Supporting information.

Direct formation of tethered Ru(II) catalysts using arene exchange.

Rina Soni, Katherine E. Jolley, Guy J. Clarkson and Martin Wills

Department of Chemistry, The University of Warwick, Coventry, CV4 7AL, UK. Fax: (+44) 24 7652 3260. E-mail: m.wills@warwick.ac.uk

Contents:

General experimental conditions ........................................... S2
Synthesis of Complexes .................................................. S2
Asymmetric reduction reactions and reduction products ............ S30
X-ray crystallographic structure of (R,R)-4 and (R,R)-8 .......... S44
1H and 13C-NMR Spectra ............................................... S47
Chiral GC and HPLC data ............................................ S61
**General experimental details.**

**General:** Solvents and reagents for the synthesis of complexes and catalytic reactions were degassed prior to use and all reactions were carried out under either a nitrogen or argon atmosphere. Room temperature refers to ambient room temperature (20-22 °C), 0 °C refers to an ice slush bath and –78 °C refers to a dry ice-acetone bath. Heated experiments were conducted using thermostatically controlled oil baths. Reactions were monitored by TLC using aluminum backed silica gel 60 (F254) plates, visualized using uv at 254 nm and phosphomolybdic acid, ninhydrin, potassium permanganate or vanillin dips as appropriate. Flash column chromatography was carried out routinely using 60 Å silica gel (organic compounds) or 100-200 mesh Florisil (complexes). Reagents were used as received from commercial sources unless otherwise stated. NMR spectra were recorded on a Bruker DPX (300 or 400 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform. Coupling constants (J) are measured in Hertz. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Mass spectra were recorded on a Bruker Esquire 2000, Agilent 6130B or a Bruker MicroTOF mass spectrometer. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected. GC analysis was performed using a Hewlett-Packard 5890 or a Perkin Elmer 8500 instrument and HPLC analyses on a Hewlett-Packard 1050 instrument. Optical rotations were measured on an AA-1000 polarimeter. Dry solvents were purchased and used as received.

**Synthesis of complexes.**

Throughout these examples, [Ru(C₆H₅CO₂Et)Cl₂], or a similar complex (i.e. containing at least one electron-withdrawing group) was used as the Ru(II) source. This known complex can be prepared in large quantities through an established route as shown below, which is published elsewhere (see main paper for references). The complex [RuCl₂{(EtO₂C)₂C₆H₄}]₂ also works well in this application whilst [RuCl₂{(EtO₂C)(CH₃)C₆H₄}]₂ is less effective.

![Synthesis of complexes](image)

**Preparation of ruthenium dimer from ethyl 1,4-cyclohexadene-1-carboxylate.**

To ethyl 1,4-cyclohexadene-1-carboxylate (1.6 g, 10.5 mmol) in a dried, nitrogen purged flask connected to a condenser, was added RuCl₃.xH₂O (679 mg, 2.6 mmol assuming x=3). Dry EtOH (40 mL) was then added and the reaction was stirred at reflux for 18 hours. The reaction was cooled and filtered and the solid residue was washed with hexane and Et₂O to leave the product as an orange solid (735 mg, 1.1 mmol, 42%). δₜ₅ (300 MHz, dₛ-DMSO) 7.69 (2H, d J 6.0Hz, CHAr-Ru), 6.29 (1H, t J 6.0Hz, CHAr-Ru) 6.04...
Complex 2 (n=1):

In this example, the reaction of 3-phenyl-1-propanol with trifluoromethanesulfonic (triflic) anhydride results in formation of triflate, which is not isolated but employed directly in the next step in a reaction with diamine TsDPEN which gives 6a. Reaction of 6a with complex [Ru(C₆H₅CO₂Et)Cl₂]₂ under the conditions shown results in formation of complex 2 (n=1).

N-[1R,2R]-1,2-Diphenyl-2-[3-phenylpropylamino)ethyl]-4-methylbenzenesulfonamide 6a. To a mixture of 3-phenyl-1-propanol (0.149 mL, 1.093 mmol, 1.6 eq) and 2,6-lutidine (0.167 mL, 1.434 mmol, 2.10 eq) in dry DCM (5 mL) was added a solution of triflic anhydride (0.195 mL, 1.161 mmol, 1.70 eq) in dry DCM (1.5 mL), dropwise at 0 °C under an inert atmosphere. The resulting light pink solution was stirred at 0 °C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 °C. To this, a solution of (1R,2R)-TsDPEN (0.250 g, 0.683 mmol, 1.0 eq) and triethylamine (TEA) (0.228 mL, 1.639 mmol, 2.4 eq) in dry DCM (1.5 mL) was added dropwise at 0 °C. The resulting yellow colored mixture was stirred at 0 °C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO₃ solution (3 x 10 mL). The organic layer was separated, washed with H₂O (2 x 10 mL), brine (10 mL), dried over anhydrous Na₂SO₄, filtered and concentrated to give a crude compound which was purified by column chromatography over silica gel using EtOAc: Pet. ether (25:75) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give a solid. The solid was filtered, washed with n-pentane and dried under vacuum to give compound 6a as white solid (0.280 g, 0.579 mmol, 84.7%). Mp 106-108 °C; [α]D²⁸ = -17.8 (c 0.225 in CHCl₃); δ(H (300 MHz, CDCl₃) 7.36 (2H, d, J 8.4, -CH of phenyl), 7.28-7.23 (2H, m, -CH of phenyl), 7.19-7.09 (5H, m, -CH of phenyl), 7.07-7.00 (6H, m, -CH of phenyl), 6.95-6.87 (4H, m, -CH of phenyl), 6.25 (1H, br s, -NHTs), 4.25 (1H, d, J 7.8, -CHNHTs), 3.59 (1H, d, J 7.8, -CHN(CH₃)₂), 2.61-2.49 (2H, m, -NH-CH₂CH₂CH₂CH₂), 2.47-2.39 (1H, m, -NH-CH₂CH₂CH₂CH₂), 2.34-2.25 (1H, m, -NH-CH₂CH₂CH₂CH₂), 2.32 (3H, s, -CH₃), 1.80-1.62 (2H, m, -NH-CH₃CH₂CH₂CH₂), 1.29 (1H, br s, -NH(CH₃)₂), 6C (75 MHz, CDCl₃) 142.65(C), 141.75(C), 139.24(C), 138.30(C), 137.01(C), 129.05(2CH), 128.31(4CH), 128.28(2CH), 127.89(2CH), 127.51(2CH), 127.42(CH), 127.34(2CH), 127.25(CH), 127.07(2CH), 125.79(CH), 67.70(CH), 53
63.02(CH), 46.45(CH₂), 33.26(CH₂), 31.47(CH₂), 21.41(CH₃); m/z ESI-MS [M+H]⁺ 485.1; HRMS found 485.2259(C₃₀H₃₂N₂O₂S H⁺ requires 485.2257, error = 0.1 ppm). Known and fully characterised: J. E. D. Martins, D. J. Morris, M. Wills, Tetrahedron Lett. 2009, 50, 688-692.

\{N-[(1R,2R)-1,2-Diphenyl-2-(3-phenylpropylamino)ethyl]-4-methylbenzenesulphonamide\} ruthenium chloride 2 (n=1).

Compound 6a (0.050 g, 0.103 mmol, 1.0 eq) was added to [Ru(C₆H₅CO₂Et)Cl₂]₂ (0.033 g, 0.052 mmol, 0.5 eq) in dry DCM (1.5 mL) in a glass tube under N₂. The tube was sealed and the mixture was stirred at room temperature for 30 min to give a brick red solution and then heated at 90 °C for 49 h. The reaction was followed by TLC and mass spectrometry. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 88:12) to give 2 (n=1) as a brown solid (0.034 g, 0.055 mmol, 53%). δH (300 MHz, CDCl₃) 7.24 (2H, d, J 7.2, -CH of phenyl), 7.11-7.04 (4H, m, -CH of phenyl), 6.86-6.69 (6H, m, -CH of phenyl), 6.61-6.59 (2H, m, -CH of phenyl), 6.23-6.16 (3H, m, -CH of Ru-Ar), 5.22 (1H, s, -CH of Ru-Ar), 5.03 (1H, m, -CH of Ru-Ar), 4.43(1H, br d, -NH(CH₂)₂), 4.03 (1H, d, J 10.8, -CHNTs), 3.65-3.62 (1H, m, -CHNH(CH₂)₁), 2.87-2.75 (1H, m, -NH-CHHCH₂CH₂-), 2.70-2.46 (2H, m, -NH-CHHCH₂CHH-), 2.34-2.26 (1H, m, -NH-CH₂CH₂CHH-), 2.25 (3H, s, -CH₃), 2.19-2.10 (2H, m, -NH-CH₂CH₂CH₂-). m/z ESI-MS [M-Cl]⁺ 585.1.

Known and fully characterised: A. M. Hayes, D. J. Morris, G. J. Clarkson, M. Wills, J. Am. Chem. Soc. 2005, 127, 7318–731.

Examples how the reaction can be followed by mass spectrometry are given below. The peak at m/z 485 is the ligand 6a, whilst the product ([M-Cl]⁺)appears as a complex set of peaks at ca. m/z 585. Although not quantitative (the ligand gives a very strong signal) the ESI-MS indicates the clean conversion of ligand to tethered complex under the conditions used, without significant formation of the unwanted bidentate complex (which gives a signal at m/z 735 visible transiently in the first MS but which later is lost).
2 (n=1) ESI-MS after 6h:

![ESI-MS after 6h](image)

2 (n=1) ESI-MS after 22h:

![ESI-MS after 22h](image)
Alternative variations on this step which have been evaluated: (i) Reaction of 6a with [RuCl₂(1,4-\{EtO₂C\}_2C₆H₄)]₂ in DCM at room temperature for 30 min and heated at 90 °C for 49h, showed the formation of required complex 2 (n=1) to a similar extent to the reaction with [Ru(C₆H₅CO₂Et)Cl₂]₂ (the reaction was followed by TLC and ESI-MS); (ii) reaction of 6a with [RuCl₂(1,4-(EtO₂C)(CH₃)C₆H₄)]₂ in DCM at room temperature for 30 min and heated at 90 °C for 49h, showed the formation of required complex but the conversion was very low (reaction was followed by TLC and ESI-MS); (iii) reaction of 6a with [Ru(C₆H₅CO₂Et)Cl₂]₂ in 1,2-dichloroethane (DCE) and a few drops of THF at room temperature for 60 min and heated at 120 °C for 19h, showed the formation of required complex but conversion was low (ca 7:1 ligand:2 (n=1) ratio by ESI-MS analysis of the crude product) and impurities were formed (reaction was followed by TLC and ESI-MS); (iv) reaction of 6a with [Ru(C₆H₅CO₂Et)Cl₂]₂ in DCM at room temperature for 30 min followed by heating in chlorobenzene (13 mL per 100 mg of ligand 6a used) at 140 °C for 2h, showed the formation of required complex 2 (n=1) to a similar extent to that observed in DCM at 90 °C after 49 h (reaction was followed by TLC and ESI-MS). (v) reaction of 6a with [Ru(C₆H₅CO₂Et)Cl₂]₂ in 1,2-dichloroethane (DCE) and a few drops of THF at room temperature for 60 min and heated at 85 °C for 19h, showed only low conversion to the required complex (reaction was followed by TLC and ESI-MS).
The thin layer chromatography (TLC) plate below illustrates the effect of temperature and reaction time on the product formation (reaction of C$_{30}$H$_{32}$N$_{4}$O$_{2}$S 6a with [Ru(C$_{6}$H$_{5}$CO$_{2}$Et)Cl$_{2}$]).

Left to right: A-E.

A: Pure sample of 2 (n=1), for reference.

B. Chlorobenzene, 140 °C, 2h – (iv) above. Clear formation of product, with an impurity above.

C: 1,2-dichloroethane+THF, 85 °C, 48h- (v) above. Low conversion to product, impurities visible.

D: 1,2-dichloroethane+THF, 120 °C, 19h- (iii) above. Low conversion to product, extensive impurities.

E: Dichloromethane, 90 °C, 49h- conditions in main procedure. Clear formation of product, with impurities above.
Complex 4.

