Easy-to-synthesise, robust, organo-osmium asymmetric transfer hydrogenation catalysts**

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Supporting Information

- Instrumentation
- Synthetic methods
- Catalytic reductions
- ^{1}H and ^{13}C NMR for **4a** / **4b** / **5a** / **5b**
- ^{1}H NMR of osmium hydride species
- Identification of dichlorido species **4a** / **4b**
- Crystallographic data for [Os(η^{6}-*p*-cymene)((*R,R*)-TsDPEN)] **5a**
- Crystallographic data for [Os(η^{6}-*p*-cymene)((*S,S*)-TsDPEN)] **5b**

Instrumentation

Nuclear magnetic resonance. Samples of complexes **4a**, **4b**, **5a** and **5b** were prepared in $CDCl_3$. 5 mm NMR tubes were used to record spectra at 298 K on Bruker DPX-400 or AV-600 spectrometers. Data processing was carried out using TOPSPIN version 2.0 (Bruker UK Ltd.).

Elemental analysis. Elemental analysis of complexes **4a**, **4b**, **5a** and **5b** (C, H, N) was carried out by Warwick Analytical Services on an Exeter elemental analyser CE440.

High resolution mass spectrometry. HRMS of complexes **4a**, **4b**, **5a** and **5b** in acetonitrile were obtained using a Bruker UHR-Q-TOF MaXis. A positive ion scan range of *m/z* 50-3000 with a spectra rate of 1 Hz was selected. Analysis was carried out through direct infusion (2 µL/min) with a syringe pump, with sodium formate (10 mM) calibration. Source conditions: ESI (+); end plate offset: -500 V; capillary: -3000 V; nebulizer gas (N_2): 0.4 bar; dry gas (N_2): 4 L/min; dry temperature: 453 K; funnel RF: 200 Vpp; multiple RF: 200Vpp; quadruple low mass: 55 *m/z*; collision energy: 5.0 eV; collision RF: 600 Vpp; ion cooler RF: 50-250 Vpp ramping; transfer time: 121 µs; pre-pulse storage time: 1 µs.

Ultraviolet-visible spectroscopy. The ultraviolet-visible spectra for complexes **4a**, **4b**, **5a** and **5b** in DCM (0.1 - 0.3 mM) were recorded using a Cary 300 scan spectrophotometer. Path length of cell 1 cm, range 800-200 nm, average time 0.1 s, data interval 1 nm; scan rate 600 nm/min.

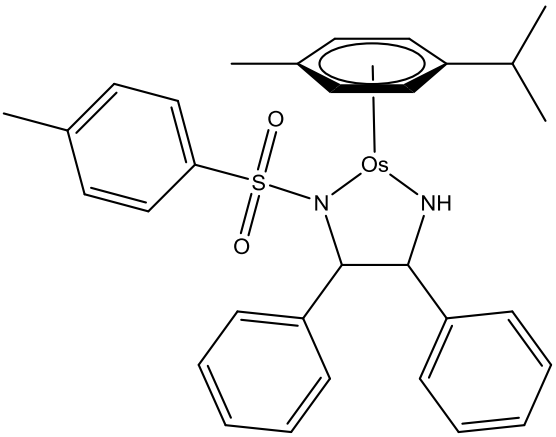
Gas chromatography. Reduction products of **6**-**9**: Chrompac cyclodextrin-β-236M-19, 50 m x 0.25 mm x 0.25 µm, *P* = 15 psi, gas H_2. Temperature varied depending on substrate. Reduction products of **10**: Chrompac-chirasil-DEX CB, 25 m x 0.25 mm x 0.25 µm, *T* = 383 K, *P* = 18 psi, gas He.

Synthetic Methods

[Os(η^6-*p*-cymene)Cl$_2$]$_2$. Osmium trichloride trihydrate (1.00 g, 2.8 mmol, 2 mol equiv) was dissolved in degassed methanol (10 mL). To this was added α-phellandrene (3.8 g, 28 mmol, 20 mol equiv) with stirring. The reaction vessel was placed in a CEM Discovery-SP microwave reactor for 10 min (413 K, 150 W, 250 psi) after which a precipitate of a crystalline orange solid was observed. The solution was washed with n-pentane (3 × 10 mL) before the solid was collected, washed with additional n-pentane (3 × 10 mL) and dried with diethyl ether yielding a bright orange crystalline solid (863 mg, 1.1 mmol, 79%).

[OsCl$_2$(η^6-*p*-cymene)(TsDPEN)] (4a and 4b). To a stirred solution of osmium p-cymene-chlorido dimer (50 mg, 0.06 mmol, 1 mol equiv) in dry DCM (2.5 mL) was added either (1*R*,2*R*)-TsDPEN (for **4a**) or (1S,2S)-TsDPEN (for **4b**) (50 mg, 0.14 mmol, 2.05 mol equiv). The resulting yellow solution was placed in a CEM Discovery-SP microwave reactor for 10 min (393 K, 150 W, 250 psi) after which the colour changed to red. After cooling and concentration in vacuo, a large excess of hexane was added to precipitate the product as an amorphous yellow solid (88 mg, 0.12 mmol, 89%). ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ=7.41 (d, ^3J(H,H)=7.9 Hz, 2H), 7.17-7.22 (m, 2H), 7.04-7.08 (m, 2H), 6.89-6.96 (m, 3H), 6.81-6.86 (m, 3H), 6.64 (d, ^3J(H,H)=7.6, 2H), 6.38 (d, ^3J(H,H)=8.3 Hz, H; TsNH), 5.60 (d, ^3J(H,H)=5.3 Hz, 1H; Os-ArH), 5.32-5.37 (m, 2H; Os-ArH), 5.23 (d, ^3J(H,H)=5.3 Hz, 1H; Os-ArH), 5.20 (d, ^3J(H,H)=11.6 Hz, 1H; NH_2), 4.50-4.58 (m, 1H; $CHNH_2$), 4.43-4.50 (m, 1H; CHNHTs), 4.20 (t, ^3J(H,H)=10.7 Hz, 1H; NH_2), 2.59 (sept, ^3J(H,H)=6.9 Hz, 1H; $CH(CH_3)_2$), 2.20 (s, 3H; CH_3), 2.02 (s, 3H; CH_3), 1.13 (d, ^3J(H,H)=6.9 Hz, 3H; $CH(CH_3)_2$), 1.08 (d, ^3J(H,H)=6.9 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ 129.3, 128.9, 128.2, 127.7, 127.4, 127.2, 72.6, 71.5, 70.9, 70.8, 65.1, 63.8, 31.0, 22.6,

22.4, 21.4, 18.7; UV/Vis: λmax 264 and 337 nm; HRMS (*m/z*): [M-H]- calcd. for $C_{31}H_{35}Cl_2N_2O_2OsS$, 761.1406; found, 761.1347; [M-HCl-Cl]+ calcd. for $C_{31}H_{35}N_2O_2OsS$, 691.2028; found, 691.2036; analysis (calcd., found for **4a** $C_{31}H_{36}Cl_2N_2O_2OsS$): C (48.87, 48.72), H (4.76, 4.73), N (3.68, 3.76); analysis (calcd., found for **4b** $C_{31}H_{36}Cl_2N_2O_2OsS$): C (48.87, 48.78), H (4.76, 4.75), N (3.68, 3.74).



