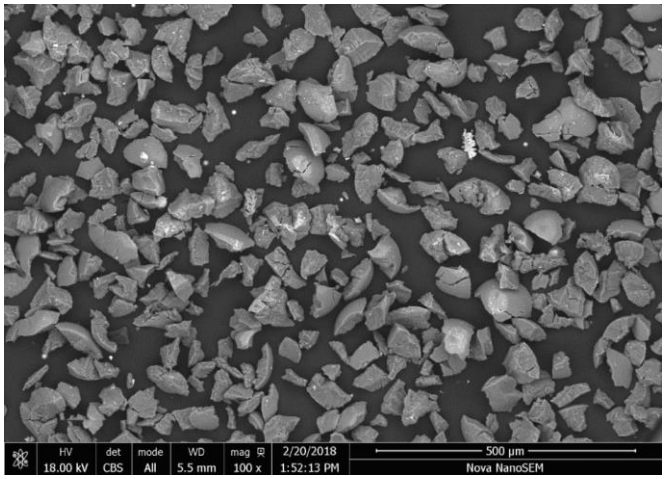


Figure S8. SEM data of the immobilized catalyst after using in batch reaction

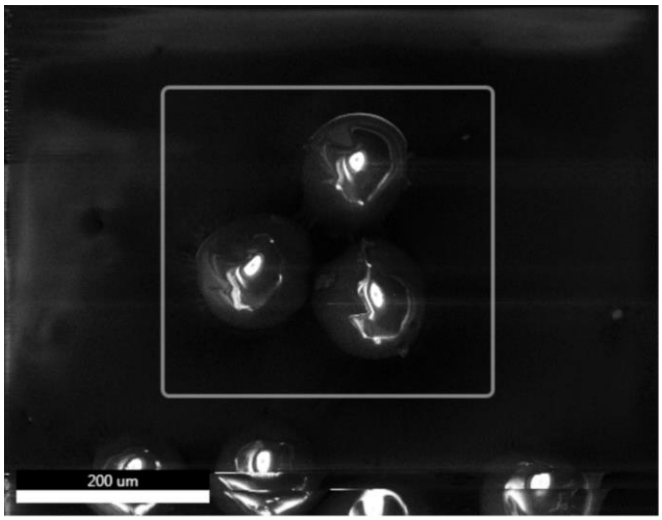


Figure S9. SEM image of immobilized iridium catalyst (**4a**) before packing into fixed-bed

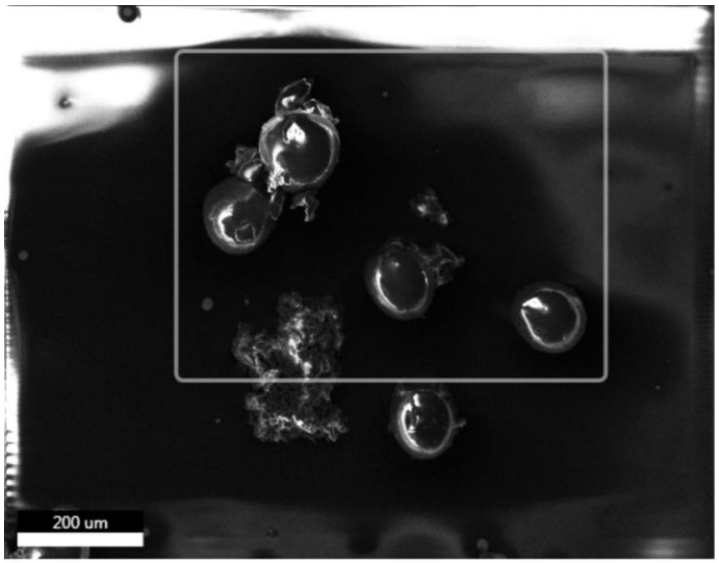


Figure S10. SEM image of immobilized iridium catalyst (**4b**) after 5 days operation in continuous flow.

10 EDX TEM data of the immobilized catalyst

Immobilized iridium catalyst was analysed by EDX TEM, whose system has SEM and Energy-dispersive X-ray spectroscopy (EDX) to characterize element of the specific area of the sample. It was found that Iridium catalyst was well dispersed on Wang resin from this data.