This compound was prepared through the sequence shown below:

\[
\text{MeO} \quad \text{MeO} \quad \text{Ru-N(CH}_2\text{CH}_2\text{CO})_2\text{EtCl}_2 \quad \text{TsDPEN} \quad \text{N-[(1R,2R)-2-[3-(4-Methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide 6b.}
\]

To a mixture of 3-(4-methoxyphenyl)-1-propanol (0.362 g, 2.186 mmol, 1.6 eq) and 2,6-lutidine (0.334 mL, 2.869 mmol, 2.10 eq) in dry DCM (10 mL) was added a solution of triflic anhydride (0.390 mL, 2.322 mmol, 1.70 eq) in dry DCM (2.5 mL) dropwise at 0 °C under an inert atmosphere. The resulting light pink solution was stirred at 0 °C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 °C. To this, a solution of (1R,2R)-TsDPEN (0.500 g, 1.366 mmol, 1.0 eq) and TEA (0.456 mL, 3.278 mmol, 2.4 eq) in dry DCM (2.5 mL) was added dropwise at 0 °C. The resulting yellow colored mixture was stirred at 0 °C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO₃ solution (3 x 25 mL). The organic layer was separated, washed with H₂O (2 x 15 mL), brine (25 mL), dried over anhydrous Na₂SO₄, filtered and concentrated to give crude compound. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (25:75) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give a solid. The solid was filtered, washed with n-pentane and dried under vacuum to give pure compound 6b as a white solid (0.625 g, 1.216 mmol, 89%). Mp 102-104 °C; [α]D28 = -21.8 (c 0.590 in CHCl₃); νmax 3280, 3032, 2929, 2845, 1611, 1512, 1454, 1348, 1328, 1246, 1157, 1088, 1034, 671 cm⁻¹; δH(300 MHz, CDCl₃) 7.36 (2H, d, J 8.1, -CH of phenyl), 7.14-7.11 (3H, m, -CH of phenyl), 7.07-6.98 (7H, m, -CH of phenyl), 6.94-6.87 (4H, m, -CH of phenyl), 6.80 (2H, d, J 8.7, -CH of phenyl), 6.27 (1H, br s, -NH₃), 4.24 (1H, d, J 8.0, -CHNH₃), 3.78 (3H, S, -OCH₃), 3.58 (1H, d, J 7.8, -CHNH(CH₂)₂), 2.55-2.37 (3H, m, -CH₂CH₂CH₂), 2.32 (3H, s, -CH₃), 2.29-2.23 (1H, m, -NH-CH₂CH₂CH₂), 1.74-1.60 (2H, m, -NH-CH₂CH₂CH₂), 1.32 (1H, br s, -NH(CH₃)₂); δc (75 MHz, CDCI₃) 157.71(C), 142.64(C), 139.25(C), 138.31(C), 137.01(C), 129.17(CH), 129.04(CH), 128.26(CH), 127.88(CH), 127.51(CH), 127.40(CH), 127.34(CH), 127.24(CH), 127.07(CH), 113.72(CH), 67.70(CH), 63.02(CH), 55.22(OCH₃), 46.39(CH₃), 32.31(CH₃), 31.66(CH₃), 21.3(CH₃); m/z ESI-MS [M+H]+ 515.1; HRMS found 515.2377 (C₃₁H₃₄N₂O₃S H+ requires 515.2363, error = -2.7 ppm).

\{N-[(1R,2R)-2-[3-(4-Methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide\} ruthenium chloride 4. Compound 6b (0.200 g, 0.389 mmol, 1.0 eq) and [Ru(C₆H₅CO₂Et)Cl₂]₂ (0.125 g,
0.195 mmol, 0.5 eq) were added to dry DCM (5 mL) in a glass tube under N₂. The tube was sealed and the mixture was stirred at room temperature for 30 min to give a brick red solution and heated at 90 °C for 54 h. The reaction was followed by TLC and mass spectrometry. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 90:10) to give a brown solid. The solid was recrystallized from MeOH to give 4 as a golden orange solid (0.108 g, 0.166 mmol, 42.7%). Mp decomposition >264 °C; [α]D₂₈ = -284.4 (c 0.016 in CHCl₃); νmax 3194, 3064, 3028, 2991, 2933, 2890, 2847, 1600, 1532, 1466, 1272, 1256, 1128, 1082, 1040, 1017, 937, 905, 850, 817, 799, 700, 693, 685 cm⁻¹; δH (300 MHz, CDCl₃) 7.27 (2H, d, J 8.1, -CH of phenyl), 7.18-7.07 (3H, m, -CH of phenyl), 6.84-6.77 (2H, m, -CH of phenyl), 6.73 (2H, d, J 8.1, m-CH of -SO₂C₆H₄CH₃), 6.63-6.58 (3H, m, -CH of phenyl), 6.54 (2H, d, J 7.2, -CH of phenyl), 5.55 (1H, dd, J 6.0, 1.2, -CH of Ru-Ar), 5.47 (1H, d, J 6.0, -CH of Ru-Ar), 5.34 (1H, dd, J 6.0, 1.2, -CH of Ru-Ar), 5.27 (1H, dd, J 6.0, -CH of Ru-Ar), 4.32 (1H, d, J 11.1, -CHNTs), 4.05 (1H, br d, -NH(CH₂)₃), 3.98 (3H, s, -OCH₃), 3.61-3.53 (1H, m, -CHNH(CH₂)₃), 2.81-2.73 (1H, m, -NH-CHHCH₂CH₂-), 2.53-2.25 (3H, m, -NH-CHHCH₂CH₂-), 2.20 (3H, s, -CH₃), 2.12-1.98 (2H, m, -NH-CH₂CH₂CH₂-); δc (75 MHz, CDCl₃) 143.81(C), 138.62(C), 138.11(C), 136.34(C), 134.65(C), 128.64(CH₄), 128.61(CH₂), 128.29(CH), 127.65(CH), 127.00(CH), 126.80(CH), 125.94(CH), 91.10(C), 84.65(CH), 81.43(CH), 78.70(CH), 72.09(CH), 68.87(CH), 56.76(CH), 49.35(CH₂), 30.27(CH₂), 27.27(CH₃), 21.10(CH₃); m/z ESI-MS [M-Cl]+ 615.1; HRMS found 615.1258 (C₃₁H₃₃N₂O₃RuS-Cl+ requires 615.1257, error = -0.2 ppm).

4-Methoxy 4 ESI-MS after 5h (ligand 6b is at m/z 515, complex 4 [M-Cl] is at m/z 615:}

![Image](image-url)
4-Methoxy 4 ESI-MS after 24h (ligand 6b is at m/z 515, complex 4 [M-Cl] is at m/z 615:}
4-Methoxy 4 ESI-MS after 51.5h (ligand 6b is at m/z 515, complex 4 [M-Cl] is at m/z 615:

Alternative variations on this step which have been evaluated: (i) Reaction of 6b with [RuCl₂(1,4-(EtO₂)C₆H₄)]₂ in DCM at room temperature for 30 min and heated at 90 °C for 49h, showed the formation of required complex (the reaction was analysed by TLC and ESI-MS); (ii) reaction of 6b with [RuCl₂(1,4-(EtO₂)C(CH₃)C₆H₄)]₂ in DCM at room temperature for 30 min and heated at 90 °C for 49h, showed the formation of required complex but the conversion was very low (the reaction was analysed by TLC and ESI-MS); (iii) reaction of 6b with and [Ru(C₆H₅CO₂Et)Cl₂]₂ in DCM at room temperature for 30 min followed by reaction in chlorobenzene (13 mL per 100 mg 6b) at 140 °C for 2h, showed the formation of the required complex 4 to an extent similar to that observed in DCM at 90 °C after 49 h (0.105 g, 0.164 mmol, 41.5%).

In contrast, stirring of 6b and and [Ru(C₆H₅CO₂Et)Cl₂]₂ in DCM at room temperature was found to form only the bidentate complex 5 (reaction was followed by ¹H-NMR; ca 30% conversion in 8h, 50% conversion in 64h), and none of the tethered complex 4. Overlaid NMR spectra for this reaction, and data for 5, are given in a later section of the SI.

The synthesis of 4 illustrates the need for careful selection of the temperature and the selection of solvent. The use of chlorobenzene gave improved results over dichloromethane or dichloroethane. In chlorobenzene, product formation was typically complete, at 90 °C, within 5 h whereas in dichloromethane, at the same temperature, full conversion typically required >48h. In further
experiments, ligand 6b and Ru dimer and [Ru(C_6H_5CO_2Et)Cl_2]_2 were stirred for 1 hour in DCM (typically 5 mL per 100 mg 6b), then DCM was removed and replaced with chlorobenzene (typically 13 mL per 100 mg 6b) and heated. The yield for formation of complex 4 by 1hr DCM room temp followed by 6 h chlorobenzene at 90 °C: 100 mg ligand gave 90 mg product from column (69%), recrystallized to give 50 mg solid (38%). Only 1 column was needed prior to recrystallization and it appears to be a cleaner procedure than with the DCM/chlorobenzene/140°C methods which led to formation of side products, although a similar yield of isolated product.

At other temperatures: 75 °C - 4 was formed, clean TLC plate, reaction appeared complete after 6 hours of heating in chlorobenzene, 90 °C – 4 was formed, clean TLC plate, reaction appeared complete after 5 h heating in chlorobenzene, 100 °C - 4 was formed, more impurities by TLC, reaction was complete in 3 h of heating in chlorobenzene, 120 and 140 °C, - 4 was formed, multiple impurities by TLC, reaction complete in 2 h of heating in chlorobenzene.

The TLC plate below (run in 6% MeOH in DCM) illustrates the crude products of reactions at different temperature ranges in chlorobenzene. The left hand column contains ligand (no color) and column 2 is a standard of the target complex. Columns 3-5 are the crude reaction after heating at 90 °C (6 h), 120 °C (2 h) and 140 °C (2 h) respectively. More impurities are formed at the higher temperatures and the cleanest product at 90 °C, however both furnish similar yields of purified product.
The reaction can also be conducted by combining the ruthenium dimer and the organic ligand directly in chlorobenzene in the ratios previously stated and heating this mixture directly to 90 °C for 5 h. This mixture can be placed directly into a heating bath at 90 °C or the mixture can be prepared at room temperature and then heated up to 90 °C over 30 minutes and held at 90 °C for 5 h. Hence there is no requirement for pre-combination in dichloromethane before the reaction mixture is heated to the temperature required for arene exchange. Under these conditions, none of the bidentate complex 5 was observed by mass spectrometry.

Alternative solvents to chlorobenzene, all at 90 °C, were tested, evaluated by TLC and examined by mass spectrometry after 2 h of heating. There was no evidence of the 4 forming with chloroform, water, THF, iso-propanol or acetonitrile, but there was evidence of 4 forming in xylene, however there were multiple impurities by TLC at the temperatures of >110 °C which were required for the reaction to proceed at an appreciable rate.

For best results, the η⁶ arene exchange should be conducted in chlorobenzene within a temperature range of 75-120 °C for a period of 6-4 h, without a base. The reaction should be heated immediately or within 30 min of combining the reagents, i.e. minimising the room temperature contact time, because the unproductive complex 5 is formed at room temperature.

Certain bases can be added to the arene-exchange reaction however strong bases are detrimental. The results of a series of tests are given below (1 eq base unless otherwise stated, initial reaction in DCM, 30 min, rt, then in PhCl at 90 °C for 6h, one equivalent of base added relative to ligand):

| Base          | None | Ca(OH)₂ 1 eq. | Ca(OH)₂ 2 eq. | NaHCO₃ | K₂CO₃ | NaOH | Mg(OH)₂ | Et₃N** |
|---------------|------|---------------|---------------|--------|-------|------|---------|--------|
| Ratio of 6b:4 by mass spec.* | 4:1  | 3:2           | 3:1           | 4:1    | 4:1   | 3:1  | 6:1     | 4:1    |
| 5 formed?     | No   | No            | No            | No     | Yes   | No   | Yes (ca 7:3 4:5) |

* the mass spectrometry test is not quantitative (because the ligand 6b gives a stronger signal) but provides a qualitative measure of the relative conversion of ligand to the desired complex. ** This reaction was conducted in DCM for 24h, 90 °C, the same reaction without Et₃N gave a 4:1 ratio of 6b:4 but no 5 was visible.

Mass spectrometry traces of reactions with added base. Ligand 6b is at m/z 515.2, the complex is a complicated signal centred on by 615.1 ([M-Cl]+, reflecting a major Ru isotope). Where observed, the complicated signal represented by 765.2 is the undesired and unproductive bidentate complex 5.
Although not quantitative (the ligand gives a very strong signal) the ESI-MS qualitatively indicates conversion of ligand 6b to tethered complex 4 under the conditions used, and formation of the unwanted bidentate complex 5 (m/z [M-Cl]+ at 765) under certain conditions.

1 eq. Ca(OH)$_2$ relative to ligand.

1 eq. K$_2$CO$_3$ relative to ligand.
1 eq. NaOH relative to ligand – significant 5 formed.

1 eq. Mg(OH)$_2$ relative to ligand.
2 eq. Ca(OH)$_2$ relative to ligand.