[Os(η^6-*p*-cymene)(TsDPEN)] (5a and 5b). Osmium p-cymene-chlorido dimer (51.4 mg, 0.065 mmol 1 mol equiv) and either (1*R*,2*R*)-TsDPEN (for **5a**) or (1*S*,2*S*)-TsDPEN (for **5b**) (51.3 mg, 0.14 mmol, 2.1 mol equiv) were stirred in chloroform (5 mL) with freshly ground KOH (56.1 mg, 1 mmol, 15 mol equiv). A colour change from yellow to red was observed < 1 min. After 5 min, H_2O (5 mL) was added with stirring for a further 10 min. The organic layer was removed by syringe and concentrated in vacuo to yield a red oil, which was dissolved in the minimum amount of DCM, followed by addition of a large excess of n-hexane. Formation of red needle crystals was observed (sometimes requiring further reduction in the volume of solvent in vacuo), and larger crystals were grown by leaving the DCM / hexane solution in a freezer at 253 K. A significant reduction in yield was observed when the product was collected as a red solid (73 mg, 0.105 mmol, 81%). ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ=7.41 (d, ^3J(H,H)=7.6 Hz, 2H), 7.05-7.20 (m, 10H), 6.82 (d, ^3J(H,H)=8.0 Hz, 2H), 6.80 (br s, 1H; NH), 5.79 (d, ^3J(H,H)=5.6 Hz, 1H; Os-ArH), 5.62 (d, ^3J(H,H)=5.6 Hz, 1H; Os-ArH), 5.52 (d, ^3J(H,H)=5.6 Hz, 1H; Os-ArH), 5.42 (d, ^3J(H,H)=5.6 Hz, 1H; Os-ArH), 4.42 (s, 1H; $CHCHNH_2$), 3.94 (d, ^3J(H,H)=4.3 Hz, 1H; TsNCH), 2.45 (sept, ^3J(H,H)=6.9 Hz, 1H; $CH(CH_3)_2$), 2.23 (s, 3H; CH_3), 2.22 (s, 3H; CH_3), 1.23 (d, ^3J(H,H)=6.9 Hz, 3H; $CH(CH_3)_2$), 1.17 (d, ^3J(H,H)=6.9 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ 127.4, 127.0, 126.8, 126.0, 125.9, 125.9, 125.4, 81.7, 76.2, 72.4, 70.7, 70.0, 66.2, 22.5, 22.4, 20.2; UV/Vis: λ_{max} 260, 410 and 478 nm; HRMS (*m/z*): $[M+H]^+$ calcd.

for $C_{31}H_{35}N_2O_2OsS$, 691.2; found, 691.2; analysis (calcd., found for **5a** $C_{31}H_{34}N_2O_2OsS$): C (54.05, 53.66), H (4.97, 4.88), N (4.07, 3.95); analysis (calcd., found for **5b** $C_{31}H_{34}N_2O_2OsS$): C (54.05, 53.71), H (4.97, 4.84), N (4.07, 4.00).

Crystal growth for complexes 5a and 5b. Single crystals of $C_{31}H_{34}N_2O_2OsS$ **5a** and **5b** were grown from $CHCl_3$/hexane. A suitable crystal was selected in each case and mounted on a glass fibre with Fromblin oil and placed on an Oxford Diffraction Gemini diffractometer with a Ruby CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2[1], the structure was solved with the ShelXS[2] structure solution program using Direct Methods and refined with the ShelXL[2] refinement package using Least Squares minimisation. Both complexes had a Flack parameter greater than 2σ from zero however this is within an acceptable range for complexes synthesised from compounds of known chirality.

Catalytic Reductions

ATH reductions were conducted under N_2 for 24 h unless stated otherwise. Aliquots of reaction solution for analysis were placed into 1 mL EtOAc and 1 mL $NaHCO_3$ and the organic layer was filtered through a plug of silica. Conversion and e.e. were analysed by GC-FID.

Asymmetric reduction of 6-10 (S/C = 100). Pre-catalyst **4a** / **4b** (7.61 mg, 10 µmol, 1 mol equiv) was stirred in a 5:2 formic acid / triethylamine azeotrope (0.5 mL) for 30 min to ensure the catalyst was dissolved. A prochiral ketone (**6-10**) was injected (1 mmol, 100 mol equiv) and stirred.

Asymmetric reduction of 6 (S/C = 200). Active catalyst **5a** / **5b** (3.45 mg, 5 µmol, 1 mol equiv) was stirred in a 5:2 formic acid / triethylamine azeotrope (0.5 mL) for 30 min to ensure the catalyst was completely dissolved. Acetophenone **4** (120 mg) was injected (1 mmol, 200 mol equiv) and stirred.

Racemic reduction of 7-8 with $NaBH_4$. To an ice-cold solution of sodium borohydride (100 mg, 2.53 mmol, 2 mol equiv of H^-) in ethanol (1.5 mL) was added 4'-chloro-acetophenone (0.67 mL, 5.14 mmol) or 4'-methoxy-acetophenone (771 mg, 5.14 mmol) drop-wise over 15 min. A white solid was precipitated by addition of 3 M HCl (0.5 mL). Diethyl ether (5 mL) and water (5 mL) were added and the organic layer was dried over $MgSO_4$. The solvent was evaporated, yielding a colourless liquid.

Chiral GC data for reduction products from the following ketones:

Acetophenone (6). 120 mg. **6** = 12.1 min, *S* = 19.0 min, *R* =18.4 min. *T* = 388 K, t = 0.5 h.

4'-chloro- (7). 155 mg. **7** = 10.5 min, *S* = 17.1 min, *R* = 16.5 min. *T* = 423 K, t = 0.5 h.

4'-methoxy- (8). 150 mg. **8** = 35.7 min, *S* = 40.5 min, *R* = 39.0 min. *T* = 403 K, t = 1 h.

α-chloro- (9). 155 mg. **9** not recorded, *S* = 11.4 min, *R* = 11.2 min. *T* = 388 K, t = 0.5 h.

Propiophenone (10). 134 mg. **10** = 9.4 min, *S* = 26.0 min, *R* = 24.0 min. *T* = 383 K, t = 0.5 h.