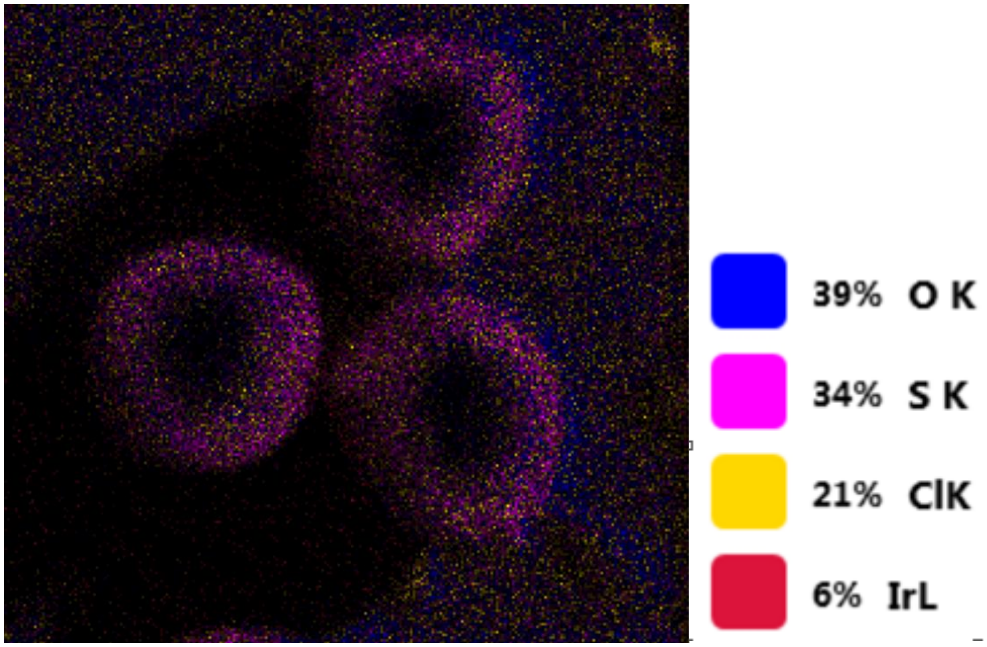


Figure S11. EDX TEM data of immobilized catalyst for all the elements

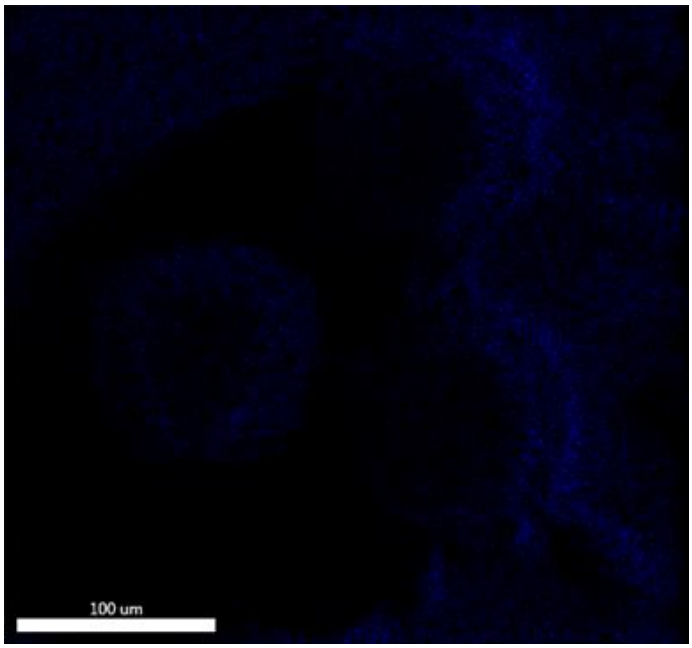


Figure S12. EDX TEM data of immobilized catalyst for oxygen

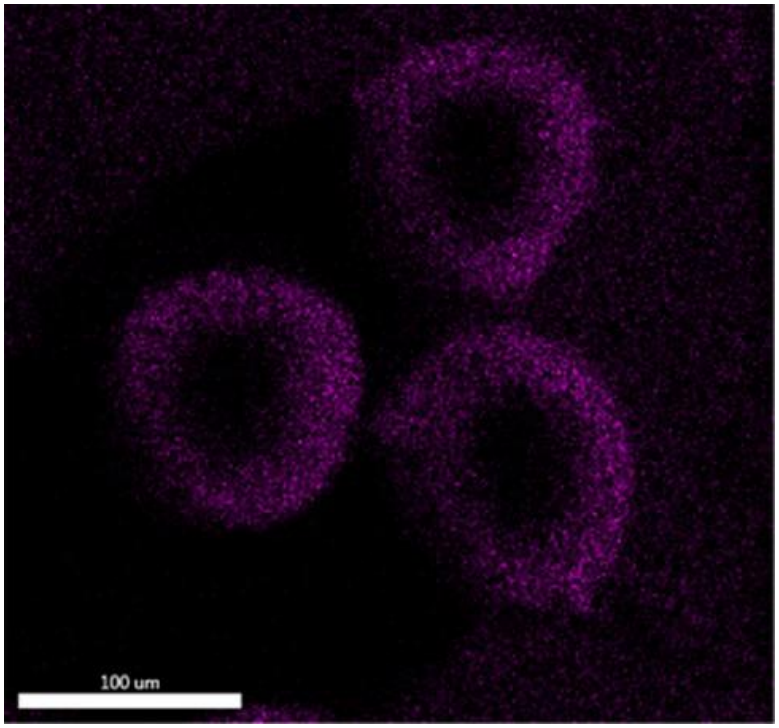


Figure S13. EDX TEM data of immobilized catalyst for sulfur

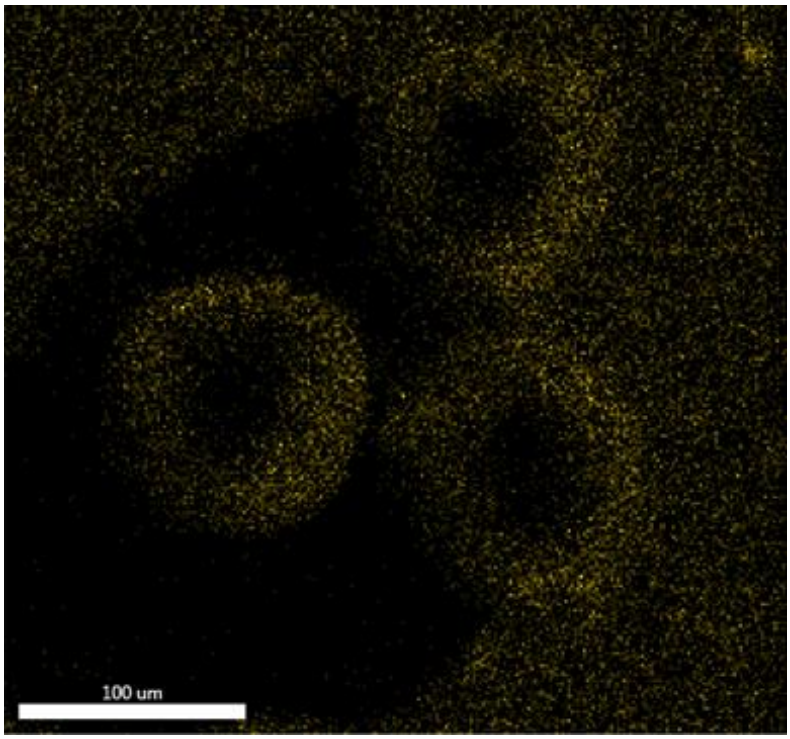


Figure S14. EDX TEM data of immobilized catalyst for chlorine

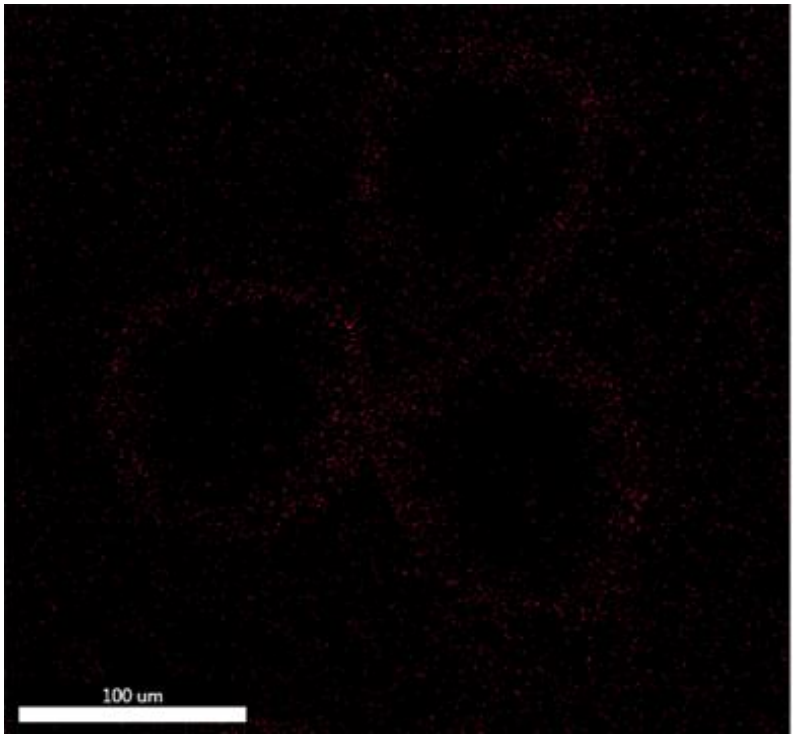


Figure S15. EDX TEM data of immobilized catalyst for iridium

11 Analytical method for Catalytic Asymmetric Transfer Hydrogenation (CATHy)

11.1 Acetophenone

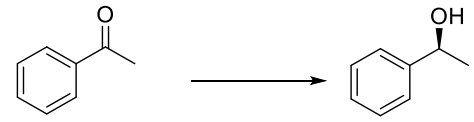


Table Analytical method (GC) for ATH of acetophenone

Column	CP-CHIRAL-DEX-CB (length:25 m, diameter:0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (5 min) - 10 °C/min - 90 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make up	N_2 (10 ml/min)	Injector split	10/1
Retention time	Acetophenone: 3.7 min, Product (minor, (*R*)-isomer): 7.0 min, Product (major, (*S*)-isomer):7.1 min		

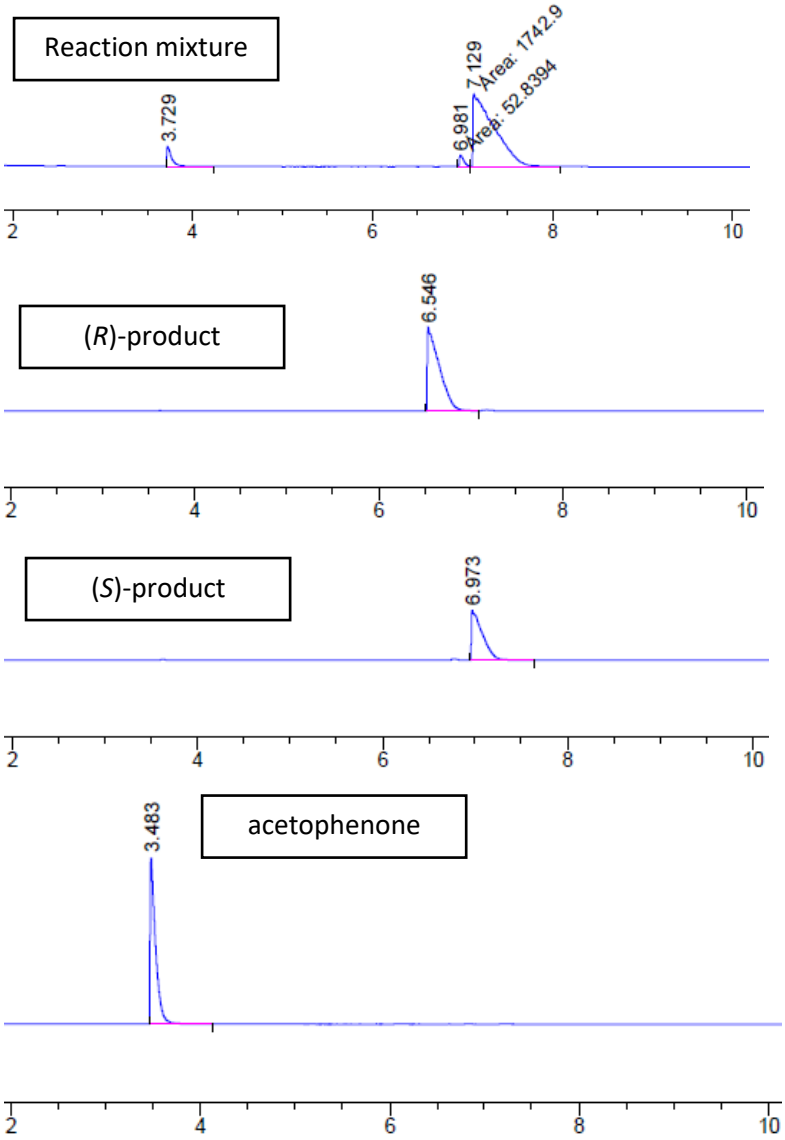
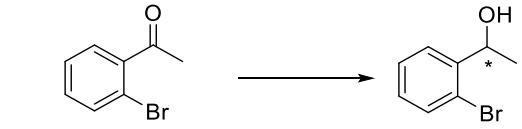


Figure GC trace of continuous flow CATHy of acetophenone

11.2 2'-Bromoacetophenone



2'-bromoacetophenone

Table Analysis method (GC) for ATH of 2'-bromoacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec

Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	2’-Bromoacetophenone: 4.6 min, Product (minor): 6.1 min, Product (major): 6.5 min		

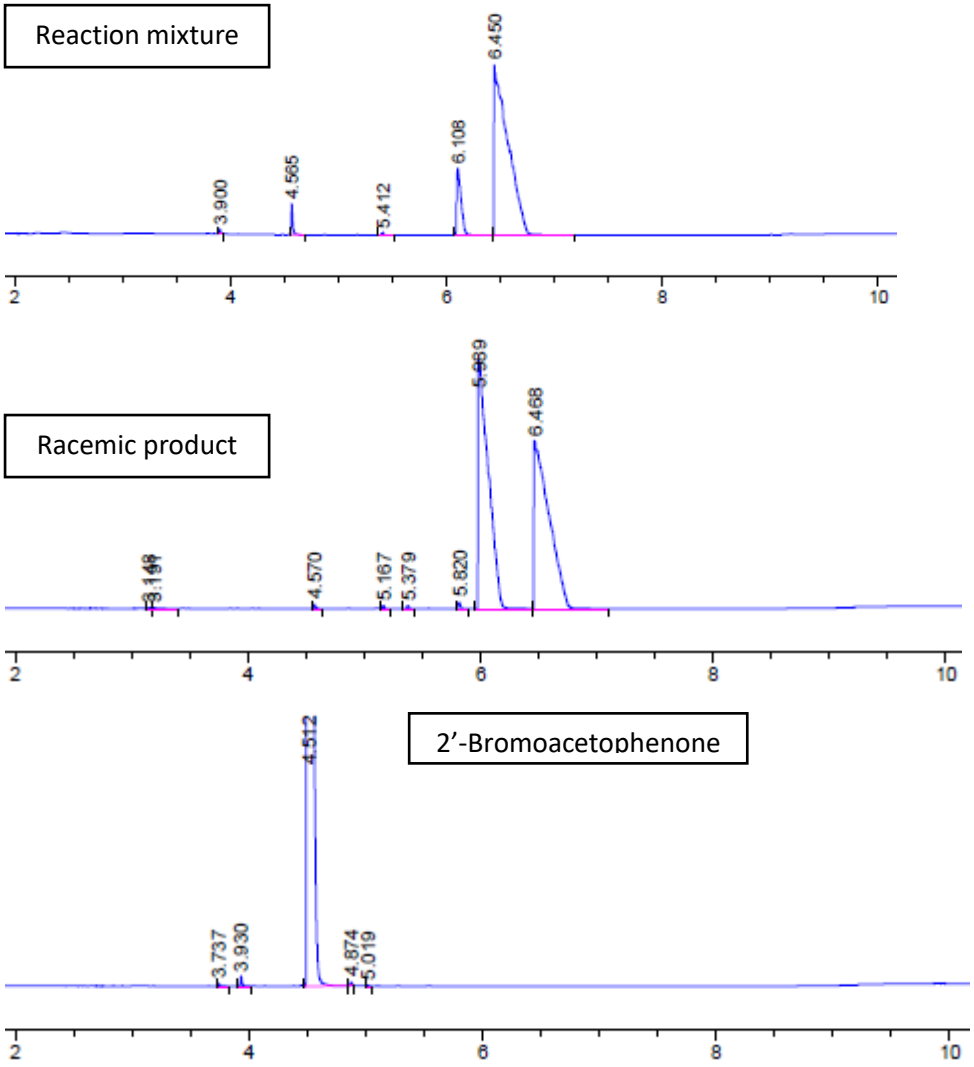
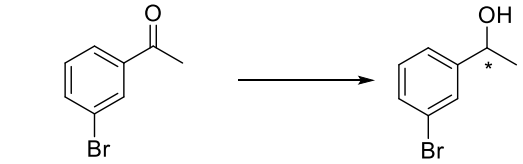