1 eq of TEA relative to ligand. Significant bidentate 5 is formed.
This compound was prepared through the sequence shown below:

\[
\text{N-}\{(1\text{R},2\text{R})-2-[3-(3,5-\text{Dimethoxyphenyl})propylamino]-1,2-\text{diphenylethyl}\}-4-\text{methylbenzenesulfonamide} \ 6c.
\]

To a mixture of 3-(3,5-(dimethoxy)phenyl)propanol (0.428 g, 2.186 mmol, 1.6 eq) and 2,6-lutidine (0.334 mL, 2.869 mmol, 2.10 eq) in dry DCM (10 mL) was added a solution of triflic anhydride (0.390 mL, 2.322 mmol, 1.70 eq) in dry DCM (2.5 mL) dropwise at 0°C under an inert atmosphere. The resulting light pink solution was stirred at 0°C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0°C. To this, a solution of (1\text{R},2\text{R})-TsDPEN (0.500 g, 1.366 mmol, 1.0 eq) and TEA (0.456 mL, 3.278 mmol, 2.4 eq) in dry DCM (2.5 mL) was added dropwise at 0°C. The resulting yellow colored mixture was stirred at 0°C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO\textsubscript{3} solution (3 x 25 mL). The organic layer was separated, washed with H\textsubscript{2}O (2 x 15 mL), brine (25 mL), dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated to give crude compound. The crude compound was purified by column chromatography on silica gel using EtOAc: Pet. ether (25:75) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give compound \( 6c \) as an oil (0.610 g, 1.121 mmol, 82%). \([\text{[\text{α}]_D^{20}} = -15.1 \ (c \ 0.550 \ \text{in CHCl}_3); \nu_{\text{max}} = 3267, 2932, 2837, 1594, 1455, 1428, 1323, 1291, 1203, 1160, 1091, 1055, 924, 831, 812, 697, 695 \ \text{cm}^{-1}; \delta_H (400 \ \text{MHz, CDCl}_3) = 7.36 (2\text{H}, \text{d, } J = 8.4, \text{C}_6\text{H}_5\text{ of } -\text{SO}_2\text{C}_6\text{H}_4\text{CH}_3), 7.14-7.09 (3\text{H}, \text{m, } -\text{C}_6\text{H}_5 \text{ of phenyl}), 7.06-7.00 (5\text{H}, \text{m, } -\text{C}_6\text{H}_5 \text{ of phenyl}), 6.93-6.88 (4\text{H}, \text{m, } -\text{C}_6\text{H}_5 \text{ of phenyl}), 6.29 (1\text{H}, \text{t, } J = 2.2, \text{ -CH of } -\text{CH}_3\text{OCH}_3), 6.27 (2\text{H}, \text{d, } J = 2.2, \text{-CH of } -\text{CH}_3\text{OCH}_3), 6.25 (1\text{H}, \text{br s, } -\text{NHTs}), 4.24 (1\text{H}, \text{d, } J = 7.8, \text{-CHNHTs}), 3.78 (6\text{H}, \text{s, } -\text{OCH}_3), 3.59 (1\text{H}, \text{d, } J = 7.8, \text{-CHNH(CH}_3)_2), 2.55-2.40 (3\text{H}, \text{m, } -\text{NH}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3), 2.34-2.28 (1\text{H}, \text{m, } -\text{NH}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3), 2.32 (3\text{H}, \text{s, } -\text{CH}_3), 1.76-1.62 (2\text{H}, \text{m, } -\text{NH}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3), 1.35 (1\text{H}, \text{br s, } -\text{NH}(\text{CH}_3)_2); \delta_c (100 \ \text{MHz, CDCl}_3) = 160.73(\text{C}), 144.22(\text{C}), 142.66(\text{C}), 139.24(\text{C}), 138.26(\text{C}), 137.03(\text{C}), 129.05(\text{CH}), 128.27(\text{CH}), 127.87(\text{CH}), 127.43(\text{CH}), 127.34(\text{CH}), 127.24(\text{CH}), 127.08(\text{CH}), 106.34(\text{CH}), 97.85(\text{CH}), 67.69(\text{CH}), 63.06(\text{CH}), 55.24(2\text{-OCH}_3), 46.52(\text{CH}_2), 33.63(\text{CH}_3), 31.30(\text{CH}_2), 21.40(\text{CH}_3); \text{m/z ESI-MS [M+H]^+} = 545.2; \text{HRMS found 545.2475 (C}_{32}\text{H}_{36}\text{N}_{2}\text{O}_{4}\text{S H}^+ \text{requires 545.2469, error = -1.1 ppm).}
\]

\( \{\text{N-}\{(1\text{R},2\text{R})-2-[3-(3,5-\text{Dimethoxyphenyl})propylamino]-1,2-\text{diphenylethyl}\}-4-\text{methylbenzenesulfonamide} \} \) -ruthenium chloride \( 9. \) Compound \( 6c \) (0.125 g, 0.230 mmol, 1.0 eq) and [Ru(C₆H₅CO₂Et)Cl₂]₂
(0.074 g, 0.115 mmol, 0.5 eq) were dissolved in dry DCM (4.5 mL) in a glass tube under N₂. The tube was sealed and the mixture was stirred at room temperature for 30 min to give a brick red solution and heated at 90 °C for 49 h. The reaction was followed by TLC and mass spectrometry. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 88:12) to give a brown solid. The solid was recrystallized from MeOH to give 9 as a golden orange solid (0.075 g, 0.110 mmol, 48%). Mp decomposition >280 °C; [α]D28 = -124.0 (c 0.025 in CHCl₃); νmax 3197, 3080, 3028, 3000, 2980, 2929, 2875, 1598, 1542, 1528, 1495, 1453, 1411, 1319, 1264, 1211, 1164, 1155, 1125, 1080, 1034, 1022, 934, 895, 833, 789, 695 cm⁻¹; δH (400 MHz, CDCl₃) 7.45 (2H, d, J 8.4, -CH of -SO₂C₆H₄CH₃), 7.12-7.07 (3H, m, -CH of phenyl), 6.86-6.84 (3H, m, -CH of phenyl), 6.77-6.73 (4H, m, -CH of phenyl), 6.64 (2H, d, J 7.2, -CH of phenyl), 5.89 (1H, s, -CH of Ru-Ar), 4.78 (1H, s, -CH of Ru-Ar), 4.76 (1H, s, -CH of Ru-Ar), 4.39 (1H, d, J 12.6, -NH(CH₃)₂), 4.17 (3H, s, OCH₃), 4.15 (3H, s, OCH₃), 4.07 (1H, d, J 10.3, -CHNTs), 3.59 (1H, m, -CHNH(CH₃)₃), 2.70-2.65 (2H, m, -NH-CH₃CH₂CH₂-), 2.62-2.58 (1H, m, -NH-CHHCH₂CH₂-), 2.24 (3H, s, -CH₃), 2.11-2.03 (1H, m, -NH-CHHCH₂CH₂-), 1.90-1.85 (1H, m, -NH-CH₂CHHCH₂-)dC (100 MHz, CDCl₃) 141.63(C), 139.99(C), 139.14(C), 136.52(C), 135.72(C), 135.38(C), 128.78(2CH), 128.62(2CH), 128.20(CH), 128.11(2CH), 127.69(4CH), 126.91(2CH), 126.32(CH), 96.05(C), 78.74(CH), 69.45(CH), 66.03(CH), 57.31(OCH₃), 57.29(OCH₃), 54.96(CH), 53.93(CH), 47.64(CH₂), 29.59(CH₃), 24.97(CH₃), 21.23(CH₃); m/z ESI-MS [M-Cl]⁺ 645.1; HRMS found 645.1365 (C₃₂H₃₅N₂O₄RuS-Cl⁺ requires 645.1363, error = -0.2 ppm).
2,4-Dimethoxy 9 ESI-MS after 5.5h:

2,4-Dimethoxy 9 ESI-MS after 48h (ligand is at m/z 545, complex 9 is at m/z 645 ([M-Cl]+):
Reaction of 6c with \([\text{Ru(C}_6\text{H}_3\text{CO}_2\text{Et})\text{Cl}_2]\) in DCM at room temperature for 30 min followed by in chlorobenzene at 140 °C for 2 h, resulted in the formation of required complex 9 in a lower conversion than that observed in DCM at 90 °C after 49 h (0.080 g, 0.118 mmol, 32%).

**Complex 10.**

This compound was prepared through the sequence shown below:

\[
\begin{align*}
\text{Ph} & \quad \text{Cl-Ru} \quad \text{Cl} \\
& \quad \begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\end{array} \\
& \quad \text{COEt} \\
\end{align*}
\]

\[\text{N-\{1R,2R\}-2-[3-(Biphenyl-4-yl)-propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6d.]

To a mixture of 3-(4-phenylphenyl)propanol (C_{15}H_{16}O, 0.232 g, 1.093 mmol, 1.6 eq) and 2,6-lutidine (0.167 mL, 1.434 mmol, 2.10 eq) in dry DCM (5 mL) was added a solution of triflic anhydride (0.195 mL, 1.161 mmol, 1.70 eq) in dry DCM (1.5 mL) dropwise at 0 °C under an inert atmosphere. The resulting light pink solution was stirred at 0 °C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 °C. To this, a solution of (1R,2R)TsDPEN (0.250 g, 0.683 mmol, 1.0 eq) and TEA (0.228 mL, 1.639 mmol, 2.4 eq) in dry DCM (1.5 mL) was added dropwise at 0 °C. The resulting yellow colored mixture was stirred at 0 °C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO₃ solution (3 x 10 mL). The organic layer was separated, washed with H₂O (2 x 10 mL), brine (10 mL), dried over anhydrous Na₂SO₄, filtered and concentrated to give a crude compound. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (25:75) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give a solid. The solid was filtered, washed with n-pentane and dried under vacuum to give pure compound 6d as a white solid (0.318 g, 0.568 mmol, 83%). Mp 98-100 °C; [\(\alpha\)]D₃₀ = -21.3 (c 0.550 in CHCl₃); \(\nu_{\text{max}}\) 3286, 3029, 2944, 1598, 1489, 1454, 1431, 1348, 1328, 1154, 1087, 1041, 841, 807, 758, 699, 670 cm⁻¹; \(\delta_{\text{H}}\) (300 MHz, CDCl₃) 7.59-7.56 (2H, m, -C₆H of phenyl), 7.36 (2H, d, \(J = 8.1\), -C₆H of -SO₂C₆H₄CH₃), 7.45-7.30 (5H, m, -C₆H of phenyl), 7.17-7.11 (5H, m, -C₆H of phenyl), 7.07-6.99 (5H, m, -C₆H of phenyl), 6.96-6.89 (4H, m, -CH of phenyl), 6.27 (1H, br s, -NH(Ts)), 4.26 (1H, d, \(J = 7.8\), -CHNH(Ts)), 3.61 (1H, d, \(J = 7.8\), -CHNH(CH₂)₂-), 2.66-2.52 (2H, m, -NH-CH₂CH₂CH₂-), 2.50-2.42 (1H, m, -NH-CHHCH₂CH₂-), 2.36-2.28 (1H, m, -NH-CHHCH₂CH₂-), 2.32 (3H, s, -CH₃), 1.81-1.66 (2H, m, -NH-CH₂CH₂CH₂-), 1.37 (1H, br s, -NH(CH₃)₂); \(\delta_{\text{C}}\) (75 MHz, CDCl₃) 142.65(C), 140.99(C), 140.86(C), 139.21(C), 138.74(C), 138.28(C), 136.98(C), 129.05(2CH), 128.74(2CH), 128.69(2CH), 128.28(2CH), 128.21(C), 127.29(C), 126.59(C), 123.34(C), 121.37(C), 114.80(C), 114.23(C), 113.79(C), 113.61(C), 103.28(C), 55.01(C), 52.63(C), 48.55(C), 45.96(C), 45.16(C), 41.59(C), 25.97(C), 23.01(C), 20.07(C).
*{1H,N}-(1R,2R)-2-[3-(biphenyl-4-yl)-propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide*} 

**ruthenium chloride 10.** Compound 6d (0.200 g, 0.357 mmol, 1.0 eq) and [Ru(C₆H₅CO)₂Et]Cl₂ (0.115 g, 0.179 mmol, 0.5 eq) were added to dry DCM (6.0 mL) in a glass tube under N₂. The tube was sealed and the mixture was stirred at room temp for 30 min to give a brick red solution that was heated at 90 °C for 49 h. The reaction was followed by TLC and mass spectrometry. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 88:12) to give 10 as a brown solid (0.079 g, 0.114 mmol, 31.8%) as a mixture of isomers with ratio 0.75:0.25 (A:B by 1H-NMR in CDCl₃). Mp decomposition >198 °C; [α]D₃₂ = +50.0 (c 0.005 in CHCl₃); νmax 3027, 2921, 1599, 1491, 1373, 1453, 1270, 1131, 1085, 935, 902, 807, 761, 699, 658 cm⁻¹; δH (400 MHz, CDCl₃) 7.98 (1.5H, d, J 7.6, A -C₆H of phenyl), 7.81 (0.5H, d, J 6.4, B -C₆H of phenyl), 7.49-7.38 (4H, m, A+B -C₆H of phenyl, A -C₆H of Ru-Ar), 7.23 (0.25H, d, J 7.8, A -C₆H of phenyl), 7.18-7.04 (5H, m, A+B -C₆H of phenyl, A -C₆H of Ru-Ar), 6.89-6.72 (2H, m, A+B -CH of phenyl, B -CH of Ru-Ar), 6.80-6.72 (4H, m, A+B -CH of phenyl), 6.57 (0.75H, d, J 7.8, A -CH of phenyl), 6.26 (0.75H, d, J 5.6, A -CH of Ru-Ar), 5.86 (0.25H, d, J 5.2, B -CH of Ru-Ar), 5.62 (0.25H, br s, B -CH of Ru-Ar), 5.41 (0.75H, d, J 5.2, A -CH of Ru-Ar), 5.23 (0.25H, br d, B -CHNTs), 5.15 (0.75H, d, J 5.6, A -CH of Ru-Ar), 4.99 (0.25H, br d, B -CHNH(CH₂)₂), 4.73 (0.75H, d, J 12.0, A -NH(CH₂)₂), 4.06 (0.75H, d, J 10.8, A -CHNTs), 3.64-3.58 (0.75H, m, A -CHNH(CH₂)₂), 2.91-2.60 (3H, m, A+B -NH-CHHCH₂CH₂-), 2.36-2.25 (1H, m, A+B -NH-CHHCH₂CH₂-), 2.20 (2.25H, s, A -CH₃), 2.12 (0.75H, s, B -CH₃), 2.11-2.04 (2H, m, -A+B NH-CHHCH₂CH₃-), (peak not identified for (0.25H) B -NH(CH₂)₃); 6c (150 MHz, CD₃NO₂) 144.25(A, C), 143.49(B, C), 142.16(B, C), 140.48(B, C), 139.57(A, C), 139.51(A, C), 137.75(A, C), 135.50(A, C), 135.71(B, C), 135.38(B, CH), 130.89(B, CH), 129.94(A, CH), 129.28(B, CH), 129.18(A, CH), 128.80(A, CH), 128.54(A, CH), 128.46(A, CH), 128.42(A, CH), 128.06(A, CH), 127.06(B, CH), 126.80(A, CH), 126.62(B, CH), 126.41(B, CH), 125.96(B, CH), 101.17(A, C), 95.83(B, C), 94.42(A, C), 92.62(A, CH), 90.66(A, CH), 90.06(B, CH), 88.11(B, CH), 81.08(B, CH), 78.41(A, CH), 76.93(B, CH), 75.93(A, CH), 75.82(A, CH), 73.14(A, CH), 70.49(B, CH), 69.37(A, CH), 46.97(B, CH), 46.85(A, CH), 29.72(B, CH₃), 29.10(B, CH₂), 28.08(A, CH₂), 24.32(A, CH₂), 20.34(B, CH₃), 20.21(A, CH₃); m/z ESI-MS [M+Cl]⁺ 661.1; HRMS found 661.1458 (C₃₆H₃₅N₂O₂RuS-Cl⁺ requires 661.1466, error = 1.5 ppm).
Complex 11.