NMR Data for complex 4a

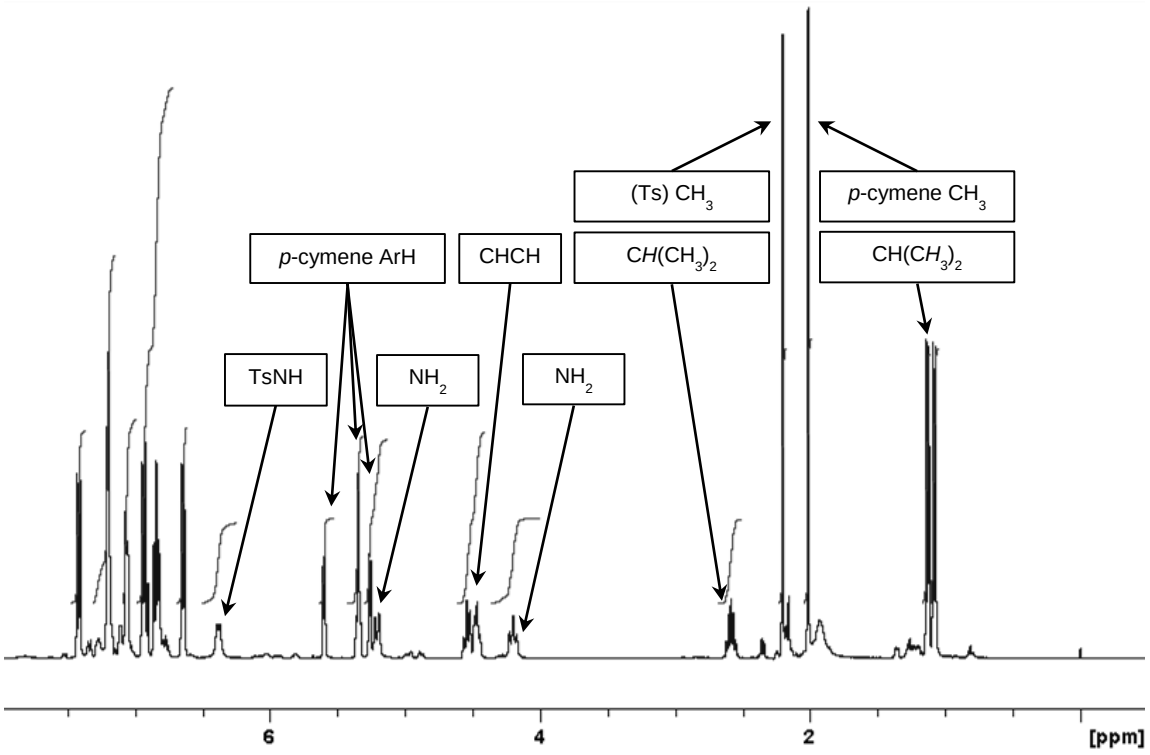


Figure S1: ^{1}H-NMR spectrum of complex **4a** (400 MHz, $CDCl_3$, TMS) with key assignments.

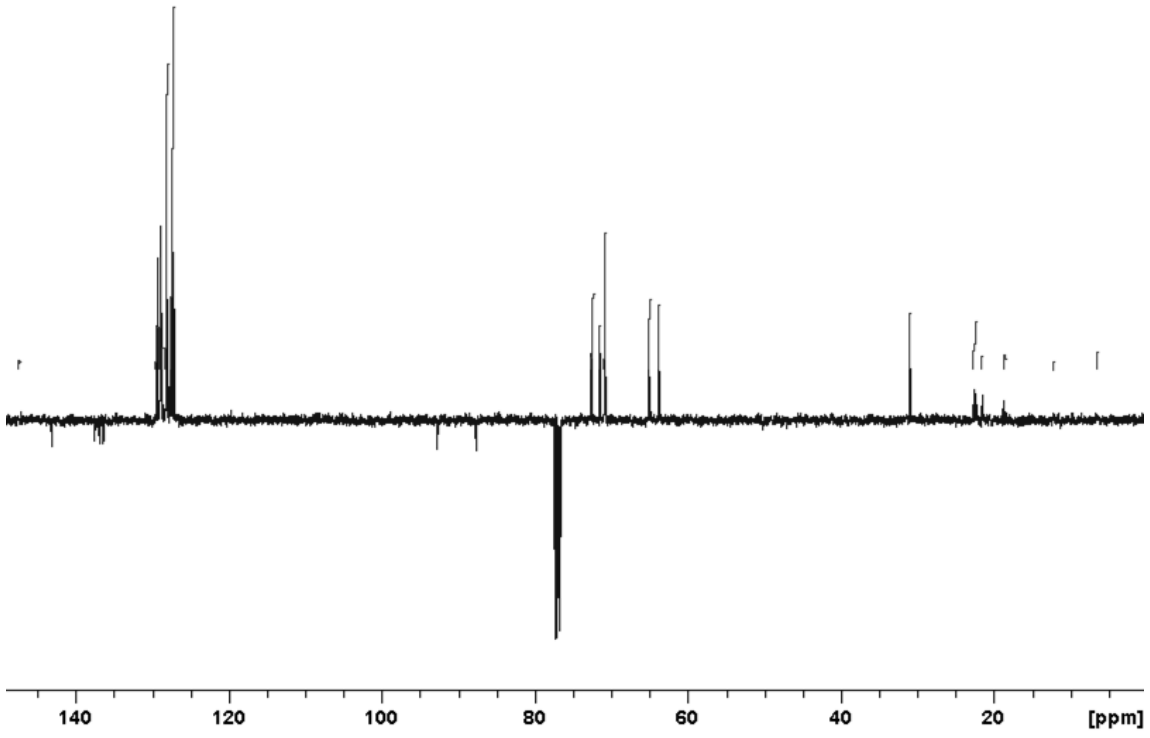


Figure S2: ^{13}C-NMR spectrum (dept 135, long acquisition) of complex **4a** (100 MHz, $CDCl_3$, TMS).