Figure GC trace of continuous flow ATH of 2’-bromoacetophenone

11.3 3’-Bromoacetophenone



3'-bromoacetophenone

Table Analysis method (GC) for ATH of 3’-bromoacetophenone

Column	CP-CHIRAL-DEX-CB

	(length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	3’-Bromoacetophenone: 4.8 min, Product (minor): 6.4 min, Product (major): 6.6 min		

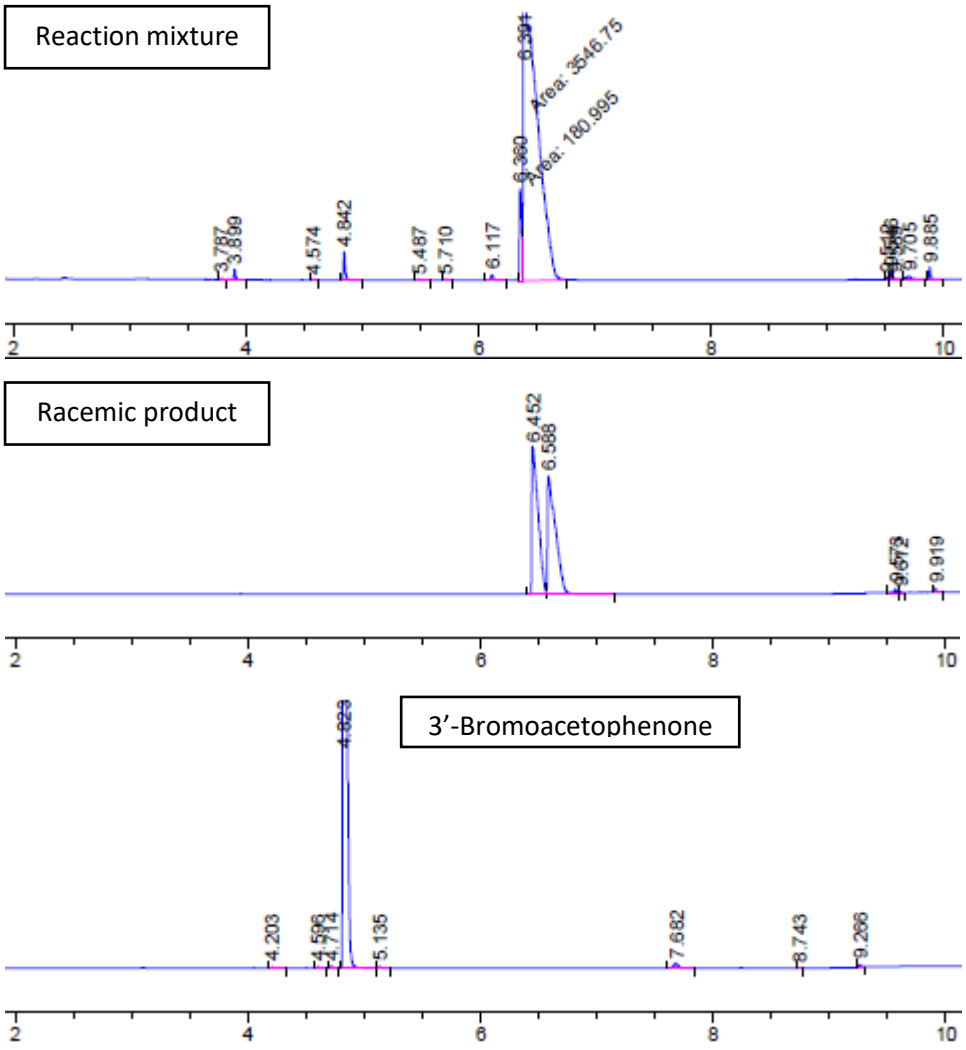
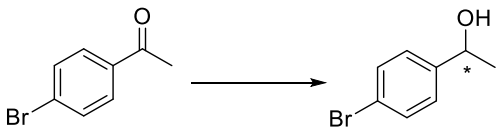


Figure GC trace of continuous flow ATH of 3’-bromoacetophenone

11.4 4’-Bromoacetophenone



4'-bromoacetophenone

Table Analysis method (GC) for ATH of 4'-bromoacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4'-Bromoacetophenone: 5.1 min, Product (minor): 6.6 min, Product (major): 6.7 min		

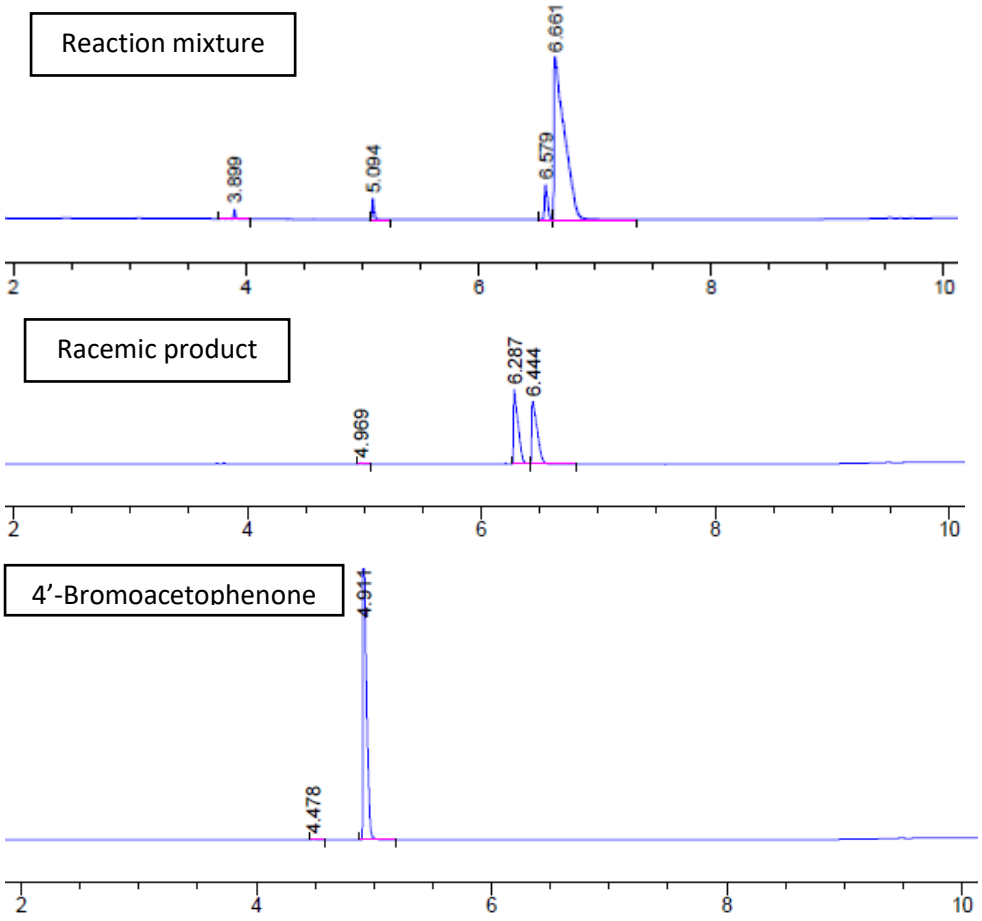
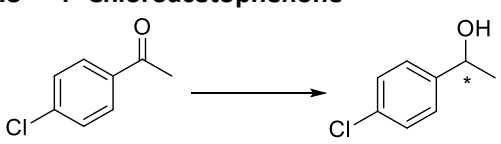


Figure GC trace of continuous flow ATH of 4'-bromoacetophenone

11.5 4'-Chloroacetophenone



4'-chloroacetophenone

Table Analysis method (GC) for ATH of 4'-chloroacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4'-Chloroacetophenone: 9.6 min, Product (minor): 11.69 min, Product (major): 11.73 min		

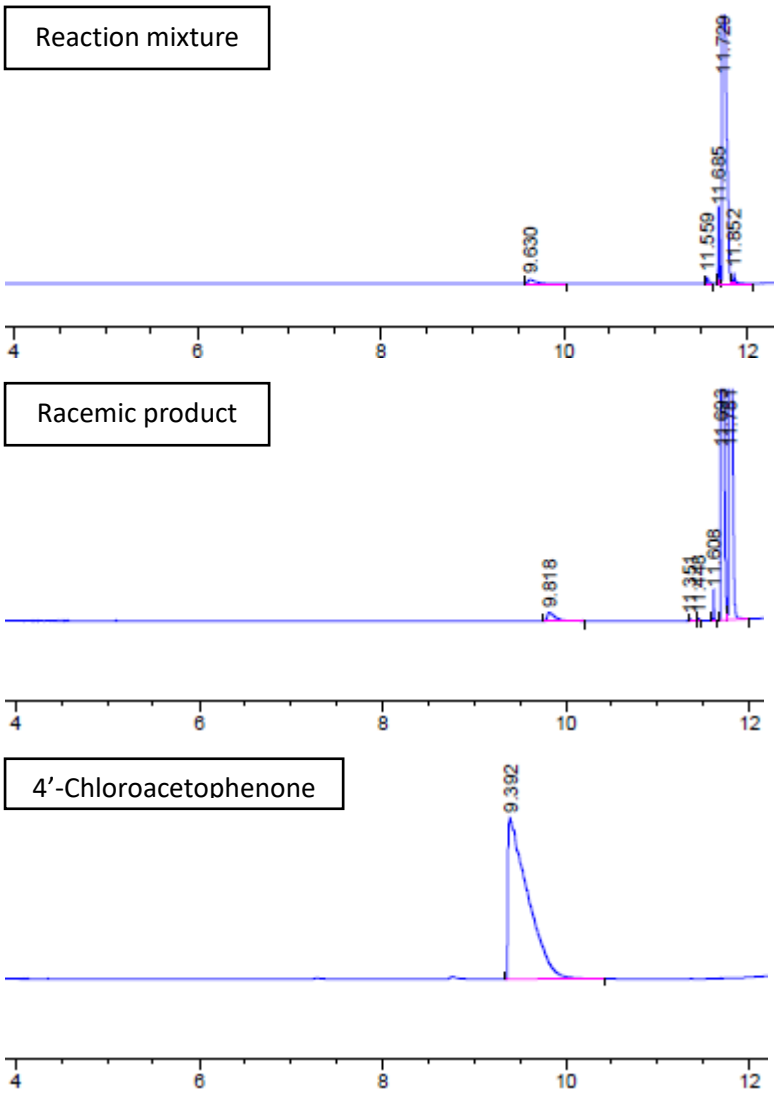
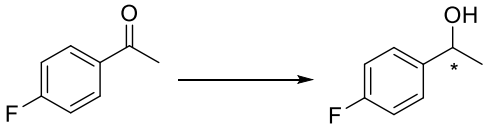