This compound was prepared through the sequence shown below:

[N-(1R,2R)-2-[3-(4-Isopropylphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide 6e. To a mixture of 3-(4-isopropylphenyl)propanol (C\textsubscript{12}H\textsubscript{18}O, 0.195 g, 1.093 mmol, 1.6 eq) and 2,6-lutidine (0.167 mL, 1.434 mmol, 2.10 eq) in dry DCM (5 mL) was added a solution of triflic anhydride (0.195 mL, 1.161 mmol, 1.70 eq) in dry DCM (1.5 mL) dropwise at 0 °C under an inert atmosphere. The resulting light pink solution was stirred at 0 °C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 °C. To this, solution of (1R,2R)-TsDPEN (0.250 g, 0.683 mmol, 1.0 eq) and TEA (0.228 mL, 1.639 mmol, 2.4 eq) into dry DCM (1.5 mL) was added dropwise at 0 °C. The resulting yellow colored mixture was stirred at 0 °C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO\textsubscript{3} solution (3 x 10 mL). The organic layer was separated, washed with H\textsubscript{2}O (2 x 10 mL), brine (10 mL), dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated to give a crude compound. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (25:75) as an eluent to give residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give a solid. The solid was filtered, washed with n-pentane and dried under vacuum to give pure compound 6e as a white solid (0.340 g, 0.646 mmol, 94.6%). Mp 106-108 °C; [α]\textsubscript{D}\textsuperscript{30} = -19.6 (c 0.5850 in CHCl\textsubscript{3}); ν\textsubscript{max} 3352, 3029, 2959, 2926, 2855, 2806, 1598, 1512, 1494, 1454, 1433, 1339, 1324, 1153, 1093, 1081, 1051, 932, 811, 766, 699, 663 cm\textsuperscript{-1}; δ\textsubscript{H} (300 MHz, CDCl\textsubscript{3}) 7.37 (2H, d, J 8.1, -C\textsubscript{6}H\textsubscript{4}CH\textsubscript{3}), 7.14-7.09 (5H, m, -C\textsubscript{6}H\textsubscript{4} of phenyl), 7.07-6.99 (7H, m, -C\textsubscript{6}H\textsubscript{4} of phenyl), 6.96-6.87 (4H, m, -C\textsubscript{6}H\textsubscript{4} of phenyl), 6.28 (1H, br s, -NH\textsubscript{T}s), 4.24 (1H, d, J 7.7, -C\textsubscript{6}H\textsubscript{4}NHTs), 3.59 (1H, d, J 7.7, -C\textsubscript{6}H\textsubscript{4}NH(CH\textsubscript{2})\textsubscript{3}-), 2.94-2.80 (1H, m, -CH(CH\textsubscript{3})\textsubscript{2}), 2.57-2.39 (3H, m, -NH-CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}-), 2.34-2.25 (1H, m, -NH-CHHCH\textsubscript{2}CH\textsubscript{2}-), 2.32 (3H, s, -CH\textsubscript{3}), 1.78-1.60 (2H, m, -NH-CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}-), 1.23 (6H, d, J 6.9, -CH\textsubscript{2}(CH\textsubscript{3})\textsubscript{2}), ( peak not identified for -NH(CH\textsubscript{2})\textsubscript{3}-); δ\textsubscript{C} (75 MHz, CDCl\textsubscript{3}) 146.30(C), 142.65(C), 139.24(C), 139.03(C), 138.33(C), 137.00(C), 129.05(2CH), 128.27(2CH), 128.19(2CH), 127.89(2CH), 127.51(2CH), 127.41(CH), 127.34(2CH), 127.25(CH), 127.08(2CH), 126.34(2CH), 67.66(CH), 63.01(CH), 46.50(CH\textsubscript{3}), 32.65(CH\textsubscript{3}), 32.80(CH\textsubscript{3}), 31.50(CH\textsubscript{3}), 24.05(CH\textsubscript{3}), 14.05(CH\textsubscript{3}); m/z ESI-MS [M+H]\textsuperscript{+} 527.2; HRMS found 527.2735(C\textsubscript{33}H\textsubscript{38}N\textsubscript{2}O\textsubscript{2}S H+ requires 527.2727, error = -0.6 ppm).
\{N-[(1R,2R)-2-[3-(4-isopropylphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide}\}

**ruthenium chloride 11.** Compound 6e (C_{33}H_{38}N_{2}O_{2}S, 0.200 g, 0.380 mmol, 1.0 eq) and [Ru(C_{6}H_{5}CO_{2}Et)Cl_{2}] (0.122 g, 0.190 mmol, 0.5 eq) were dissolved in dry DCM (6.0 mL) in a glass tube under N_{2}. The tube was sealed and the mixture was stirred at room temp for 30 min to give brick red solution and heated at 90 °C for 49 h. The reaction was followed by TLC and mass spectra analysis. The reaction mixture was cooled to room temperature and concentrated to give a brown residue. The solid was precipitated from diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 88:12) to give 11 as a brown solid (0.073 g, 0.110 mmol, 28%) as a mixture of isomers with ratio 0.8:0.2 (A:B by \(^{1}H\)-NMR in CDCl\(_{3}\)). Mp decomposition >168 °C; \([\alpha]_{D}^{28}\) = +137.50 (c 0.004 in CHCl\(_{3}\)); \(\nu_{\text{max}}\) 3191, 3028, 2937, 1599, 1494, 1453, 1269, 1130, 1085, 1056, 935, 903, 807, 759, 679 cm\(^{-1}\); \(\delta_{\text{H}}\) (400 MHz, CDCl\(_{3}\)) 7.39-7.29 (2H, m, A+B -CH of phenyl), 7.18-7.04 (4H, m, A+B -CH of phenyl), 6.87-6.77 (4H, m, A+B -CH of phenyl), 6.75-6.65 (2H, m, A+B -CH of phenyl), 6.60-6.58 (2H, m, A+B -CH of phenyl), 6.44 (0.2H, d, \(J = 4.8\), B -CH of Ru-Ar), 6.36 (0.8H, d, J 5.6, A -CH of Ru-Ar), 5.96 (0.8H, d, J 6.0, A -CH of Ru-Ar), 5.91 (0.2H, d, J 5.6, B -CH of Ru-Ar), 5.46 (0.2H, br d, B -CH of Ru-Ar), 5.36 (0.2H, br d, B -CH of Ru-Ar), 5.18 (1H, d, J 5.6, A -CH of Ru-Ar, B -CHNTs), 4.99 (0.8H, d, J 6.0, A -CH of Ru-Ar), 4.83 (0.2H, d, J 12, B -CHNH(CH\(_{2}\))\(_{3}\)-), 4.53 (0.8H, d, J 12.0, A -CH(NH(CH\(_{2}\))\(_{3}\)-), 4.10 (0.8H, d, J 10.8, A -CHNTs), 3.73-3.67 (0.8H, m, A -CHNH(CH\(_{2}\))\(_{3}\)-), 3.62-3.52 (0.8H, m, A -CH(CH\(_{3}\))\(_{2}\)-), 2.87-2.59 (3H, m, A+B -NH-CH\(_{2}\)CH\(_{2}\)C\(_{6}\)H\(_{5}\)-), 2.29-2.13 (2H, m, A+B -NH-CH\(_{2}\)H\(_{2}\)C\(_{6}\)H\(_{5}\)-), 2.24 (2.4H, s, A -CH\(_{3}\)), 2.15 (0.6H, s, B -CH\(_{3}\)), 2.08-2.02 (1H, m, A+B -NH-CH\(_{2}\)CH\(_{2}\)H\(_{2}\)C\(_{6}\)H\(_{5}\)-), 1.58 (2.4H, d, J 6.8, A -CH(CH\(_{3}\))\(_{2}\)), 1.40 (0.6H, d, J 6.4, B -CH(CH\(_{3}\))\(_{2}\), 1.58 (0.6H, d, J 6.8, B -CH(CH\(_{3}\))\(_{2}\)), 1.25 (2.4H, d, J 6.8, A -CH(CH\(_{3}\))\(_{2}\)), (peak not identified for (0.2H) B -NH(CH\(_{2}\))\(_{3}\)-); \(\delta_{C}\) (150 MHz, CD\(_{3}\)NO\(_{2}\)) 144.30(A, C), 143.55(B, C), 141.06(B, C), 140.38(B, C), 139.76(A, C), 139.73(A, C), 137.43(A, C), 135.92(B, C), 131.08(B, CH), 130.86(B, CH), 129.84(A, CH), 128.80(A, CH), 128.67(B, CH), 128.45(A, CH), 128.27(A, CH), 127.06(A, CH), 126.89(A, CH), 126.77(B, CH), 126.41(A, CH), 125.96(B, CH), 106.38(B, C), 104.25(A, C), 100.26(A, C), 91.10(A, CH), 89.72(B, C), 88.05(A, CH), 85.70(B, CH), 81.16(B, CH), 77.86(A, CH), 77.57(B, CH), 76.08(B, CH), 75.97(A, CH), 72.08(A, CH), 70.26(B, CH), 70.15(B, CH), 69.41(B, CH), 46.72(A, CH\(_{2}\)), 45.11(B, CH\(_{2}\)), 31.28(B, CH), 31.07(B, CH), 29.72(B, CH\(_{2}\), 29.00(B, CH\(_{3}\)), 28.18(A, CH\(_{3}\)), 26.18(B, CH\(_{3}\)), 25.90(A, CH\(_{3}\)), 23.88(A, CH\(_{3}\)), 23.44(B, CH\(_{3}\)), 23.34(B, CH\(_{3}\)), 20.24(A, CH\(_{3}\)), 19.83(A, CH\(_{3}\)), 19.68(B, CH\(_{3}\)); m/z ESI-MS [M-Cl]\(^{+}\) 627.1; HRMS found 627.1611 (C\(_{33}\)H\(_{37}\)N\(_{2}\)O\(_{2}\)RuS-Cl\(^{+}\) requires 627.1622, error = 1.3 ppm).
**Complex 12.**

This compound was prepared through the sequence shown below:

\[ \text{N-\{1R,2R\}-2-\{3-(4-tert-butylphenyl)propylamino\}-1,2-diphenylethyl\}-4-methylbenzenesulfon-amide 6f.} \]