NMR Data for complex 4b

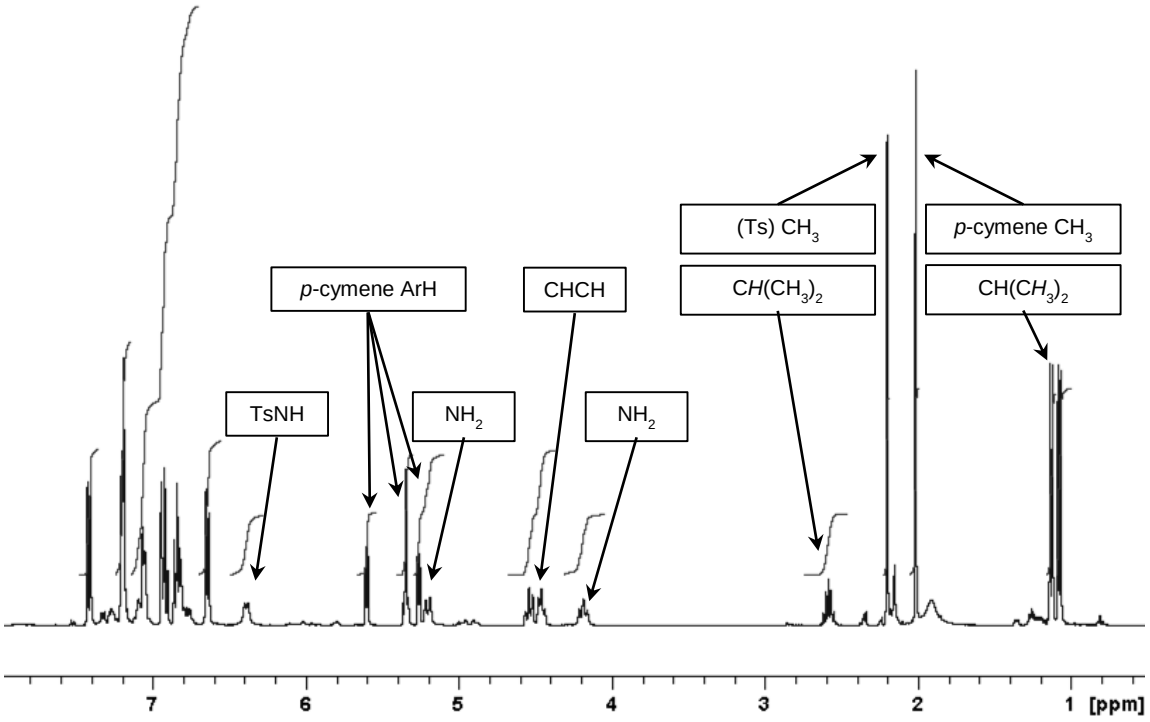


Figure S3: ^{1}H-NMR spectrum of complex **4b** (400 MHz, $CDCl_3$, TMS) with key assignments.

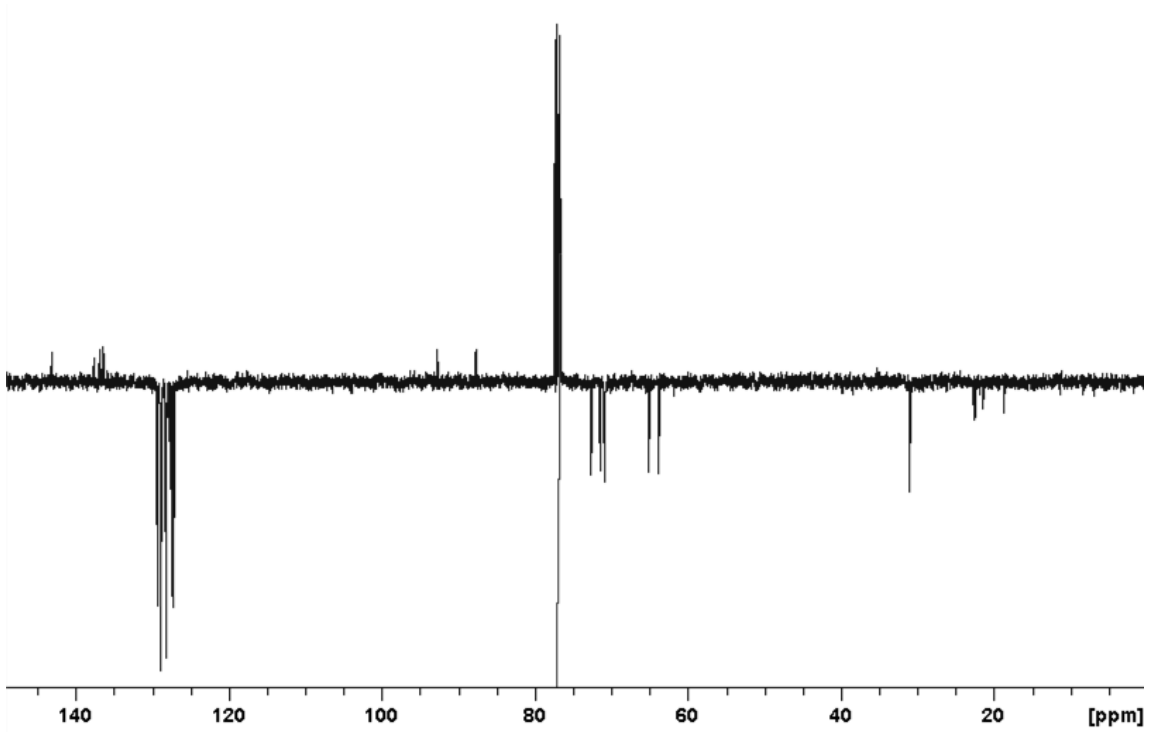


Figure S4: ^{13}C-NMR spectrum (dept 135, long acquisition) of complex **4b** (100 MHz, $CDCl_3$, TMS).

NMR for complex 5a

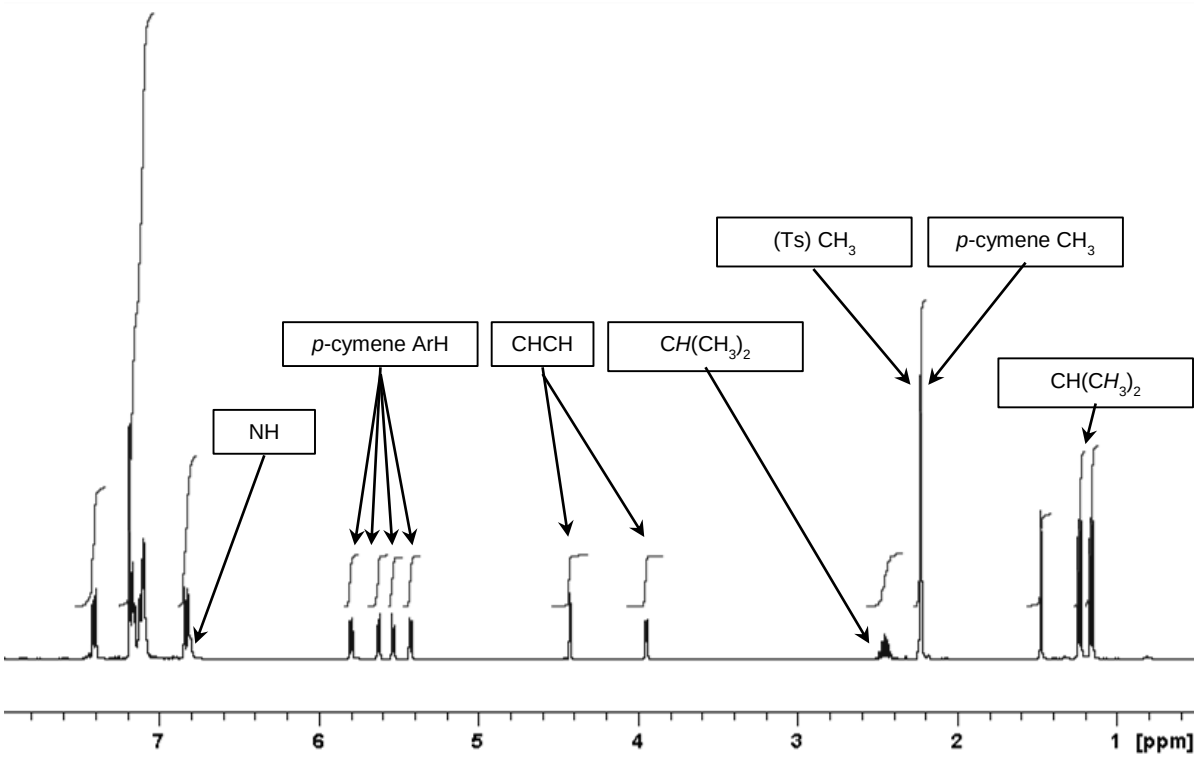


Figure S5: ^{1}H-NMR spectrum of complex **5a** (400 MHz, $CDCl_3$, TMS) with key assignments.