Figure GC trace of continuous flow ATH of 4'-chloroacetophenone

11.6 4’-Fluoroacetophenone



4'-fluoroacetophenone

Table Analytical method (GC) for ATH of 4’-fluoroacetophenone

Column	CP-CHIRAL-DEX-CB (length:25 m, diameter:0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (5 min) - 10 °C/min - 90 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4’-Fluoroacetophenone: 3.8 min, Product (minor): 8.1 min, Product (major): 8.5 min		

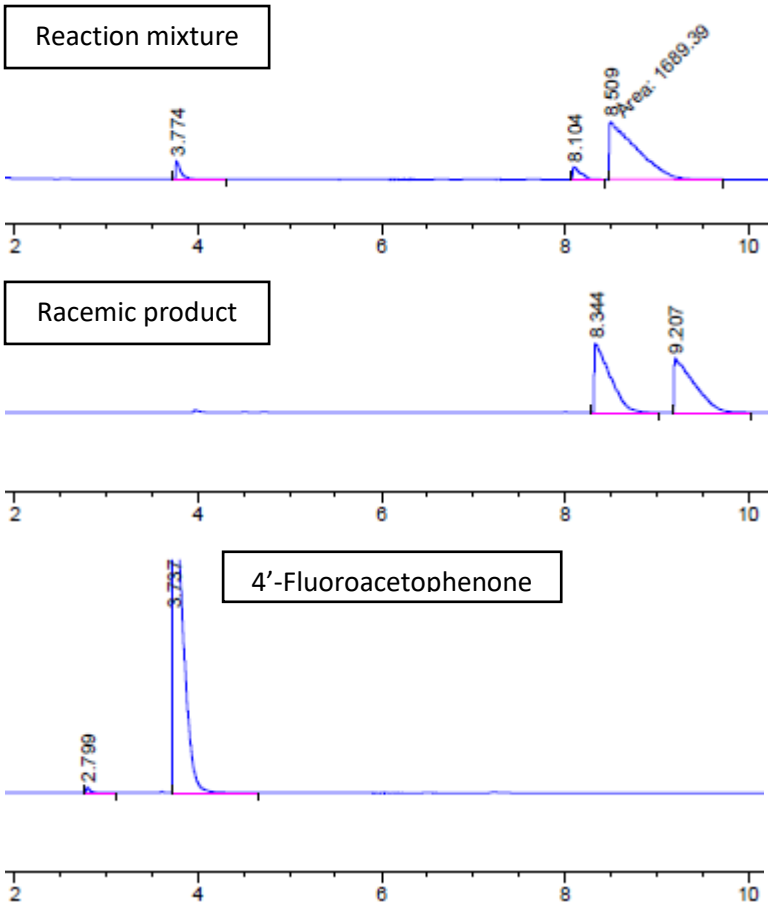
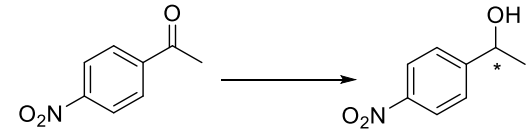


Figure GC trace of continuous flow ATH of 4’-fluoroacetophenone

11.7 4’-Nitroacetophenone



4'-nitroacetophenone

Table Analysis method (GC) for ATH of 4’-niotroacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4’-Nitroacetophenone: 7.3 min, Product (minor): 9.57 min, Product (major): 9.62 min		

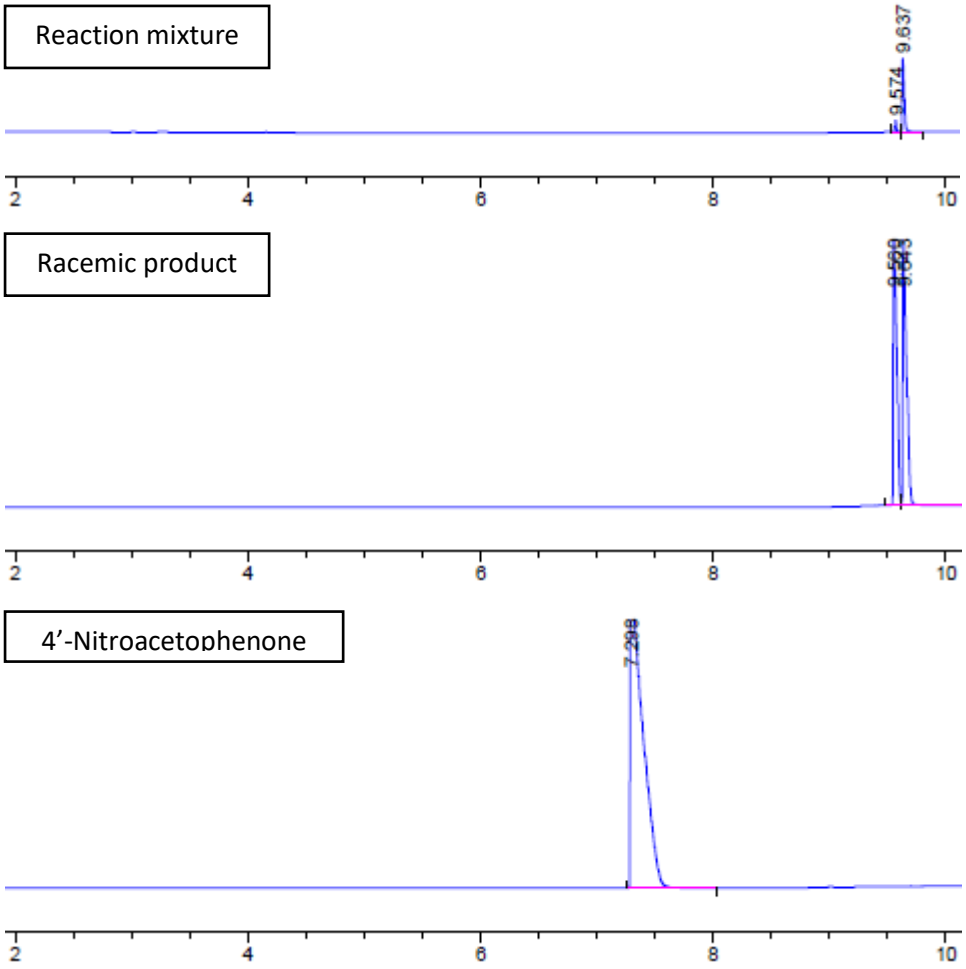


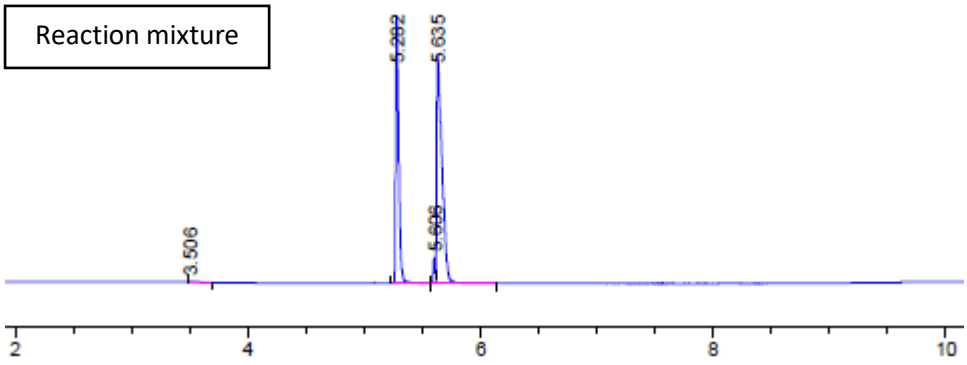
Figure GC trace of continuous flow ATH of 4’-nitroacetophenone

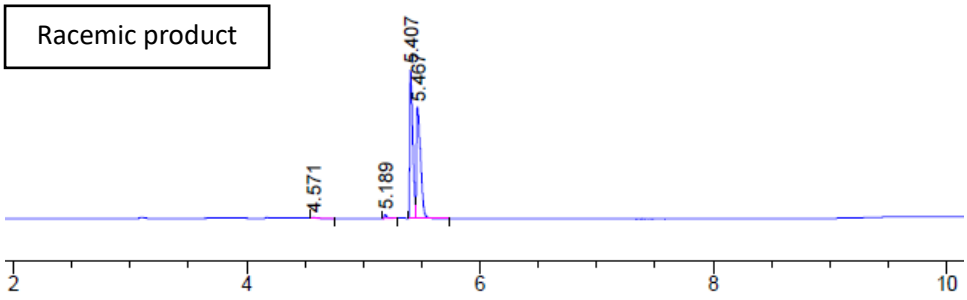
11.8 4’-Methoxyacetophenone

4'-methoxyacetophenone

Table Analysis method (GC) for ATH of 4’-methoxyacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (2 min) - 30 °C/min - 140 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make Up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4’-Methoxyacetophenone: 5.2 min, Product (minor): 5.61 min, Product (major): 5.64 min		





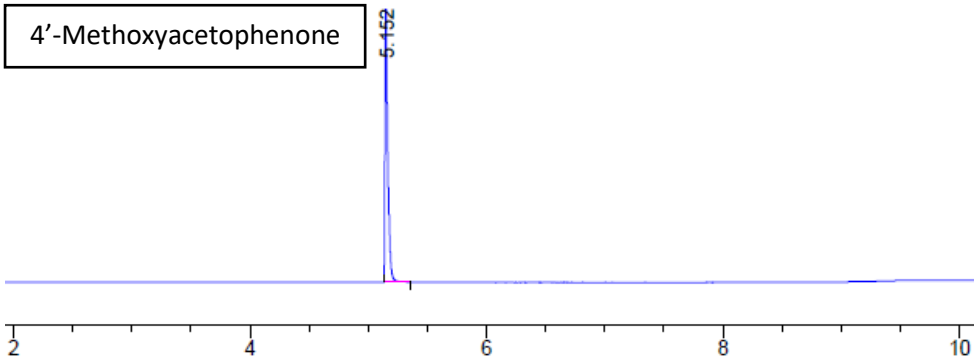
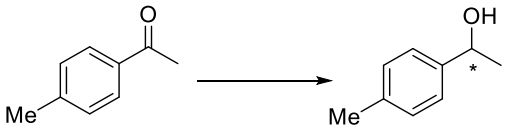