To a mixture of 3-(4-tert-butylphenyl)propanol (C\(_{13}\)H\(_{20}\)O, 0.210 g, 1.093 mmol, 1.6 eq) and 2,6-lutidine (0.167 mL, 1.434 mmol, 2.10 eq) in dry DCM (5 mL) was added a solution of triflic anhydride (0.195 mL, 1.161 mmol, 1.70 eq) in dry DCM (1.5 mL) dropwise at 0 °C under an inert atmosphere. The resulting light pink solution was stirred at 0 °C for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 °C. To this, a solution of (1R,2R)-TsDPEN (0.250 g, 0.683 mmol, 1.0 eq) and TEA (0.228 mL, 1.639 mmol, 2.4 eq) in dry DCM (1.5 mL) was added dropwise at 0 °C. The resulting yellow colored mixture was stirred at 0 °C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. NaHCO\(_3\) solution (3 x 10 mL). The organic layer was separated, washed with H\(_2\)O (2 x 10 mL), brine (10 mL), dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated to give a crude compound. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (25:75) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) to give a solid. The solid was filtered, washed with n-pentane and dried under vacuum to give pure compound 6f as a white solid (0.312 g, 0.578 mmol, 84.6%). Mp 84-86 °C; [\(\alpha\)]\(_D\)\(^{30}\) = -19.3 (c 0.580 in CHCl\(_3\)); \(\nu_{\text{max}}\) 3250, 3063, 3031, 2959, 2915, 2863, 2815, 1599, 1509, 1494, 1455, 1435, 1323, 1157, 1092, 1037, 1025, 918, 806, 754, 699, 685 cm\(^{-1}\); \(\delta_h\) (300 MHz, CDCl\(_3\)) 7.37 (2H, d, \(J\) 8.4, -C\(\text{H}\)of -SO\(_2\)C\(\text{H}\)_4CH\(_3\)), 7.29-7.25 (2H, m, -C\(\text{H}\) of phenyl), 7.14-7.11 (3H, m, -C\(\text{H}\) of phenyl), 7.05-7.00 (7H, m, -C\(\text{H}\) of phenyl), 6.96-6.87 (4H, m, -CH of phenyl), 6.28 (1H, br s, -NHTs), 4.24 (1H, d, \(J\) 8.0, -CHNHTs), 3.59 (1H, d, \(J\) 8.0, -CHNH(CH\(_2\))\(_3\)-), 2.57-2.39 (3H, m, -NH-CHHCH\(_2\)CH\(_2\)-), 2.34-2.26 (1H, m, -NH-CHHCH\(_2\)CH\(_2\)-), 2.32 (3H, s, -CH\(_3\)), 1.76-1.63 (2H, m, -NH-CH\(_2\)CH\(_2\)CH\(_2\)-), 1.30 (10H, br s, -C(CH\(_3\))\(_3\) and -NH(CH\(_2\))\(_3\)-); \(\delta_c\) (75 MHz, CDCl\(_3\)) 148.57(C), 142.65(C), 139.24(C), 138.65(C), 138.33(C), 137.00(C), 129.06(2CH), 128.27(2CH), 127.94(2CH), 127.89(2CH), 127.52(2CH), 127.41(CH), 127.34(2CH), 127.25(CH), 127.08(2CH), 125.20(2CH), 67.65(CH), 63.01(CH), 46.53(CH\(_3\)), 34.31(C), 32.68(CH\(_2\)), 31.43(CH\(_2\)), 31.38(3CH\(_3\)), 21.41(CH\(_3\)); m/z ESI-MS [M+H]\(^+\) 541.2; HRMS found 541.2888 (C\(_{34}\)H\(_{40}\)N\(_2\)O\(_2\)S) H+ requires 541.2883, error = -0.6 ppm).
\{N-[(1R,2R)-2-[3-(4-tert-butylphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide\} ruthenium chloride. Compound 6f \((C_{34}H_{40}N_2O_2S, 0.200 \text{ g}, 0.370 \text{ mmol}, 1.0 \text{ eq})\) and \([Ru(C_6H_5CO_2Et)Cl_2]_2\) \((0.119 \text{ g}, 0.185 \text{ mmol}, 0.5 \text{ eq})\) were added to dry DCM \((6.0 \text{ mL})\) in a glass tube under N\(_2\). The tube was sealed and the mixture was stirred at room temperature for 30 min to give a brick red solution which was heated at 90 °C for 49 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH \((97:3 \text{ to } 88:12)\) to give 12 as a brown solid \((0.052 \text{ g}, 0.078 \text{ mmol}, 20.8\%)\) as a mixture of isomers with ratio 0.55:0.45 \((\text{A:B}}\) by \(^1\text{H-NMR in CDCl}_3\). Mp decomposition >174 °C; \([\alpha]_\text{D}^{32} = +516.7 \text{ (c 0.003 in CHCl}_3\); \(\nu_{\text{max}}\) 2941, 1599, 1494, 1454, 1374, 1263, 1129, 1085, 935, 901, 808, 661 cm\(^{-1}\); \(\delta_\text{H}(400 \text{ MHz, CDCl}_3)\) 7.30 (1.1H, d, J 8.0, A -C \_H of phenyl), 7.22 (0.9H, d, J 8.0, B -C \_H of phenyl), 7.09-7.02 (3H, m, A+B -C \_H of phenyl), 6.99-6.98 (1H, m, A+B -C \_H of phenyl), 6.77-6.75 (2H, m, A+B -C \_H of phenyl), 6.71-6.33 (3H, m, A+B -C \_H of phenyl, A+B -C \_H of Ru-Ar), 6.58-6.54 (2H, m, A+B -C \_H of phenyl), 5.87-5.84 (1H, m, A+B -C \_H of Ru-Ar), 5.69 (0.45H, br s, B -C \_H of Ru-Ar), 5.60 (0.55H, d, J 5.2, A -C \_H of Ru-Ar), 5.48 (0.45H, br s, B -C \_H of Ru-Ar), 5.21-5.17 (1H, m, A -C \_H of Ru-Ar, B -C \_HNTs), 4.78 (0.45H, br d, B -C \_HNTs), 4.68 (0.55H, d, J 10.8, A -C \_HNTs), 4.30 (0.55H, br d, A NH(CH\(_3\))\(_3\)), 3.87-3.81 (0.55H, m, A -C \_HNTs(CH\(_3\))\(_3\)), 2.85-2.54 (3H, m, A+B -CN(CH\(_2\))\(_2\)), 2.23-2.02 (2H, m, A+B -CN(CH\(_2\))\(_2\)), 2.19 (1.65H, s, A -C\(_3\)), 2.13 (1.35H, s, B -C\(_3\)), 1.60 (4.95H, s, A -C(CH\(_3\))\(_3\)), 1.55 (4.05H, s, B -C(CH\(_3\))\(_3\)), (peak not identified for (0.45H) B -CN(CH\(_2\))\(_2\)); \(\delta_\text{H}(100 \text{ MHz, CDCl}_3)\) 142.93(C), 141.63(C), 139.43(C), 139.37(C), 138.97(C), 137.90(C), 136.32(C), 135.25(C), 131.57(CH), 130.37(CH), 128.61(CH), 128.32(CH), 128.24(CH), 127.99(CH), 127.92(CH), 127.80(CH), 127.27(CH), 126.90(CH), 126.57(CH), 126.25(CH), 126.11(CH), 125.39(CH), 109.97(C), 106.41(C), 95.88(C), 89.50(CH), 89.04(C), 88.63(CH), 88.30(CH), 85.21(CH), 80.50(CH), 77.96(CH), 75.32(CH), 73.98(CH), 71.00(CH), 69.47(CH), 67.96(CH), 62.50(CH), 47.48(CH\(_3\)), 44.82(CH\(_3\)), 34.55(C), 34.28(C), 31.12(CH\(_3\)), 30.87(CH\(_3\)), 29.12(CH\(_3\)), 28.67(CH\(_3\)), 26.85(CH\(_3\)), 26.60(CH\(_3\)), 21.17(CH\(_3\)), 21.13(CH\(_3\)); m/z ESI-MS [M-Cl]\(^+\) 641.1; HRMS found 641.1777 \((C_{33}H_{38}N_2O_2RuS-Cl)^+\) requires 641.1778, error = 0.3 ppm).
Mechanistic discussion and evidence of intermediates formed in cyclisation:

The results described above (particularly the observation for unsuccessful attempted conversion of 5 to 4) indicates that complexation of both nitrogens of the diamine to the Ru(II) is unlikely to be the first step in the successful complexation process. A proposed mechanism is shown below, in which the basic amine initially promotes conversion of the dimer to a monomer complex, then arene displacement takes place, finally followed by the second N-Ru bond formation via loss of HCl. The addition of a base, such as triethylamine, does not improve the conversion because a strong base will reduce the level of product by promoting premature cyclisation through deprotonation to give the unwanted bidentate product e.g. 5. This mechanism is distinct from those previously employed in the synthesis of this class of tethered complexes.
The results from a study of the room temperature reaction are given below:

A mixture of compound 6b (10 mg, 1.0 eq) and [Ru(C6H5CO2Et)Cl2]2 (6.3 mg, 0.5 eq) was dissolved in CDCl3 (0.6 mL) in a NMR tube at room temperature. The mixture was analysed by 1H-NMR after 0.5 h, 8 h, 19h and 64 h. The 1H-NMR spectra are overlaid below.

1= NMR after 0.5 h; 2= NMR after 8 h; 3= NMR after 19h; 4= NMR after 64 h; 5 = NMR of complex 5. The formation of 5 can be seen, with conversion levelling off at ca. 50%. Hence stirring at rt results in formation of the unproductive complex 5. (triplet at 1.35-1.55 is characteristic of 5: ca. 10% at 0.5h, 40% at 8h, 50% at 19h, 50% at 64h). Full 1H-NMR spectrum for 5 is given in the main spectroscopy section of this supporting information.
Evidence of monodentate intermediate: We have obtained $^1$H-NMR data for the initial monodentate complex B - see below.

1 (lower) = $^1$H-NMR of compound 5.

2 (middle) = $^1$H-NMR of compound 6b.

3 (upper) = $^1$H-NMR of intermediate formed after 0.5 h on stirring compound 6b (1.0 eq) and [Ru(C$_6$H$_5$CO$_2$Et)Cl$_2$]$_2$ (0.5 eq) in DCM. At this point, a new complex, but not 5, is observed. This may be the speculated monodentate intermediate B, which is converted to 4 upon rapid heating.
N-{[(1R,2R)-2-[3-(4-methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide}-\eta^6-(ethyl benzoate) ruthenium chloride 5.

To a nitrogen purged, dried flask was added ligand 6b (50 mg, 0.1 mmol) and ruthenium dimer [Ru(C₆H₅CO₂Et)Cl₂]₂ (32 mg, 0.05 mmol). To this was then added triethylamine (20 mg, 0.2 mmol) and anhydrous iso-propanol (4 mL). The resulting solution was stirred at reflux under nitrogen for 2 hours. The reaction was cooled to room temperature and the solvent and triethylamine were removed under reduced pressure to leave an orange/brown solid. The solid was purified by column chromatography (florosil, 0-5% MeOH in DCM, TLC: 5% MeOH in DCM with product Rf = 0.35) to give the product 5 as a red solid (33 mg, 0.04 mmol, 40%). Mp 210°C (decomposed 170°C); [α]D 28 -30 (c 0.005 in CHCl₃); υmax 3028, 2923, 1729, 1512, 1454, 1268, 1125,1103, 1082, 903, 817, 806, 697, 576 cm⁻¹; δH (400 MHz, CDCl₃) 7.18 (2H, d J 8.0 Hz, C₆H₄), 7.04-6.92 (6H, m, 5 x C₆H₄ and C₆H₄-Ru); 6.75-6.65 (6H, m, C₆H₄), 6.60 (1H, br s, C₆H₄), 6.54 (2H, t J 7.5 Hz, C₆H₄), 6.41-4.34 (1H, m, CH₂CH₃), 4.01 (1H, d J 11.0 Hz, CH), 3.82 (1H, t J 11.0 Hz, NH), 3.70 (3H, s, OC₆H₃), 3.55-3.49 (1H, m, CH), 3.31-3.22 (1H, m, CH₂), 2.75-2.67 (1H, m, CH₂), 2.64-2.57 (1H, m, CH₂), 2.24-2.16 (1H, m, CH₂), 2.13 (3H, s, CH₃), 2.02-1.97 (1H, m, CH₂), 1.86-1.79 (1H, m, CH₂), 1.45 (3H, m, CH₂), 1.12-1.04 (1H, m, CH₂), 0.86 (3H, t J 7.2 Hz, CH₂CH₃); δC (100 MHz, CDCl₃) 166.49 (C=O), 158.22(C), 142.03(C), 139.35(C), 138.29(C), 136.60(C), 132.78(C), 129.52(2CH), 128.90(2CH), 128.60(2CH), 128.30(CH), 127.84(2CH), 127.49(2CH), 126.86(2CH), 126.28(CH), 114.08(4CH), 94.95(CH), 93.72(CH), 89.25(CH), 81.08(CH), 79.21(CH), 79.13(CH), 75.38(C), 69.68(CH), 62.76(CH₃), 55.34(CH₃), 53.48(CH₃), 32.08(CH₂), 30.55(CH₂). m/z (ESI) 765.2 (M⁺ + 1). m/z ESI-MS [M+H-Cl]+ 765; HRMS found 765.1944 C₄₀H₃₉N₂O₇RuS ([M+H-Cl]+) requires M, 765.1942.

Attempted synthesis of N-{[(1R,2R)-2-[3-(4-methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride 4 from N-{[(1R,2R)-2-[3-(4-methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide}-\eta^6-(ethyl benzoate) ruthenium chloride 5.