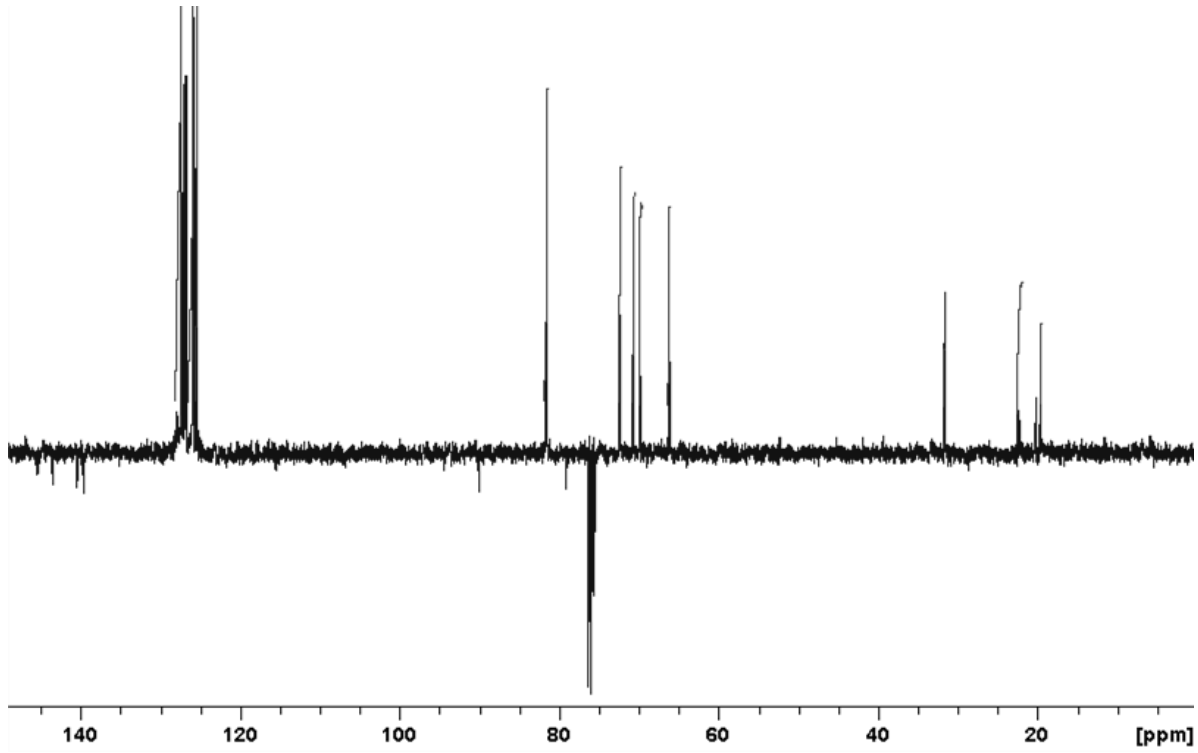


Figure S6: ^{13}C-NMR spectrum (dept 135, long acquisition) of complex **5a** (100 MHz, $CDCl_3$, TMS).

NMR for complex 5b

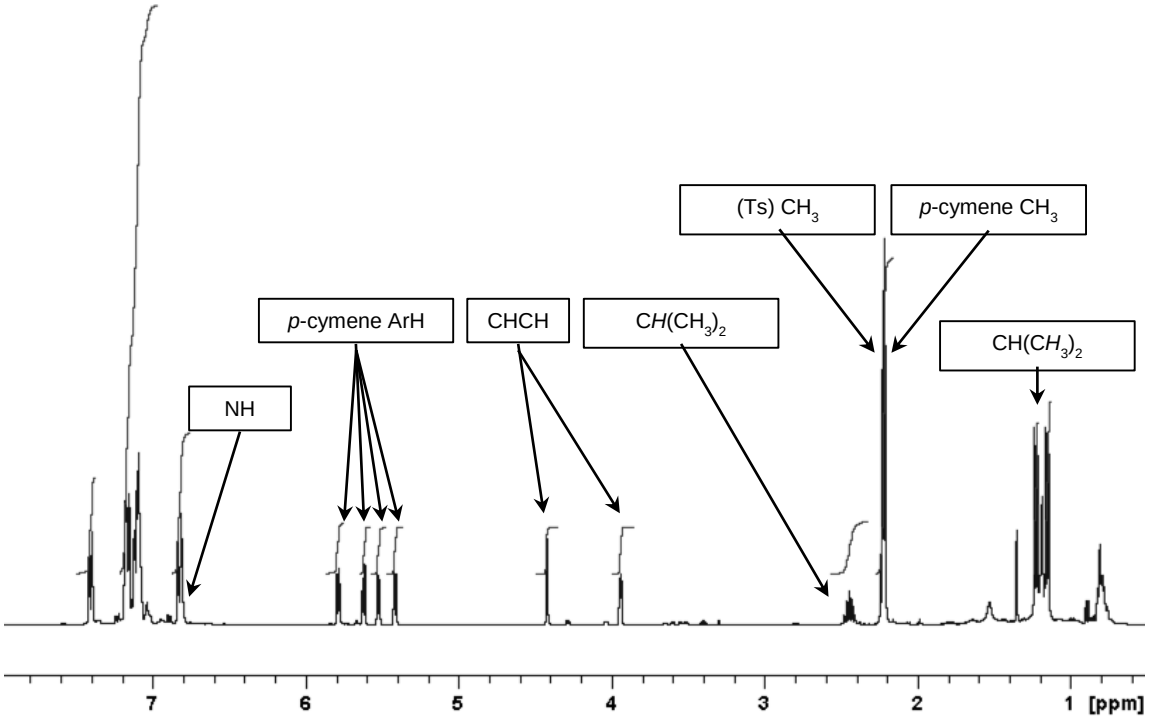


Figure S7: ^{1}H-NMR spectrum of complex **5b** (400 MHz, $CDCl_3$, TMS) with key assignments.