Figure GC trace of continuous flow ATH of 4’-methoxyacetophenone

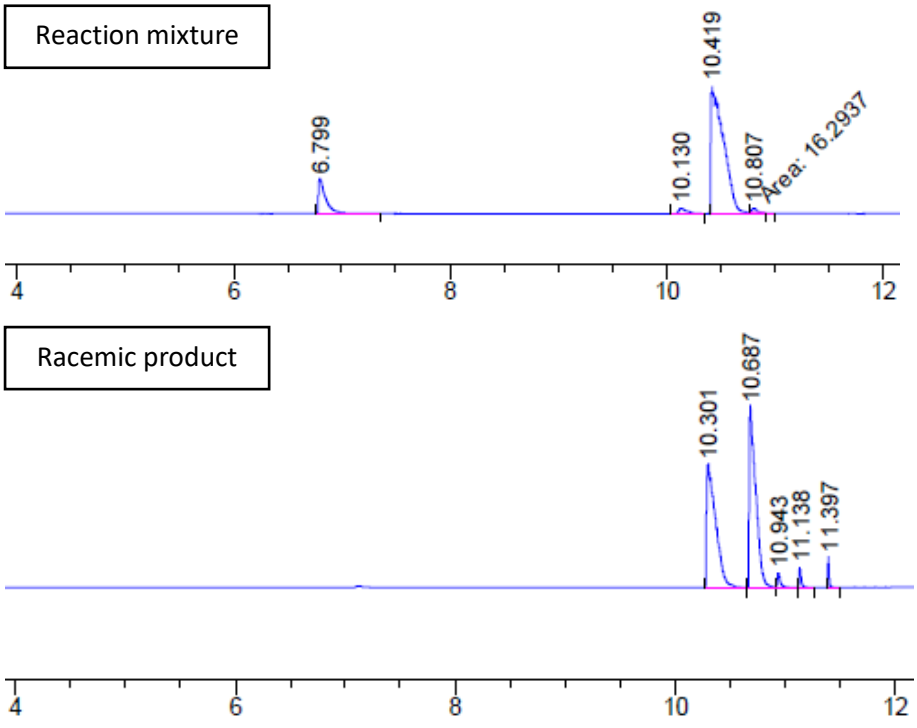
11.9 4’-Methylacetophenone



4'-methylacetophenone

Table Analytical method (GC) for ATH of 4’-metylacetophenone

Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)		
Column temp.	80 °C (5 min) - 10 °C/min - 90 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 78 cm/sec
Make up	N_2 (10 ml/min)	Injector split	10/1
Retention time	4’-Methylacetophenone: 6.8 min, Product (minor): 10.1 min, Product (major): 10.4 min		



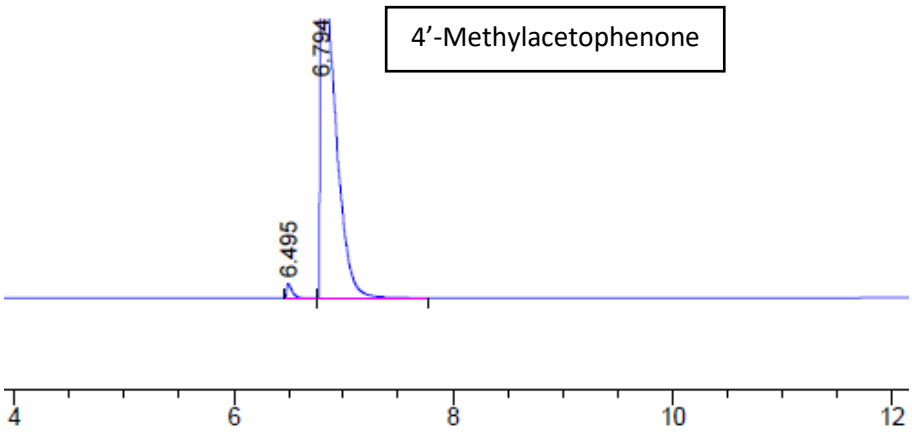
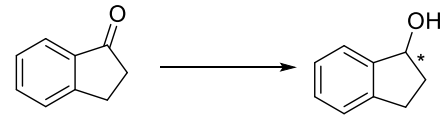


Figure GC trace of continuous flow ATH of 4'-methylacetophenone

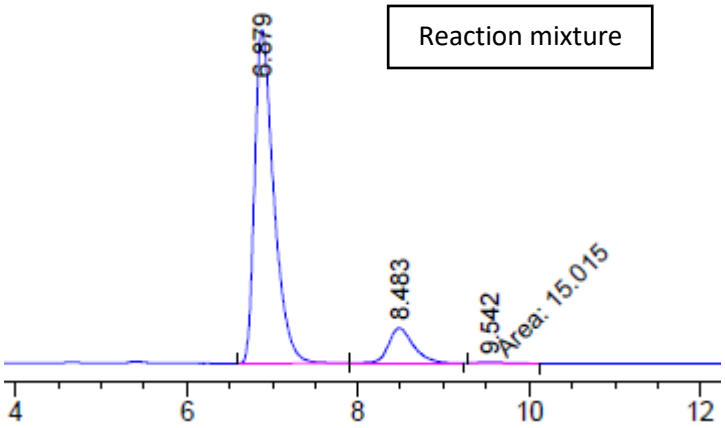
11.10 1-Indanone



1-indanone

Table Analytical method (HPLC) for ATH of 1-indanone

Column	CHIRALCEL-OD (length: 250 mm, diameter: 4.6 mm, particle size: 10 µm)		
Mobile phase	*n*-hexane / IPA = 95 / 5		
Flow rate	1 ml/min	Wavelength	254 nm
Retention time	1-Indanone: 6.9 min, Product (major): 8.5 min, Product (minor): 9.5 min		



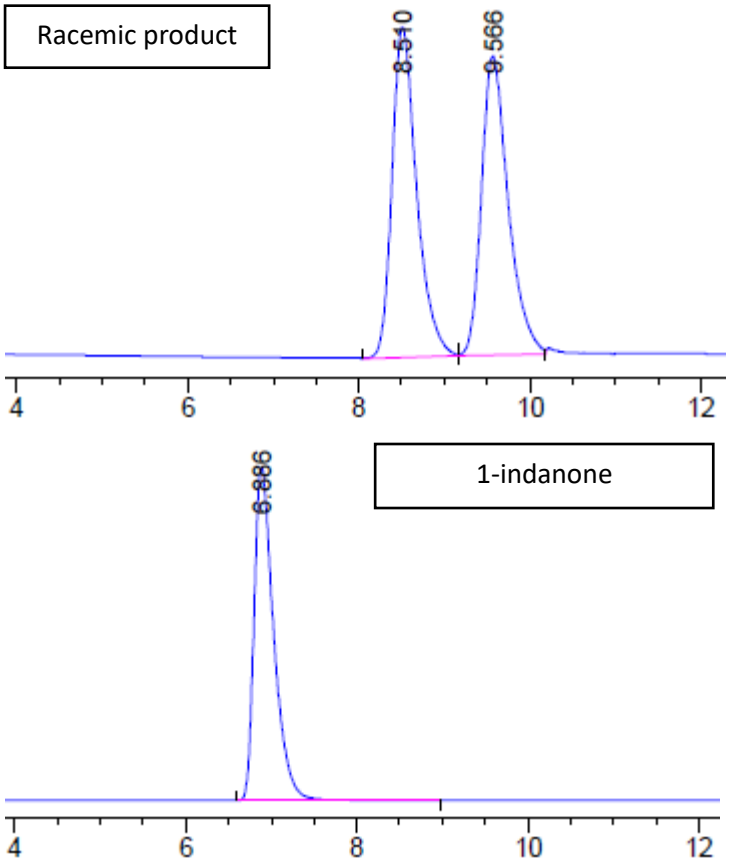
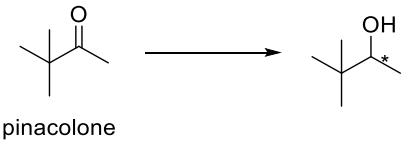


Figure HPLC trace of continuous flow ATH of 1-indanone

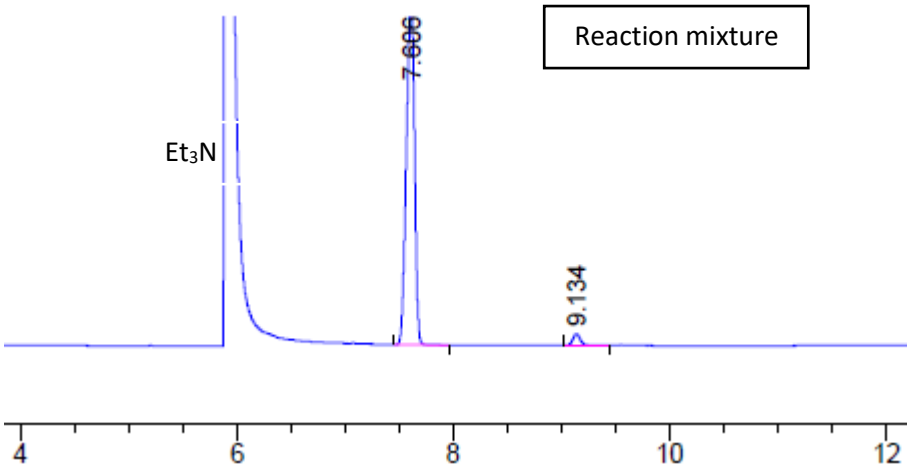
11.11 Pinacolone (3,3-dimethyl-2-butanone)