Compound 5 (0.050 g, 0.061 mmol) was dissolved in dry DCM (1.5 mL) in a glass tube under N₂. The tube was sealed and the mixture was heated at 90 °C for 49 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The residue was precipitated from diethyl ether, filtered and dried to give a dark brown solid (0.045 g). The crude compound was analysed by ¹H-NMR to give the conversion to desired compound 4. The ¹H-NMR spectrum is given below, and indicated a ca. <15% conversion to 4. The majority of the visible material is uncyclised 5.
$^1$H-NMR for attempted intramolecular reaction (Scheme 1 in main paper).

Cyclised product 4 visible at 5.5, 5.4. Starting material 5 peaks dominate the spectrum. Full spectra of 5 and 4 are given in the spectroscopic data section of this supporting information.
Asymmetric reduction reactions.

Reduction with formic acid/triethylamine (ATH).

To a mixture of catalyst (0.002 mmol) in FA:TEA (5:2) (1.0 mL) was added ketone/imine (2.0 mmol) and the mixture was stirred at 60 °C for 1h-31h under an inert atmosphere. The reaction was monitored by chiral GC. For chiral GC analysis, the small sample from reaction mixture was filtered through a plug of silica using hexane: EtOAc (1:1). The filtrate was analysed by chiral GC. After completion of reaction; (i) for ketone reduction: reaction mixture was filtered through silica using EtOAc. The filtrate was concentrated to give a crude alcohol. The crude compound was purified by flash column chromatography over silica gel to give pure alcohol; (ii) for imine reduction: reaction mixture was concentrated, diluted with DCM and washed with sat. NaHCO₃ solution. The organic layer was separated, dried over anhydrous Na₂SO₄, filtered and concentrated to give the amine.

Table 1a: ATH of ketones and imines using (R,R) 4-methoxy 4 and (R,R) 3,5-dimethoxy 9 catalysts in FA:TEA(2M solution of ketone) at 60°C using S/C ratio 1000/1.

| Substrate | Catalyst | Time | % Conv | % ee<sup>a</sup> |
|-----------|----------|------|--------|------------------|
| 13        | 4-Methoxy 4 | 1h   | 83     | 97(R)           |
|           |          | 1.5h | 93     | 97(R)           |
|           |          | 2h   | 100    | 96(R)           |
|           | 3,5-Dimethoxy 9 | 1h   | 24     | 90(R)           |
|           |          | 2h   | 79     | 89(R)           |
|           |          | 3h   | 98     | 90(R)           |
|           |          | 4h   | 100    | 89(R)           |
| 14        | 4-Methoxy 4 | 1.5h | 60     | 96(R)           |
|           |          | 3.5h | 100    | 97(R)           |
|           | 3,5-Dimethoxy 9 | 1h   | 17     | 89(R)           |
|           |          | 3h   | 88     | 88(R)           |
|           |          | 5h   | 100    | 88(R)           |
| 15        | 4-Methoxy 4 | 1h   | 99     | 96(R)           |
|           |          | 1.5h | 100    | 96(R)           |
|           | 3,5-Dimethoxy 9 | 5h   | 21     | 75(R)           |
|           |          | 8h   | 50     | 73(R)           |
|           |          | 23h  | 97     | 70(R)           |
|           |          | 31h  | 99     | 69(R)           |
| 16        | 4-Methoxy 4 | 1h   | 64     | 98(R)           |
|           |          | 2h   | 100    | 98(R)           |
| Compound | Time | Value | Enantiomer |
|----------|------|-------|------------|
| 3,5-Dimethoxy 9 | 1h | 24 | 95(R) |
| 3,5-Dimethoxy 9 | 2h | 84 | 96(R) |
| 3,5-Dimethoxy 9 | 3h | 99 | 96(R) |
| 4-Methoxy 4 | 1h | 99 | 95(S) |
| 4-Methoxy 4 | 2h | 100 | 98(S) |
| 3,5-Dimethoxy 9 | 1h | 100 | 96(S) |
| 3,5-Dimethoxy 9 | 2h | 100 | 95(S) |
| 4-Methoxy 4 | 1h | 99 | 97°(S) |
| 3,5-Dimethoxy 9 | 1h | 88 | 94(S) |
| 3,5-Dimethoxy 9 | 2h | 99 | 94(S) |
| 4-Methoxy 4 | 1h | 49 | 99(R) |
| 4-Methoxy 4 | 2h | 99 | 99(R) |
| 4-Methoxy 4 | 3h | 100 | 99(R) |
| 3,5-Dimethoxy 9 | 1h | 2 | 25(R) |
| 3,5-Dimethoxy 9 | 3h | 31 | 18(R) |
| 3,5-Dimethoxy 9 | 6h | 62 | 22(R) |
| 3,5-Dimethoxy 9 | 8h | 64 | 21(R) |
| 3,5-Dimethoxy 9 | 23h | 90 | 20(R) |
| 3,5-Dimethoxy 9 | 31h | 96 | 21(R) |
| 4-Methoxy 4 | 1h | 79 | 95(R) |
| 4-Methoxy 4 | 2h | 100 | 94°(R) |
| 3,5-Dimethoxy 9 | 1h | 27 | 89(R) |
| 3,5-Dimethoxy 9 | 2h | 86 | 83(R) |
| 3,5-Dimethoxy 9 | 3h | 99 | 80(R) |
| 3,5-Dimethoxy 9 | 4h | 100 | 81(R) |
| 3,5-Dimethoxy 9 | 4h | 100 | 87°(R) |
| 4-Methoxy 4 | 1h | 43 | 99°(R) |
| 3,5-Dimethoxy 9 | 1h | 77 | 99°(R) |
| 3,5-Dimethoxy 9 | 2h | 100 | >99°(R) |
| 3,5-Dimethoxy 9 | 3h | 100 | >99°(R) |
|                   | 1h  | 2h  | 3h  | 4h  | 5h  | %ee  |
|-------------------|-----|-----|-----|-----|-----|------|
| 4-Methoxy 4       |     |     |     |     |     | 21   |
|                   |     |     |     |     |     | 67   |
| 3,5-Dimethoxy 9   |     |     |     |     |     | 23   |
|                   |     |     |     |     |     | 64   |
| **4-Methoxy 4**   | 0.5h|     |     |     |     | 37   |
|                   | 1h  |     |     |     |     | 98   |
| **3,5-Dimethoxy 9** |    |     |     |     |     | 78   |
|                   | 1h  |     |     |     |     | 99   |
|                   | 2h  |     |     |     |     | 100  | 99(R) |
| **4-Methoxy 4**   | 2h  |     |     |     |     | 41   |
|                   |     |     |     |     |     | 93   |
|                   |     |     |     |     |     | 100  | 99(R) |
| **3,5-Dimethoxy 9** | 7h |     |     |     |     | 100  | 96(R) |
| **4-Methoxy 4**   | 2h  |     |     |     |     | 76   |
|                   |     |     |     |     |     | 99   |
|                   |     |     |     |     |     | 100  | 37(S) |
| **3,5-Dimethoxy 9** | 2h |     |     |     |     | 57   |
|                   |     |     |     |     |     | 96   |
|                   |     |     |     |     |     | 99   |
|                   |     |     |     |     |     | 100  | 73(S) |
| **4-Methoxy 4**   | 1h  |     |     |     |     | 92   |
|                   |     |     |     |     |     | 99   |
|                   |     |     |     |     |     | 100  | 35(S) |
| **3,5-Dimethoxy 9** | 1h |     |     |     |     | 95   | 75(S) |
|                   |     |     |     |     |     | 99   | 76(S) |

a %Conv and %ee were calculated by chiral GC analysis; b %ee was calculated by chiral HPLC analysis; c For this compound %ee was given for the chiral GC analysis carried out after final work up of the reaction; d %ee was calculated for acetate derivative. Note: figures for conversion and ee given in the main paper are rounded from the GC/HPLC figures to the nearest whole number, with the exception of cases where the ee is >99.4%, in which case it is given as >99%.
Table 1b: ATH of acetophenone and acetylcyclohexane using five novel catalysts (2M) in FA:TEA at 28 °C using complexes at S/C ratio 100/1.

| Catalyst | Ketone     | Time | % Conv | % ee   |
|----------|------------|------|--------|--------|
| ![Catalyst 4](chart1.png) | ![Ketone 4](chart2.png) | 4.5 h | >99%   | 97%(R) |
| ![Catalyst 9](chart3.png) | ![Ketone 9](chart4.png) | 22 h  | >99%   | 41%(S) |
| ![Catalyst 11](chart5.png) | ![Ketone 11](chart6.png) | 8 h   | 99%    | 91%(R) |
| ![Catalyst 11](chart5.png) | ![Ketone 11](chart6.png) | 21.5 h| 99%    | 74%(S) |
| ![Catalyst 12](chart7.png) | ![Ketone 12](chart8.png) | 22 h  | 100%   | 97%(R) |
| ![Catalyst 12](chart7.png) | ![Ketone 12](chart8.png) | 20 h  | 99%    | 31%(S) |
| ![Catalyst 10](chart9.png) | ![Ketone 10](chart10.png) | 94 h  | 55%    | 87%(R) |
| ![Catalyst 10](chart9.png) | ![Ketone 10](chart10.png) | 44 h  | 30%    | 4%(S)  |
| ![Catalyst 10](chart9.png) | ![Ketone 10](chart10.png) | 23 h  | 100%   | 96%(R) |
| ![Catalyst 10](chart9.png) | ![Ketone 10](chart10.png) | 44 h  | 99%    | 60%(S) |
Reduction with hydrogen gas (APH):

To a pyrex test tube was added the substrate (1 mmol) followed by the catalyst (0.002 mmol). To this was then added MeOH (2 mL). The test tube was then placed into a Parr reactor which was sealed and purged with hydrogen gas. The reactor was then charged to a pressure of 30 bar hydrogen gas, heated to the required temperature (60 °C) and stirred for the required time. Once complete the reactor was allowed to cool to room temperature and the pressure released. The reaction solution was filtered through silica with 1:1 EtOAc: petroleum ether 40-60 solution to remove the catalyst. The filtrate was dried by rotary evaporation to give the product which was analysed by gas chromatography.

Table 3. Comparison of APH results for p-OMe 4 and di-OMe 3C 9 tethered (R,R)-catalysts

| Ketone | Catalyst 4 | | Catalyst 9 | |
|--------|------------|------------|------------|
|        | Time (hr.) | Conv. (%)  | e.e. (%)   | Time (hr.) | Conv. (%)  | e.e. (%)   |
| ![Image of ketone](image1) | 16 | 100 | 94 (R) | 16 | 100 | 84 (R) |
| ![Image of ketone](image2) | 48 | 99  | 37 (S)  | 48 | 40  | 81 (S)  |
| ![Image of ketone](image3) | 16 | 100 | 94 (R) | 16 | 100 | 80 (R) |
| ![Image of ketone](image4) | 16 | 98  | 92 (R)  | 16 | 99  | 74 (R)  |
| ![Image of ketone](image5) | 24 | 100 | 82 (R)  | 24 | 100 | 54 (R)  |
| ![Image of ketone](image6) | 16 | 70  | 84 (R)  | 16 | 19  | 73 (R)  |
| ![Image of ketone](image7) | 48 | 32  | 80 (R)  | 48 | 27  | 78 (R)  |
MeOH solvent with [S] 0.5M, 60°C, S/C 500/1, 30 bar H₂. Note: figures for conversion and ee given in the main paper are rounded from the GC/HPLC figures to the nearest whole number, with the exception of cases where the ee is >99.4%, in which case it is given as >99%.

Reduction products (combined references are given at end of this section).

(R)-1-Phenylethanol (reduction product of 13).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25μm, Oven Temp = 110 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 6.24 min, R isomer 13.91 min, S isomer 16.24 min. 
\[\alpha\]D 28 = +58.1 (c 0.730 in CHCl₃) for 96.3% ee [lit. value 1 \[\alpha\]D 27 = +54.9 (c 1.0 in CHCl₃) 96% ee (R)]; \(\delta\)H (300 MHz, CDCl₃) 7.38-7.24 (5H, m, Ph), 4.87 (1H, q, J 6.5, -CH), 2.07 (1H, br s, -OH), 1.48 (3H, d, J 6.5, -CH₃); \(\delta\)C (75 MHz, CDCl₃): 145.20, 127.90(2C), 126.87, 124.78, 69.81, 24.55.
For APH: Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15psi H₂, det = FID 220°C, inj = 220°C, ketone 10.2 min., R isomer 14.27 min., S isomer 15.76 min.

(R)-1-Phenyl-1-propanol (reduction product of 14).
ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 115 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 7.88 min, R isomer 19.30 min, S isomer 20.44 min. 

$\alpha_D^{32} = +52.6$ ($c$ 0.885 in CHCl$_3$) for 96.8% ee (R) [lit. value$^2$ $\alpha_D^{25} = -47.2$ ($c$ 0.65 in CHCl$_3$) 99% ee (S)]; $\delta_H$ (400 MHz, CDCl$_3$) 7.36-7.25 (5H, m, Ph), 4.58 (1H, t, $J$ 6.4, -CH), 2.03 (1H, br s, -OH), 1.87-1.68 (2H, m, -CH$_2$), 1.48 (3H, d, $J$ 7.4, -CH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 144.55, 128.36(2C), 127.46, 125.94(2C), 75.99, 31.84, 10.11.