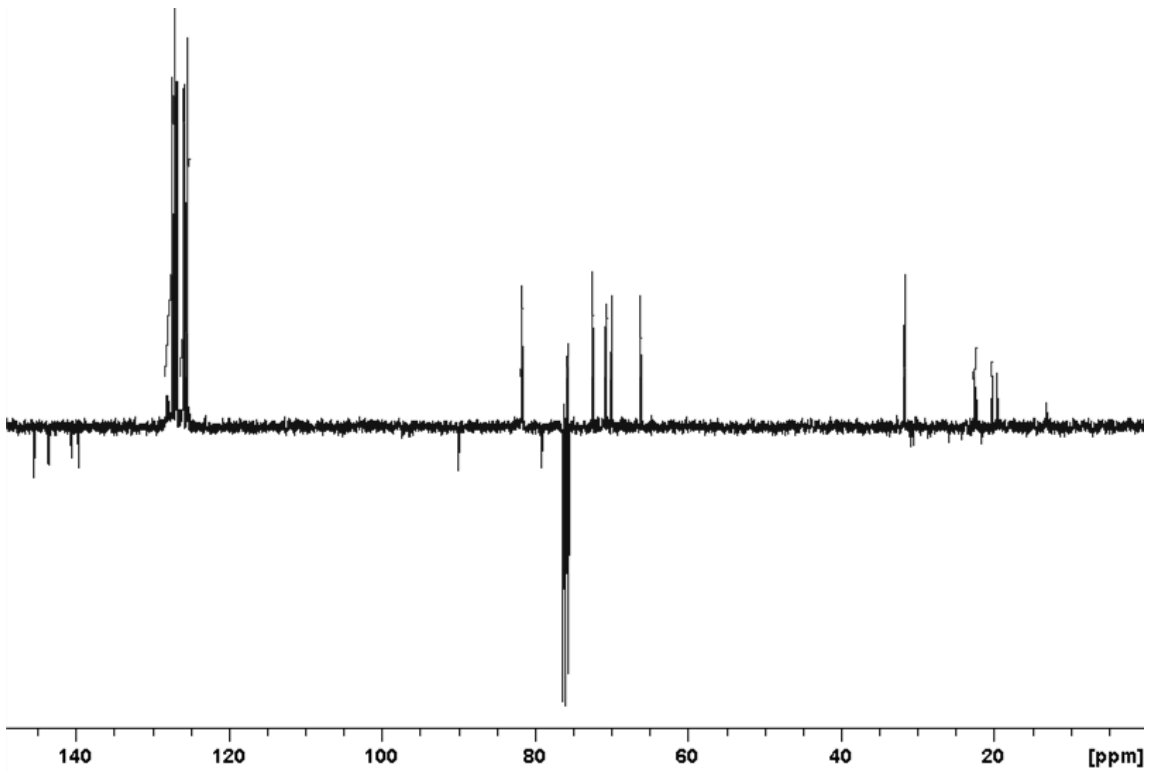


Figure S8: ^{13}C-NMR spectrum (dept 135, long acquisition) of complex **5b** (100 MHz, $CDCl_3$, TMS).

^{1}H NMR of osmium hydride species

The treatment of complex **4** with 4.0 mol equiv of triethylamine followed by the addition of 2 µL of formic acid allowed for the observation of osmium hydride resonances, observed as two singlets at -5.89 and -6.04 ppm, each having ^{187}Os satellites ($^{1}J(^{187}Os,^{1}H)$ = 44 Hz). Over a period of 30 min, the ratio between the resonances decreased from 3:1 to 1.2:1; a similar observation has been made in the case of the analogous Ru^{II} complexes.[3]

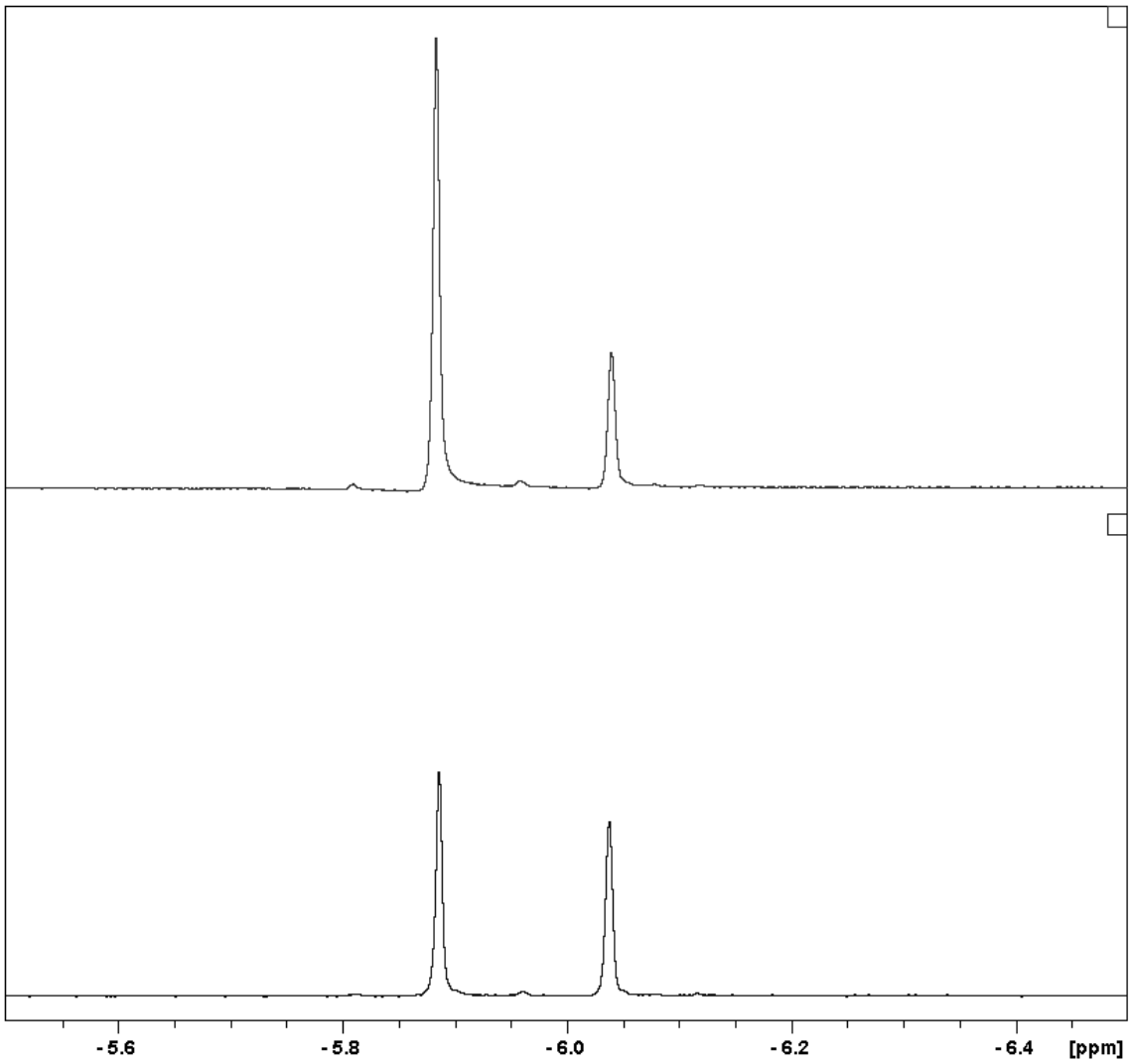


Figure S9: 600 MHz ^{1}H-NMR spectrum showing Os-H formation as two singlets with the ratio changing over time: initially 3:1 (top) and 1.2:1 after 30 min (bottom).