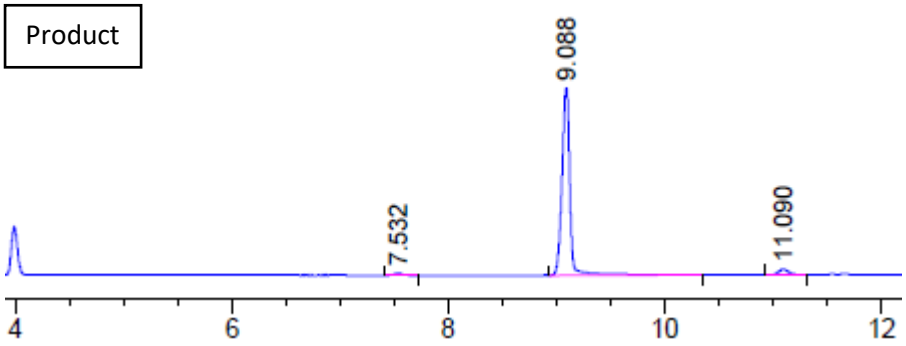


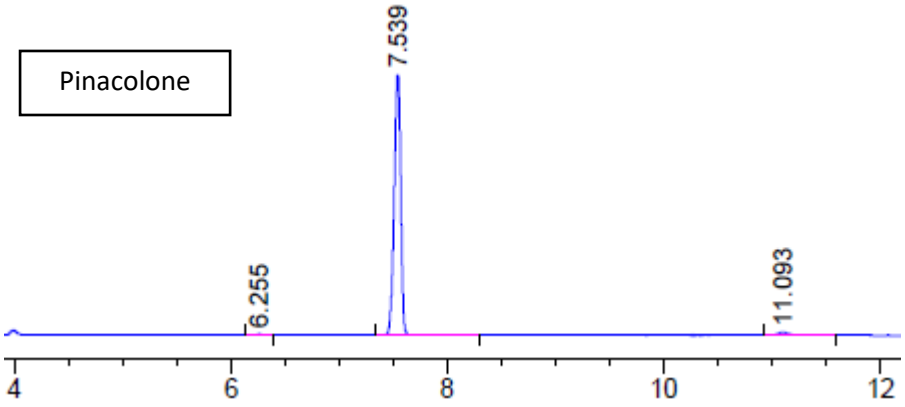
pinacolone

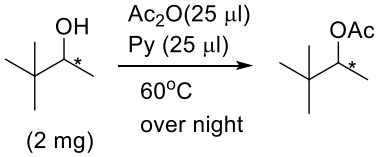
Table Analytical method (GC) for ATH of pinacolone (Conversion)

Column **(achiral)**	DB-624 (length: 30 m, diameter: 0.25 mm, film thickness: 1.4 µm)		
Column temp.	40 °C (5 min) - 10 °C/min - 60 °C (4 min) - 50 °C/min - 200 °C (2 min)		
Detector	FID (300 °C)	Carrier	H_2 69 cm/sec (constant pressure: 15 psi)
Make up	N_2 (45 ml/min)	Injector split	9.3/1
Retention time	Pinacolone: 7.6 min, Product: 9.1 min		







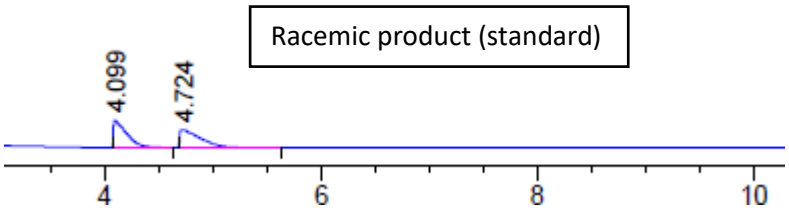


After evaporation of the sample and derivatization to the acetate[4], the acetate was analysed by GC on chiral phase to determine enantioselectivity. However target product was not observed, because original conversion from pinacolone to 3,3-dimethyl-2-butanone was very low (3%).

Table Analytical method (GC) for ATH of pinacolone (enantioselectivity)

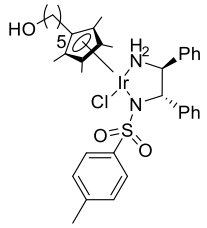
Column	CP-CHIRAL-DEX-CB (length: 25 m, diameter: 0.25 mm, film thickness: 0.25 µm)

(chiral)			
Column temp.	40 °C(5min) - 10 °C/min - 6 °C (4min) - 50 °C/min - 200 °C (2min)		
Detector	FID (300 °C)	Carrier	H_2 85 cm/sec (constant pressure: 15 psi)
Make up	N_2 (10 ml/min)	Injector split	10/1
Retention time	Product (acetate): 4.1 min and 4.7 min		

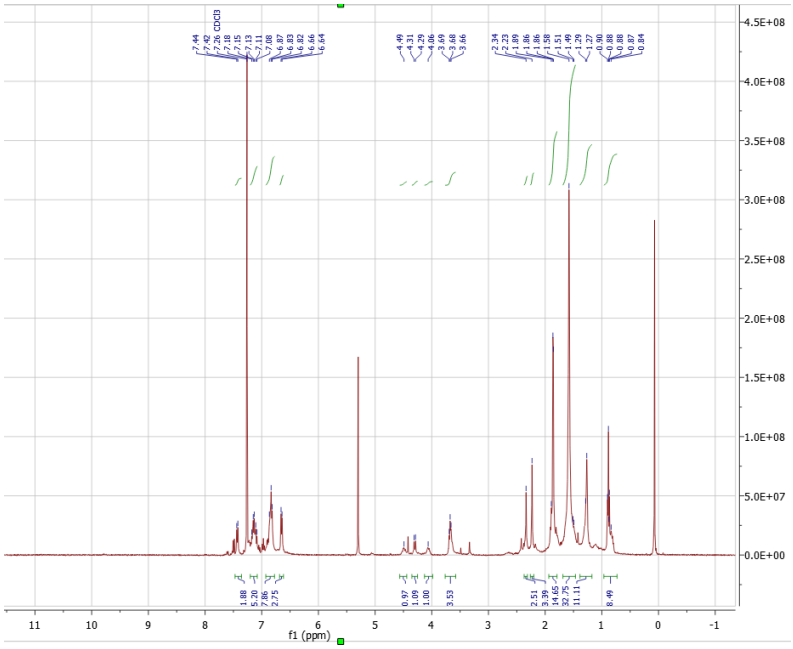


12 NMR spectra for the homogenous catalysts

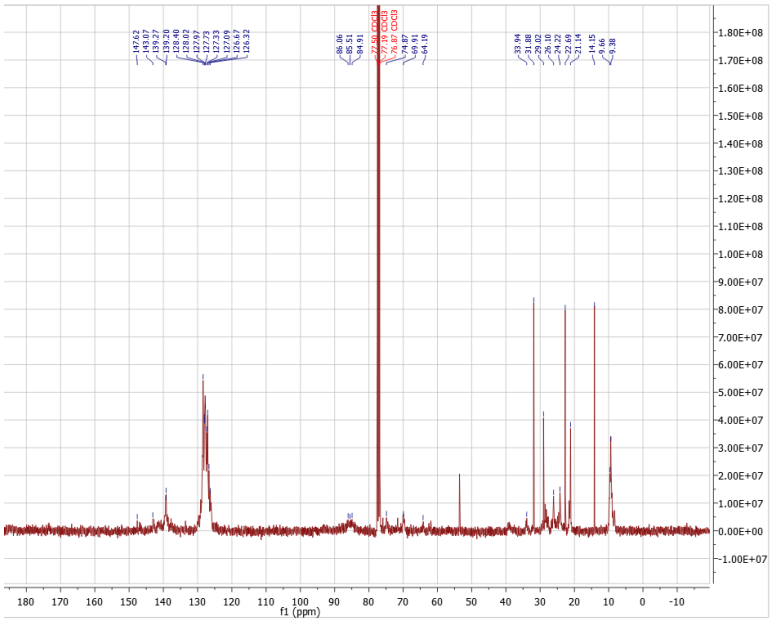
Ir(Cp*C_5H_{10}OH){(*S,S*)-TsDPEN}Cl (**3a**)



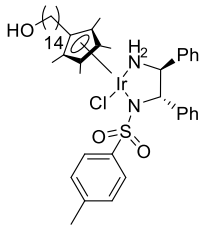
^{1}H-NMR



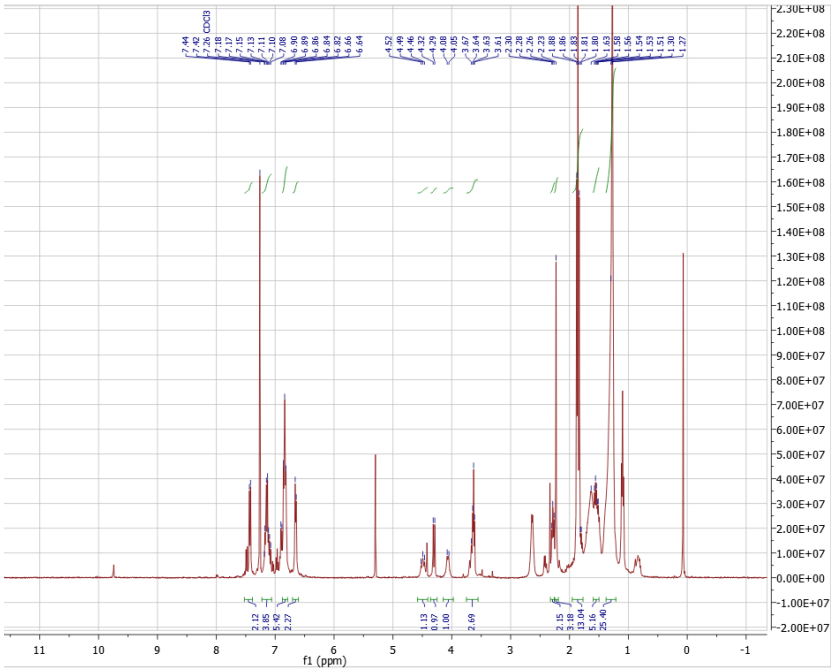
^{13}C-NMR



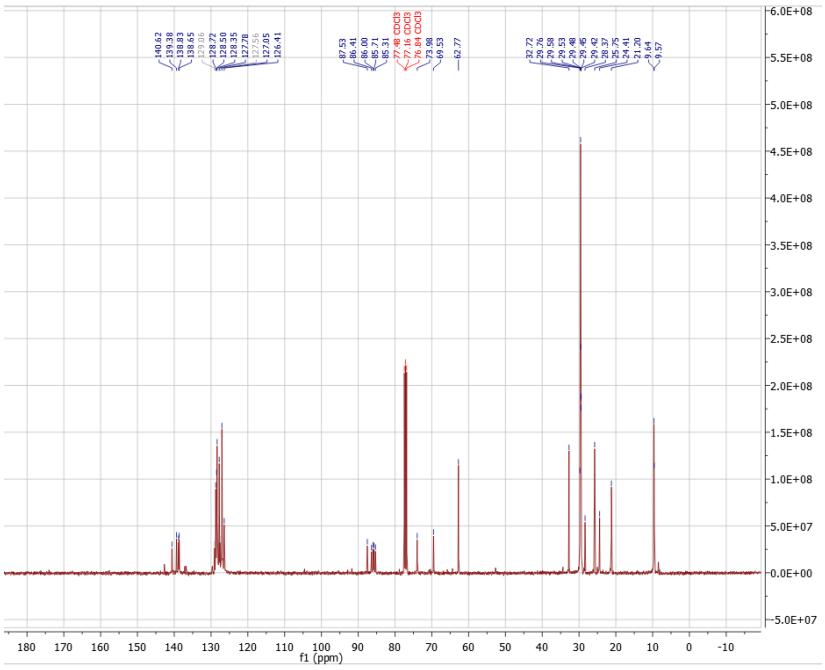
Ir(Cp*$C_{14}H_{28}OH$){(*S*,*S*)-TsDPEN}Cl (**3c**)