For APH: Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 µm, T = 115°C, P = 15psi H$_2$, det = FID 220°C, inj = 220°C, ketone 14.56 min., R isomer 23.11 min., S isomer 25.03 min.

(R)-1-(2-Methoxyphenyl)ethanol (reduction product of 15).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 4.08 min, S isomer 5.87 min, R isomer 6.08 min. 

$\alpha_D^{32} = +26.3$ ($c$ 1.225 in CHCl$_3$) for 95.5% ee (R) [lit. value$^3$ $\alpha_D^{20} = +32.3$ ($c$ 2.0 in CHCl$_3$) 94% ee (R)]; $\delta_H$ (400 MHz, CDCl$_3$) 7.36-7.25 (5H, m, Ph), 4.58 (1H, t, $J$ 6.4, -CH), 2.03 (1H, br s, -OH), 1.87-1.68 (2H, m, -CH$_2$), 1.48 (3H, d, $J$ 7.4, -CH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 156.52, 133.37, 128.26, 126.06, 120.76, 110.40, 66.51, 55.22, 22.80.

(R)-1-(2-Furyl)ethanol (reduction product of 16).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 70 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) R isomer 34.31 min, S isomer 39.45 min. 

$\alpha_D^{31} = +24.9$ ($c$ 0.895 in CHCl$_3$) for 98.2% ee (R) [lit. value$^4$ $\alpha_D^{24} = -20.1$ ($c$ 1.0 in CHCl$_3$) 99% ee (S)]; $\delta_H$ (400 MHz, CDCl$_3$) 7.37 (1H, dd, $J$ 2.0, 0.8, -CH of furyl), 6.32 (1H, dd, $J$ 3.2, 1.6, -CH of furyl), 6.22 (1H, d, $J$ 3.2, -CH of furyl), 4.58 (1H, t, $J$ 6.8, -CH), 2.24 (1H, br s, -OH), 1.53 (3H, d, $J$ 6.8, -CH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 157.54, 141.88, 110.10, 105.09, 63.06, 21.21.

(S)-1-Phenyl-1,2-ethanediol (reduction product of 17).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 140 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) R isomer 27.35 min, S isomer 29.69 min.
[\alpha]_D^{32} = +57.8 (c 0.790 in CHCl₃) for 97.8% ee (S) [lit. value² [\alpha]_D^{18} = +65.5 (c 1.25 in CHCl₃) 94% ee (S)]; δ_H (400 MHz, CDCl₃) 7.37-7.27 (5H, m, Ph), 4.78 (1H, dd, J 8.4, 3.6, -CH), 3.72 (1H, dd, J 11.4, 3.6, -CH₂OH), 3.63 (1H, dd, J 11.4, 8.4, -CH₂OH), 3.12 (2H, br s, -OH and -CH₂OH); δ_C (100 MHz, CDCl₃): 140.41, 128.49(2C), 127.94, 126.03(2C), 74.67, 68.01.

For APH: Conversion and enantiomeric excess determined by GC analysis: CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 155°C, P = 18 psi He, det = FID 220°C, inj = 220°C, ketone 5.2 min, S isomer 12.54 min, R isomer 13.45 min.

(S)-1-Phenyl-2-chloroethanol (reduction product of 18).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det . Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 5.45 min, R isomer 8.88 min, S isomer 9.56 min; [\alpha]_D^{32} = +61.8 (c 0.810 in CHCl₃) for 96.8% ee (S) [lit. value⁶ [\alpha]_D^{22} = +53.8 (c 1.0 in CHCl₃) >99% ee (S)]; δ_H (400 MHz, CDCl₃) 7.39-7.31 (5H, m, Ph), 4.89 (1H, m, -CH₂OH), 3.74 (1H, dd, J 11.4, 3.6, -CH₂Cl), 3.64 (1H, dd, J 11.4, 8.6, -CH₂Cl), 2.69 (1H, d, J 3.2, -OH); δ_C (100 MHz, CDCl₃): 139.86, 128.65(2C), 128.43, 126.02(2C), 74.03, 50.88.

(R)-3-Hydroxy-3-phenylpropionitrile (reduction product of 19).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det . Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 9.86 min, R isomer 18.28 min, S isomer 20.11 min. [\alpha]_D^{30} = +69.2 (c 0.750 in CHCl₃) for 97.8% ee (R) [lit. value⁷ [\alpha]_D^{24} = +56.9 (c 1.0 in CHCl₃) 94% ee (R)]; δ_H (400 MHz, CDCl₃) 7.49-7.30 (5H, m, Ph), 5.01 (1H, t, J 6.1, -CH), 2.74 (2H, d, J 6.1, -CH₂), 2.66 (1H, br s, -OH); δ_C (100 MHz, CDCl₃): 140.97, 128.88(2C), 128.77, 125.48(2C), 117.27, 70.02, 27.87.

(R)-1-(1-Naphthyl)ethanol (reduction product of 20).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det . Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 9.13 min, S isomer 18.99 min, R isomer 20.19 min. [\alpha]_D^{32} = +60.3 (c 0.910 in CHCl₃) for 99.1% ee (R) [lit. value⁸ [\alpha]_D = +67.3 (c 0.4 in CHCl₃) 100% ee (R)]; δ_H (400 MHz, CDCl₃) 8.10 (1H, d, J 8.4, -CH of naphthyl), 7.86 (1H, dd, J 7.2, 2, -CH of naphthyl), 7.76 (1H, d, J 8.4, -CH of naphthyl), 7.76 (1H, d, J 7.2, -CH of naphthyl), 7.53-7.44 (3H, m, -CH of naphthyl), 5.65 (1H,
q, J 6.4, -CH$_2$, 2.08 (1H, br s, -OH), 1.65 (3H, d, J 6.4, -CH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 141.30, 133.77, 130.24, 128.86, 127.90, 126.00, 125.51, 125.49, 123.12, 121.95, 67.09, 24.30.

(R)-1-(2-Naphthyl)ethanol (reduction product of 21).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) R isomer 30.64 min, S isomer 32.87 min. $[\alpha]_D^{20}$ = +46.3 (c 0.825 in CHCl$_3$) for 93.8 % ee (R) [lit. value$^9$ $[\alpha]_D^{20}$ = +46.7 (c 1.02 in CHCl$_3$) 92% ee (R)]; $\delta_H$ (400 MHz, CDCl$_3$) 7.87-7.73 (4H, m, -CH$_2$ of naphthyl), 7.54-7.40 (3H, m, -CH of naphthyl), 5.04 (1H, t, J 6.4, -CH$_2$), 1.98 (1H, br s, -OH), 1.48 (3H, d, J 6.4, -CH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 143.15, 133.29, 132.89, 128.28, 127.90, 126.11, 125.76, 123.78(2C), 70.49, 25.10.

(R)-4-Chromanol (reduction product of 22).

ATH: The conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 4.46 min, Alcohol 6.90 min; the enantiomeric excess determined by chiral HPLC analysis (ChiralPak IB Column: 0.46 cm x 25 cm, hexane:IPA 95:0.50, 1.0mL/min, 28°C) Rt(min) = 9.94 (S isomer), 10.83 min (R isomer); $[\alpha]_D^{20}$ = +72.9 (c 0.800 in CHCl$_3$) for 99.2% ee (R) [lit. value$^10$ $[\alpha]_D^{20}$ = +60.1 (c 0.2 in CHCl$_3$) 96% ee (R)]; $\delta_H$ (400 MHz, CDCl$_3$) 7.29 (1H, m, -CH of Ph), 7.20 (1H, m, -CH of Ph), 6.91 (1H, m, -CH of Ph), 7.29 (1H, m, -CH of Ph), 4.78 (1H, dd, J 8.4, 3.6, -CH), 3.72 (1H, dd, J 11.4, 3.6, -CH$_2$OH), 3.63 (1H, dd, J 11.4, 8.4, -CH$_2$OH), 3.12 (2H, br s, -OH and -CH$_2$OH); $\delta_C$ (100 MHz, CDCl$_3$): 154.86, 130.00, 129.94, 124.60, 120.87, 117.36, 63.51, 62.20, 31.09.

APH: Enantiomeric excess and conversion determined by HPLC analysis: IB column, 0.46 x 25 cm, 1 mL/min, 95:5 Hexane:2-propanol, RT, ketone 6.53 min, S isomer 8.44 min, R isomer 9.14 min. Ketone UV response is 20.12 times greater than for the alcohol; starting material peak appears on HPLC.

(R)-1-Tetralol (reduction product of 23).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 120 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 23.11 min, S isomer 40.88 min, R isomer 41.43 min. $[\alpha]_D^{20}$ = -30.7 (c 1.020 in CHCl$_3$) for 99.2 % ee (R) [lit. value$^{11}$ $[\alpha]_D^{20}$ = +34.4 (c 1.01 in CHCl$_3$) 98% ee (S)]; $\delta_C$ (400 MHz, CDCl$_3$) 7.47-7.37 (1H, m, -CH of Ph), 7.22-7.05 (3H, m, -CH of Ph), 4.78 (1H, br s, -OH), 2.03
(1H, br s, -OH), 2.89-2.65 (2H, m, -CH$_2$), 2.03-1.74 (5H, m, -CHOH-CH$_2$-CH$_2$); δ$_c$ (100 MHz, CDCl$_3$): 138.77, 137.09, 128.99, 128.62, 127.56, 126.16, 68.14, 32.24, 29.21, 18.75.

APH: Enantiomeric excess and conversion determined by GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 120°C, P = 18 psi He gas, det = FID 220°C, inj = 220°C. Ketone 24.66 min, S isomer 44.59 min, R isomer 45.62 min.

(R)-1-(4-Cyanophenyl)ethanol (reduction product of 24).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25μm, Oven Temp = 160 °C, Det Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 5.47 min, R isomer 13.48 min, S isomer 15.60 min.

[α]$^D_{30}$ = +42.22 (c 1.080 in CHCl$_3$) for 88.4% ee (R) [lit. value$^{11}$ [α]$^D_{20}$ = +77.1 (c 0.70 in CHCl$_3$) 92% ee (R)]; δ$_h$(400 MHz, CDCl$_3$) 7.62 (2H, d, J 8.0, -CH of Ph), 7.48 (2H, d, J 8.0, -CH of Ph), 4.95 (1H, t, J 6.4, -CH), 2.27 (1H, br s, -OH), 1.49 (3H, d, J 6.4, -CH$_3$); δ$_c$ (100 MHz, CDCl$_3$): 151.08, 132.30(2C), 126.20(2C), 118.82, 110.97, 69.60, 25.34.

(R)-1-(2-Hydroxyphenyl)ethanol (reduction product of 25).

ATH: The enantiomeric excess and conversion determined by GC analysis (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25μm, Oven Temp = 170 °C, Det Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) Ketone 2.18 min, R isomer 6.42 min, S isomer 7.03 min; [α]$^D_{32}$ = +22.3 (c 0.650 in CH$_2$Cl$_2$) for 98.8% ee (R) [lit. value$^{12}$ [α]$^D_{20}$ = +20.5 (c 0.2 in CH$_2$Cl$_2$) >98% ee (R)]; δ$_h$(400 MHz, CDCl$_3$) 7.98 (1H, br s, -C$_6$H$_4$OH), 7.16 (1H, dt, J 8.0, 1.6, -CH of Ph), 6.97 (1H, dd, J 7.6, 1.6, -CH of Ph), 6.87-6.80 (2H, m, -CH of Ph), 5.04 (1H, q, J 6.6, -CHOH), 2.76 (1H, br s, -CHOH), 1.57 (3H, d, J 6.6, -CH$_3$); δ$_c$ (100 MHz, CDCl$_3$): 153.32, 128.90, 128.73, 126.43, 119.87, 117.05, 71.55, 23.38.

(S)-1-Cyclohexylethanol (reduction product of 26).

ATH: the enantiomeric excess determined by GC analysis of acetate derivative (CP-Chirasil-DEX CB 25m x 0.25mm x 0.25μm, Oven Temp = 100 °C, Det Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas) S isomer 12.94 min, R isomer 17.49 min.
APH: Conversion determined by $^1$H NMR. Enantiomeric excess determined by GC analysis of the acetate derivative: CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 100°C, P = 18psi He, det = TCD 100°C, inj = 220°C, $S$ isomer 14.07 min, $R$ isomer 18.58 min.

Preparation of derivative: The reduction product (10 mg) was dissolved in 1 mL of DCM. To this was then added acetic anhydride (20 μL) and DMAP (3 crystals). The reaction was stirred overnight and then volatiles were removed by rotary evaporation. A small amount of the residue was diluted in EtOAc and then analysed by GC.

$[\alpha]^D_{26} +3.7$ (c 0.5 in CHCl$_3$) 81.4% ee ($S$) (lit.$^{14}$ $[\alpha]^D_{26} +2.7$ (c 0.5 in CHCl$_3$) 75% ee ($R$)); δ$_H$(300 MHz, CDCl$_3$) 3.54 (1H, q $J$ 6.2 Hz, CH), 1.87-1.83 (1H, m, CH), 1.79-1.73 (2H, m, CH$_2$), 1.69-1.65 (3H, m, CH + CH$_2$), 1.32-1.14 (7H, m, CH$_2$ + OH), 1.07-0.93 (2H, m, CH$_2$); δ$_C$ (75 MHz, CDCl$_3$): 72.22, 45.08, 28.67, 28.32, 26.48, 26.19, 26.0, 20.35.