Identification of Dichlorido Species 4a / 4b

Evidence for the characterisation of **4a** / **4b** as species containing two chlorido ligands was obtained, revealing the novel monodentate-TsDPEN complex that differs from Noyori-type ruthenium catalysts.

Infra-red spectroscopy

TsN-H bond stretch absorbance remains at 2859 cm^{-1}, whilst terminal amine N-H stretches are shifted from 3344 and 3281 cm^{-1} in the free ligand to 3078 and 2953 cm^{-1} in the complex.

Mass spectrometry

Dichlorido species **4** identified by high resolution MS (Bruker MaXis) with samples of the complex in acetonitrile. The mass is consistent with synthesis in the absence of base.

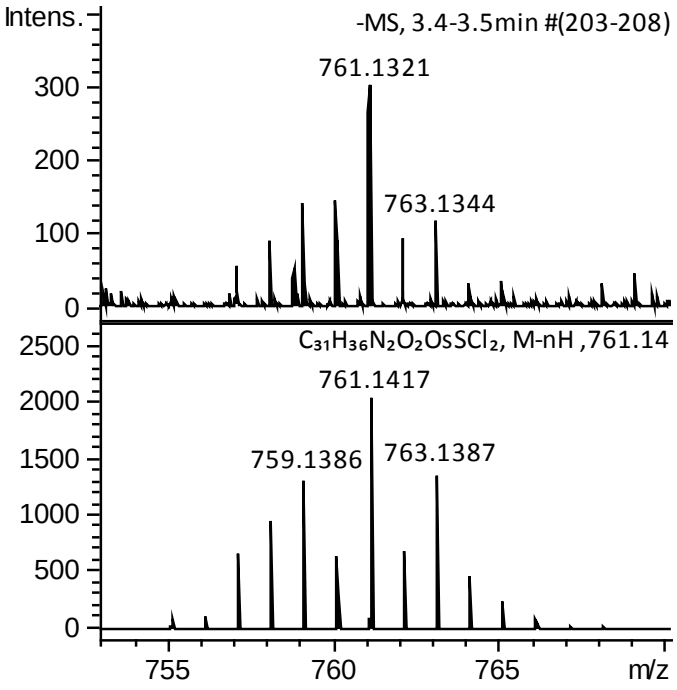


Figure S10: HRMS of [**4a**-H]$^-$ (upper) and simulated spectrum of $C_{31}H_{35}N_2O_2OsSCl_2$ (lower).

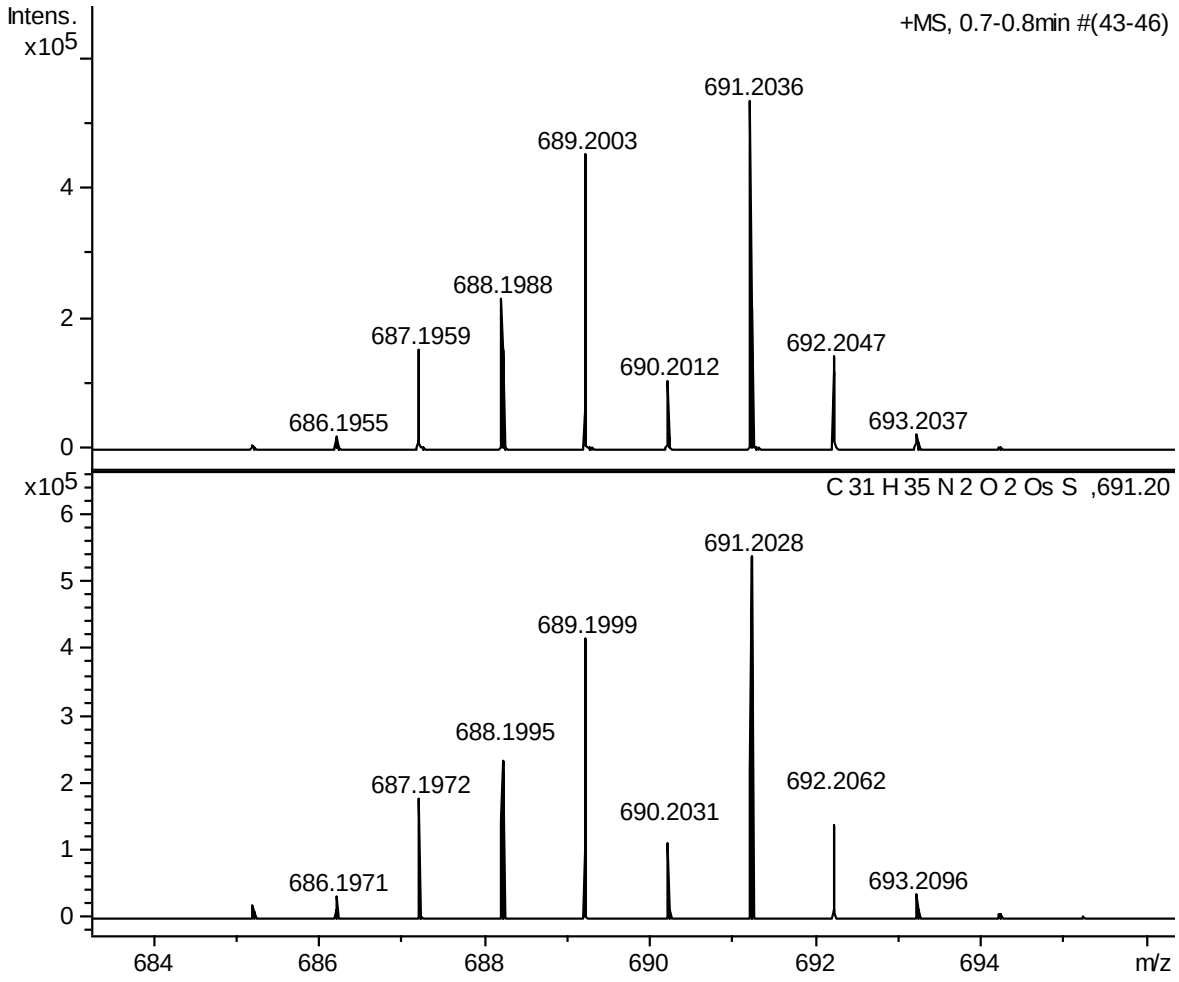


Figure S11: HRMS of [**4a**-HCl-Cl]$^+$ (top) and simulated spectrum of $C_{31}H_{35}N_2O_2OsS$ (bottom).