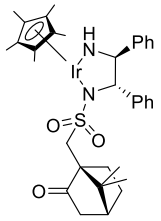
^{1}H-NMR



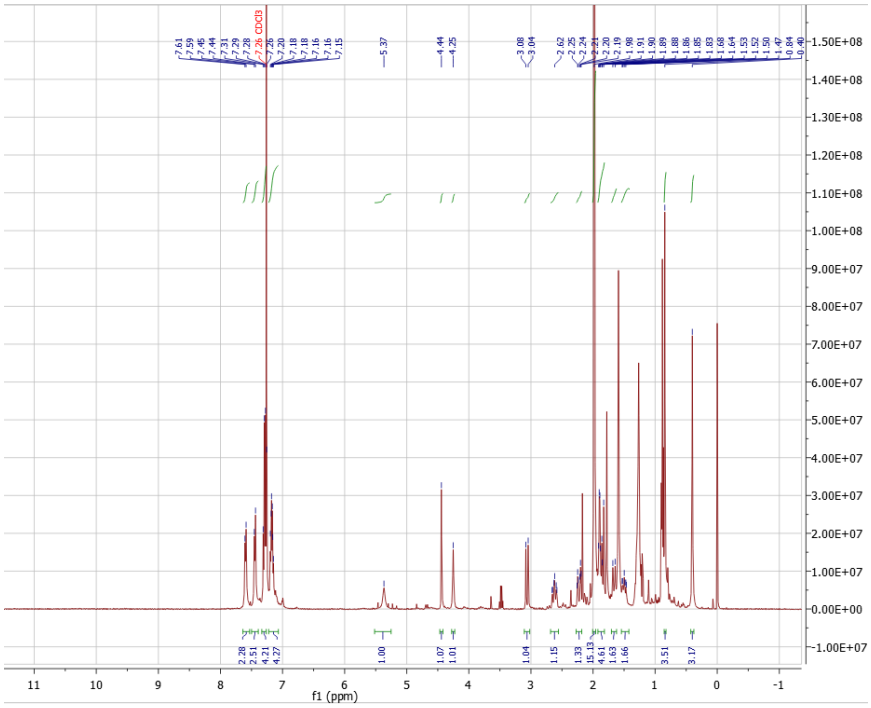
^{13}C-NMR



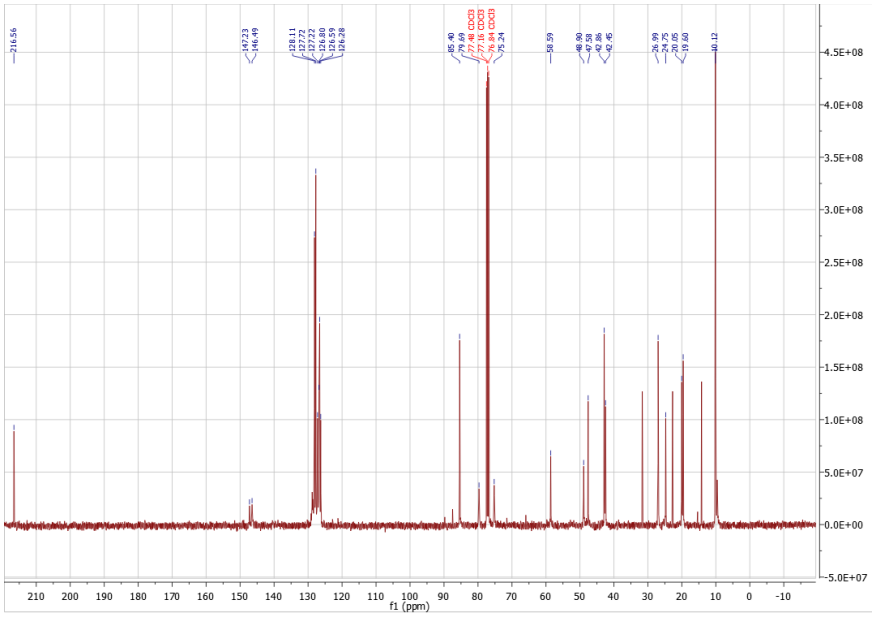
Ir(Cp*){(*S*,*S*,*S*)-CsDPEN}



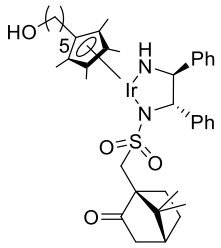
^{1}H-NMR



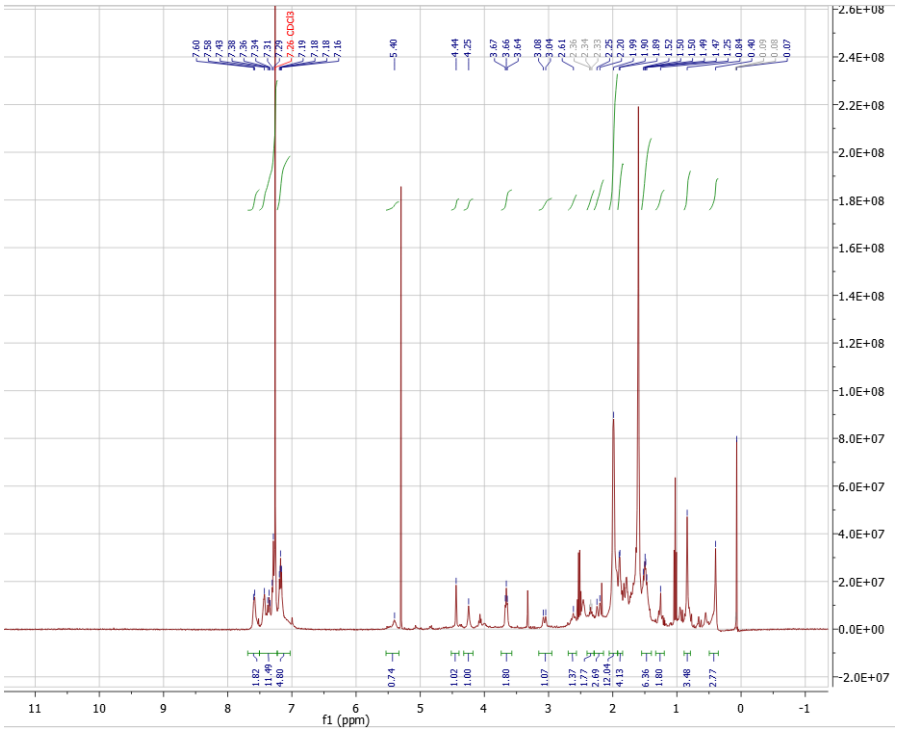
^{13}C-NMR



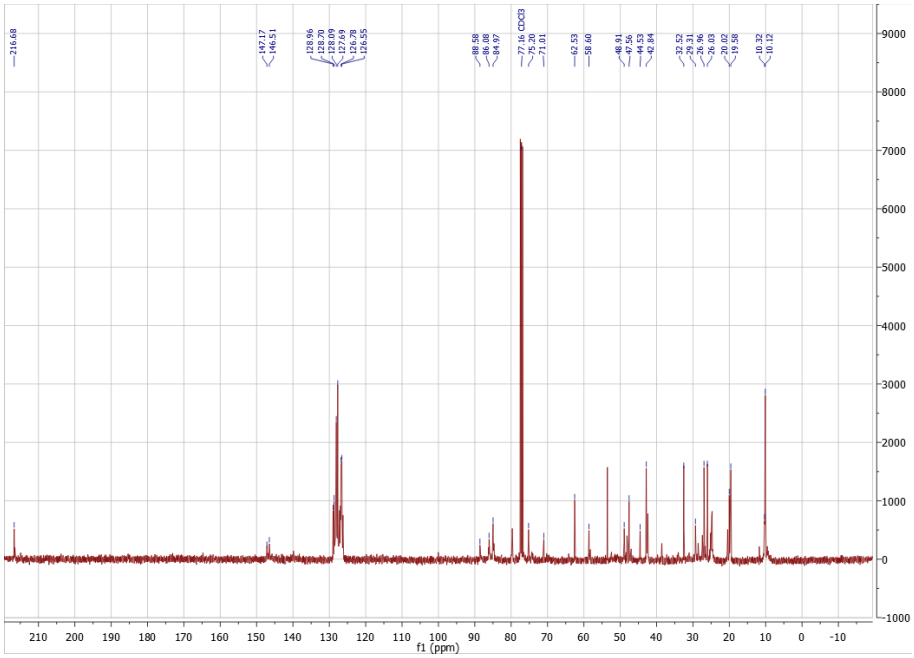
Ir(Cp*$C_5H_{10}OH$){(*S,S,S*)-CsDPEN} (**3b**)



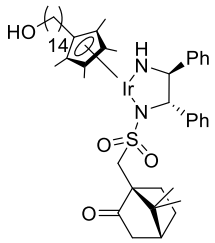
^{1}H-NMR



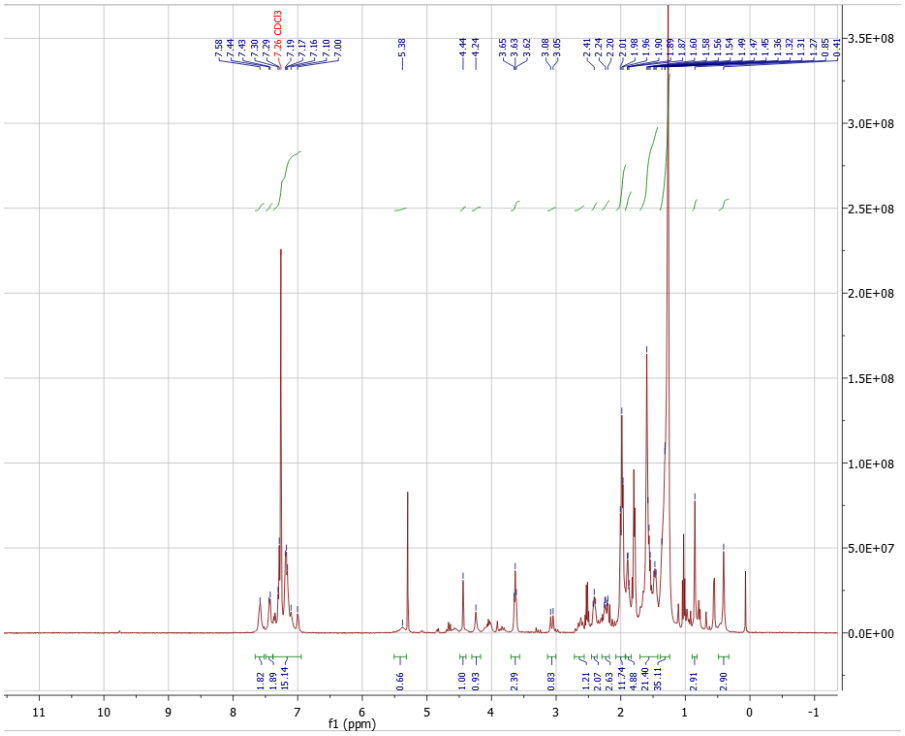
^{13}C-NMR



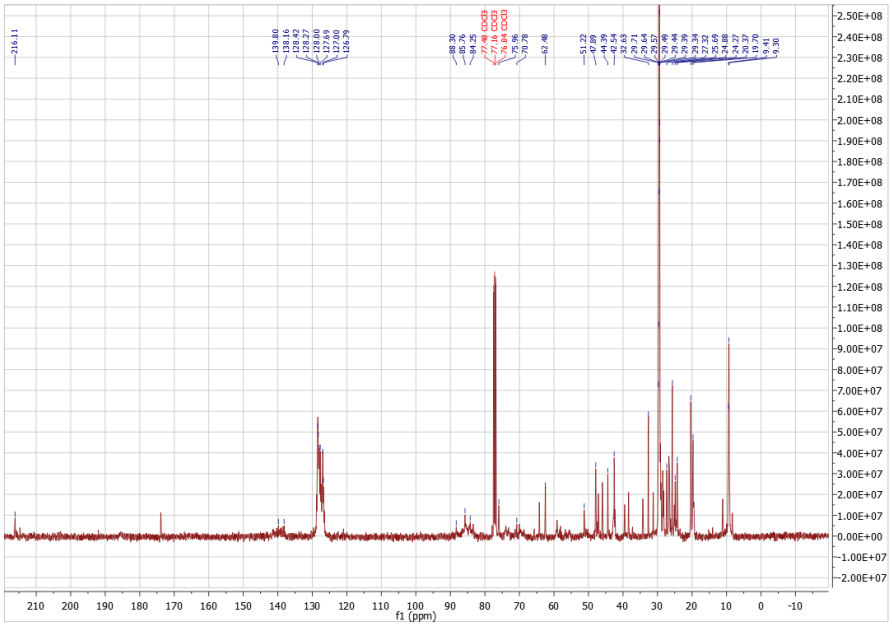
Ir(Cp*$C_{14}H_{28}OH$){(*S*,*S*,*S*)-CsDPEN}Cl (**3d**)



^{1}H-NMR

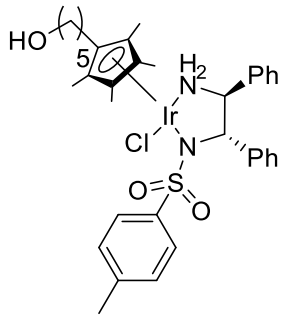


^{13}C-NMR

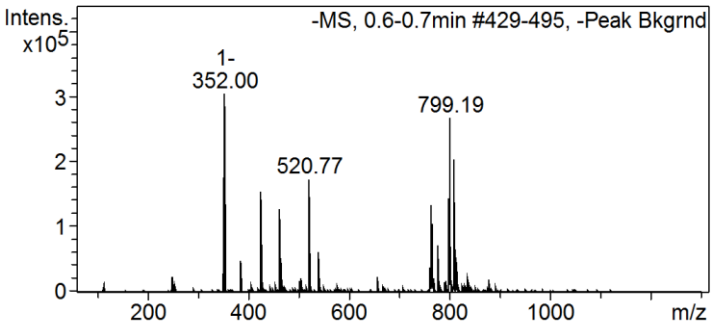


13 MS spectra for the homogenous catalysts

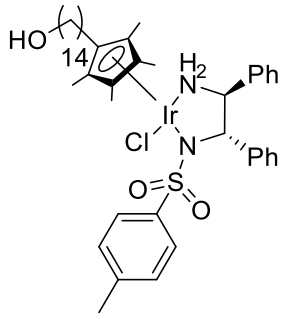
Ir(Cp*$C_5H_{10}OH$){(*S,S*)-TsDPEN}Cl (**3a**)



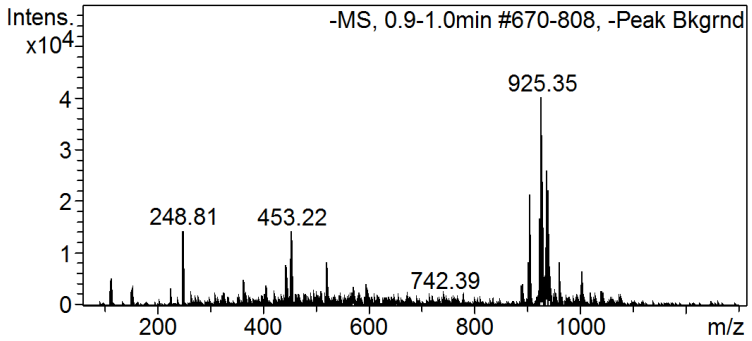
Chemical Formula: $C_{35}H_{44}ClIrN_2O_3S$, Exact MS: 800.24



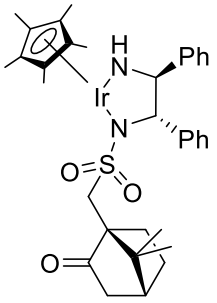
Ir(Cp*$C_{14}H_{28}OH$){(*S,S*)-TsDPEN}Cl (**3c**)



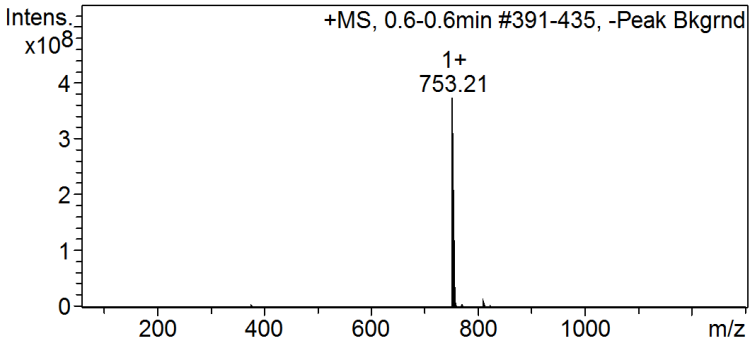
Chemical Formula: $C_{44}H_{62}ClIrN_2O_3S$, Exact MS: 926.38



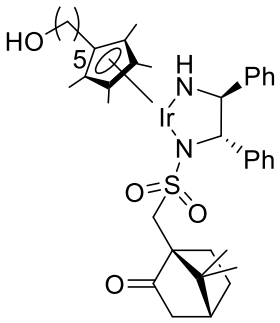
Ir(Cp*){(*S,S,S*)-CsDPEN}



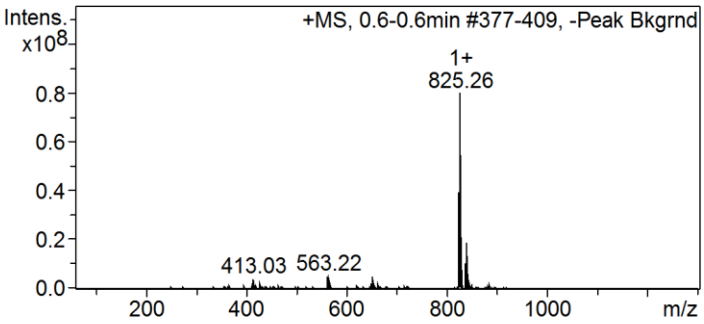
Chemical Formula: $C_{34}H_{43}IrN_2O_3S$, Exact MS: 752.26



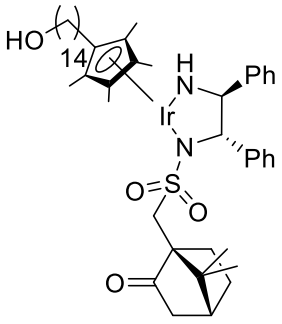
Ir(Cp*C_5H_{10}OH){(*S,S,S*)-CsDPEN} (**3b**)



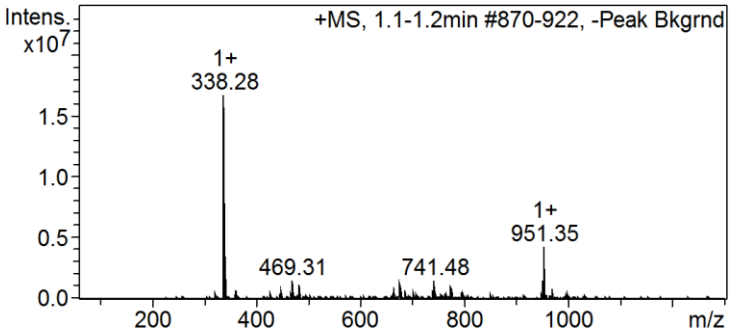
Chemical Formula: $C_{38}H_{51}IrN_2O_4S$, Exact MS: 824.32



Ir(Cp*$C_{14}H_{28}$OH){(*S,S,S*)-CsDPEN}Cl (**3d**)



Chemical Formula: $C_{47}H_{69}IrN_2O_4S$, Exact MS: 950.46



14 References

[1] Blacker A. J.; Brown S.; Clique B.; Gourlay B.; Headley C. E.; Ingham S.; Ritson D.; Screen T.; Stirling M. J.; Taylor D.; Thompson G. *Org. Process Res. Dev.* **2009**, *13*, 1370-1378.
[2] Blacker, A. J.; Treacher K.; Screen T. WO 2009/093059 A2, **2009**.
[3] Lucas, S. J.; Crossley, B. D.; Pettman, A. J.; Vassileiou, A. D.; Screen, T. E. O.; Blacker, A. J.; McGowan, P. C. *Chem. Commun*. **2013**, *49*, 5562−5564.
[4] Blacker, A. J.; Campbell, L.; Martin J.; Conference Proceedings of Scientific Update Organic Process Research and Development, Osaka, April 2004.
[5] Kaldun, J.; Krimalowski, A.; Breuning, M. *Tetrahedron. Lett.* **2016**, *57*, 2492-2495.