Crystallographic data for [Os(η^6-*p*-cymene)((*R*,*R*)-TsDPEN)] 5a - CCDC 1035611

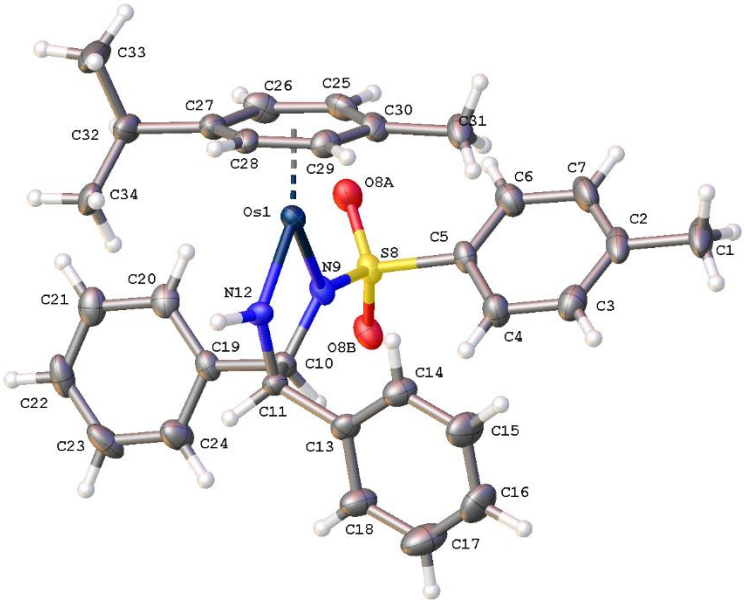


Figure S12: X-ray crystal structure of **5a** with atom labels. Thermal ellipsoids are drawn at the 50% probability level. The asymmetric unit contains the complex, there are 4 complexes in the unit cell. The hydrogen on N12 was located in a difference map. It was allowed to refine freely but given a U_{iso} 1.5 times U_{equiv} of the parent nitrogen. The Flack parameter was more than 2 sigma from zero, but is from a known chiral starting material so is within acceptable limits

Crystal Data for $C_{31}H_{34}N_2O_2OsS$ (*M* =688.86 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 10.6100(3) Å, *b* = 13.8464(3) Å, *c* = 18.9830(5) Å, *V* = 2788.79(11) Å^3, *Z* = 4, *T* = 150(2) K, μ(MoKα) = 4.678 mm^{-1}, *Dcalc* = 1.641 g/cm^3, 33345 reflections measured (4.836° ≤ 2Θ ≤ 61.698°), 8053 unique (R_{int} = 0.0557, R_{sigma} = 0.0502) which were used in all calculations. The final R_1 was 0.0333 (I > 2σ(I)) and wR_2 was 0.0927 (all data).

Flack x: 0.023(5) (Shelx); Hooft y: 0.039(5) (Olex2)

Selected distances (Å) and angles (°): Os-N12 1.916(6), Os-N9 2.046(6), N12-H12 0.96(11); N12-Os-N9 78.3(3), Os-N12-C11 121.6(5), Os-N9-C10 115.9(4).

Crystallographic data for [Os(η^6-*p*-cymene)((*S*,*S*)-TsDPEN)] 5b - CCDC 1035612

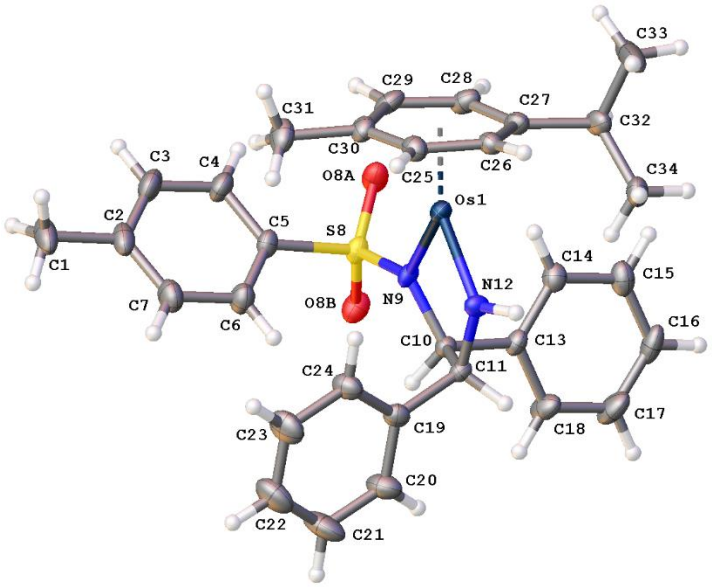


Figure S13: X-ray crystal structure of **5b** with atom labelling. Thermal ellipsoids are drawn at 50% probability level. The asymmetric unit contains the complex. There are four complexes in the unit cell. The hydrogen was located on N12 and refined with a DFIX restraint and given a U_{iso} 1.5 times the U_{equiv} of N12. The Flack parameter was more than 2 sigma from zero, but is from a known chiral starting material so is within acceptable limits (similarly for **5a**).

Crystal Data for $C_{31}H_{34}N_2O_2OsS$ (*M* =688.86 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 10.61241(15) Å, *b* = 13.8542(2) Å, *c* = 18.9999(3) Å, *V* = 2793.49(8) Å^3, *Z* = 4, *T* = 150(2) K, μ(MoKα) = 4.670 mm^{-1}, *Dcalc* = 1.638 g/cm^3, 48265 reflections measured (4.836° ≤ 2Θ ≤ 67.25°), 10419 unique (R_{int} = 0.0258, R_{sigma} = 0.0182) which were used in all calculations. The final R_1 was 0.0184 (I > 2σ(I)) and wR_2 was 0.0774 (all data).

Flack x: 0.015(2); Hooft y: 0.0070(15) (Olex2)

Selected distances (Å) and angles (°): Os-N12 1.914(3), Os-N9 2.047(4), N12-H12 0.96(3); N12-Os-N9 78.27(16), Os-N12-C11 122.1(3), Os-N9-C10 115.4(2).

[1] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339-341.

[2] G. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *64*, 112-122.

[3] a) R. Hodgkinson, V. Jurčík, A. Zanotti-Gerosa, H. G. Nedden, A. Blackaby, G. J. Clarkson, M. Wills, *Organometallics* **2014**, *33*, 5517-5524; b) N. A. Strotman, C. A. Baxter, K. M. J. Brands, E. Cleator, S. W. Krska, R. A. Reamer, D. J. Wallace, T. J. Wright, *J. Am. Chem. Soc.* **2011**, *133*, 8362-8371.