**(R)-2,3-dihydro-1H-inden-1-ol** (reduction product of 27).

![R-2,3-dihydro-1H-inden-1-ol](image)

APH: Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 100°C, P = 15psi H$_2$, det = FID 220°C, inj = 220°C, ketone 62.7 min., $R$ isomer 79.32 min., $S$ isomer 78.76 min.

$[\alpha]^D_{26} -31.6$ (c 1.0 in CHCl$_3$) 97.7% ee ($R$) (lit.$^{1}$ $[\alpha]^D_{26} -30.5$ (c 1.0 in CHCl$_3$) 84% ee ($R$)); δ$_H$(300 MHz, CDCl$_3$) 7.41-7.39 (1H, m, CH$_{Ar}$), 7.25-7.21 (3H, m, CH$_{Ar}$), 5.21 (1H, m, CH), 3.08-2.98 (1H, m, CH$_2$), 2.85-2.74 (1H, m, CH$_2$), 2.51-2.40 (1H, m, CH$_2$), 1.97-1.86 (2H, m, OH + CH$_2$); δ$_C$ (100 MHz, CDCl$_3$) 145.0, 143.3, 128.4, 126.7, 124.9, 124.2, 76.5, 36.0, 29.8.

**(R)-1-(4’-Methoxyphenyl)ethanol** (reduction product of 28).

![R-1-(4’-Methoxyphenyl)ethanol](image)

APH: Enantiomeric excess and conversion determined by GC analysis: CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 130°C, P = 18psi He, det = FID 220°C, inj = 220°C, ketone 13.5 min., $R$ isomer 18.64 min., $S$ isomer 20.28 min.

$[\alpha]^D_{22} +52.7$ (c 0.5 in CHCl$_3$) 93.7% ee ($R$) (lit.$^{1}$ $[\alpha]^D_{22} +32.3$ (c 1.0 in CHCl$_3$) 90% ee ($R$)); δ$_H$(400 MHz, CDCl$_3$) 7.32-7.30 (2H, m, CH$_{Ar}$), 6.91-6.89 (2H, m, CH$_{Ar}$), 4.85 (1H, q $J$ 6.4 Hz, CH), 3.82 (3H, s, OCH$_3$), 2.28 (1H, br s, OH), 1.49 (3H, d $J$ 6.3 Hz, CH$_3$); δ$_C$ (100 MHz, CDCl$_3$) 159.0, 138.0, 126.7, 113.9, 70.0, 55.3, 25.0.

**(R)-1-(4’-Trifluoromethylphenyl)ethanol** (reduction product of 29).

![R-1-(4’-Trifluoromethylphenyl)ethanol](image)
APH: Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 130°C, P = 15psi H₂, det = FID 220°C, inj = 220°C, ketone 7.08 min., R isomer 15.65 min., S isomer 17.42 min.

\[\alpha\]D28 +33.5 (c 1.0 in CHCl₃) 92.4% ee (R) (lit. 16 \[\alpha\]D22 +29.3 (c 1.0 in CHCl₃) >99% ee (R)); δH (400 MHz, CDCl₃) 7.62-7.60 (2H, m, CHAr), 7.48-7.46 (2H, m, CHAr), 4.93 (1H, q J 6.5 Hz, CH), 2.97 (1H, br s, OH), 1.49 (3H, d J 6.5 Hz, CH₃); δC (75 MHz, CDCl₃) 149.1, 128.9 (q J 32.3 Hz, CHCF₃), 123.6 (q J 270 Hz, CF₃), 124.9, 124.8, 124.75, 124.7, 69.1, 24.7.

(R)-1-(3',5'-Bis(trifluoromethyl)phenyl)ethanol (reduction product of 30).

APH: Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 120°C, P = 15psi H₂, det = FID 220°C, inj = 220°C, ketone 6.0 min., R isomer 16.30 min., S isomer 15.63 min.

\[\alpha\]D29 +16.5 (c 1.0 in CHCl₃) 81.8% ee (R) (lit. 17 \[\alpha\]D28 +11.9 (c 1.0 in CHCl₃) 96% ee (R)); δH (300 MHz, CDCl₃) 7.81-7.78 (3H, m, CHAr), 5.00 (1H, q J 6.3 Hz, CH), 2.92 (1H, br s, OH), 1.51 (3H, d J 6.6 Hz, CH₃); δC (100 MHz, CDCl₃) 148.2, 131.8 (q J 33 Hz, CHCF₃), 125.6, 123.4 (q J 271 Hz, CF₃), 121.3, 69.3, 25.6.

1-Phenyl-2,2-dimethyl-1-propanol (reduction product of 31).

APH: Enantiomeric excess and conversion determined by GC analysis: CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 125°C, P = 18psi He, det = TCD 100°C, inj = 220°C, ketone 6.59 min., R isomer 21.72 min., S isomer 22.42 min.

\[\alpha\]D30 +16.7 (c 1.0 in CHCl₃) 80.4% ee (R) (lit. 18 \[\alpha\]D20 +12.2 (c 1.0 in CHCl₃) 45% ee (R)); δH (300 MHz, CDCl₃) 7.31-7.25 (5H, m, CHAr), 4.39 (1H, s, CH), 1.86 (1H, br s, OH), 0.92 (9H, s, (CH₃)₃); δC (100 MHz, CDCl₃) 142.2, 127.6, 127.5, 127.3, 82.4, 35.6, 25.9.

(S)-2-phenoxy-1-phenylethanol (reduction product of 32).

APH: Conversion and enantiomeric excess determined by HPLC analysis: IB column, 0.46 x 25 cm, 0.7 mL/min, 95:5 Hexane:2-propanol, RT, ketone 14.20 min, R isomer 23.04 min, S isomer 31.93 min. Ketone UV response is 12.35 times greater than for the alcohol.

\[\alpha\]D30 +52.2 (c 1.0 in CHCl₃) 94.5% ee (S) (lit. 17 \[\alpha\]D10 +58.8 (c 1.0 in CHCl₃) 95% ee (S)); δH (300 MHz, CDCl₃) 7.45-7.24 (7H, m, CHAr), 6.98-6.89 (3H, m, CHAr), 5.10 (1H, dd J 8.8 and 3.3 Hz, CH), 4.10-4.07 (1H, m, CH₂), 4.02-3.96 (1H, m, CH₂), 2.90 (1H, br s, OH); δC (100 MHz, CDCl₃) 158.5, 139.8, 129.6, 128.6, 128.2, 126.4, 121.4, 114.7, 73.4, 72.6.
(S)-Salsolidine (reduction product of 33).

ATH: The enantiomeric excess and conversion determined by GC analysis (Chrompak cyclodextrin-β-236M-19 50m x 0.25mm x 0.25µm, Oven Temp = 170 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 15 psi, H₂ gas) Imine 49.65 min, S isomer 44.75 min, R isomer 45.69 min.

[α]D₀^28 = -40.4 (c 0.260 in CHCl₃) for 75.6% ee (S) [lit. value |α|D₀^25 = +56.5 (c 1.0 in CHCl₃) 91% ee (R)]; δH (400 MHz, CDCl₃) 6.62 (1H, s, -CH₂), 6.56 (1H, s, -CH₂), 4.04 (1H, q, J 6.8, -CH₃), 3.85 (3H, s, -OCH₃), 3.84 (3H, s, -OCH₃), 3.27-3.22 (1H, m, -CH₂HCH₂NH), 3.02-2.96 (1H, m, -CH₂CCH₂NH), 2.82-2.75 (1H, m, -CH₂CHNH₂), 2.67-2.61 (1H, m, -CH₂CHNH), 1.98 (1H, br s, -NH), 1.44 (3H, d, J 6.6, -CH₃); δC (100 MHz, CDCl₃): 147.25, 1147.17, 132.3, 126.71, 111.70, 108.99, 55.92, 55.78, 51.15, 41.27, 29.44, 22.76.

References:

(1) J. Hannedouche, G. Clarkson, M. Wills, J. Am. Chem. Soc. 2004, 126, 986-987.
(2) K. Nakamura, T. Matsuda. J. Org. Chem. 1998, 63, 8957–8964.
(3) T. S. Kaufman. Tetrahedron Lett. 1996, 37, 5329-5332.
(4) T. Ohkuma, M. Koizumi, M. Yoshida, R. Noyori. Org. Lett. 2000, 2, 1749–1751.
(5) D. J. Cross, J. A. Kenny, I. Houson, L. Campbell, T. Walsgrove, M. Wills, Tetrahedron: Asymmetry 2001, 12, 1801–1806.
(6) D. Zhu, C. Mukherjee, L. Hua. Tetrahedron: Asymmetry 2005, 16, 3275-3278.
(7) O. Soltani, M. A. Aringer, H. V-Villa, E. M. Carreira. Org. Lett. 2010, 12, 2893–2895.
(8) H. Ziffer, K. Kawai, M. Kasai, M. Imuta, C. Froussios. J. Org. Chem. 1983, 48, 3017-3021.
(9) Y. Ma, H. Liu, L. Chen, X, Cui, J. Zhu, J. Deng. Org. Lett. 2003, 5, 2103-2106.
(10) C. V. Manville, G. Docherty, R. Padda, M. Wills. Eur. J. Org. Chem. 2011, 6893–6901.
(11) M. Palmer, T. Walsgrove, M. Wills. J. Org. Chem. 1997, 62, 5226–5228.
(12) T. Kunisu, T. Oguma, T. Katsuki. J. Am. Chem. Soc. 2011, 133, 12937-12939.
(13) S. G. Davies, W. E. Hume, P. M. Roberts, J. E. Thomson. Tetrahedron 2010, 66, 8076-8088.
(14) G. Li and G. W. Kabalka, J. Organomet. Chem. 1999, 581, 66-69.
(15) F. Werner, N. Blank, T. Opatz, Eur. J. Org. Chem. 2007, 3911–3915.
(16) D. Zhu, Y. Yang, L. Hua, J. Org. Chem. 2006, 71, 4202-4205.
(17) V. Parekh, J. A. Ramsden, M. Wills, Catal. Sci. Technol. 2012, 2 (2), 406-414.
(18) D. Zhu, L. Hua, J. Org. Chem. 2006, 71, 9484–9486.
X-ray crystallographic structure of \((R,R)-4\) with atom labelling (CCDC 913682). See the .cif file for full details.

CCDC 913682 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The asymmetric unit contained the Ru complex, there are four in the unit cell. The Flack parameter refined to 0.011(7) (Shelx). The Hooft \(\gamma\) parameter refined to 0.003(4) (Olex). There are no unusual features in the crystal packing.

**Crystal Data.** \(C_{31}H_{33}ClN_2O_3RuS\), \(M = 650.17\), Orthorhombic, space group \(P2(1)2(1)2(1)\).

\[a = 6.98498(8), \quad b = 11.58675(14), \quad c = 35.3323(6) \ \text{Å}, \quad \alpha = 90^\circ, \quad \beta = 90^\circ, \quad \gamma = 90^\circ, \quad U = 2859.55(7) \ \text{Å}^3 \] (by least squares refinement on 7800 reflection positions), \(T = 100(2) \ \text{K}, \quad \lambda = 1.54184 \ \text{Å}, \quad Z = 4, \quad D(\text{cal}) = 1.510 \ \text{Mg/m}^3, \quad F(000) = 1336. \mu(\text{MoK-\(\alpha\)}) = 6.263 \ \text{mm}^{-1}. \quad \text{Crystal character: orange needle.} \quad \text{Crystal dimensions 0.61 x 0.02 x 0.01 mm.}

**Data Collection and Processing.** Oxford Diffraction Gemini four-circle system with Ruby CCD area detector. The crystal was held at 100(2) K with the Oxford Cryosystem Cryostream Cobra. Maximum theta was 70.83°. The hkl ranges were -8/5, -12/14, -39/41. 14757 reflections measured, 5366 unique \([R(\text{int}) = 0.0331]\). Absorption correction by Semi-empirical from equivalents; minimum and maximum transmission factors: 0.68; 1.00. No crystal decay.

**Structure Analysis and Refinement.** Systematic absences indicated space group \(P2(1)2(1)2(1)\) and shown to be correct by successful refinement. The structure was solved by direct methods using SHELXS.
(Sheldrick, 1990) (TREF) with additional light atoms found by Fourier methods. Hydrogen atoms were added at calculated positions and refined using a riding model except the NH. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameter equal to 1.2 (or 1.5 for methyl and NH H-atoms) times the equivalent isotropic displacement parameter of the atom to which they are attached. The NH was located in a difference map and allowed to refine freely but give thermal parameters equal to 1.5 times the equivalent isotropic displacement parameter of the atom to which it is attached. The absolute structure of the individual crystal chosen was checked by refinement of a delta-f” multiplier. Absolute structure parameter x = 0.011(7). R1[for 5211 reflections with l>2sigma(l)] = 0.0280, wR2 = 0.0678. Largest difference Fourier peak and hole 0.678 and -0.494 e. Å

X-ray crystallographic structure of (R,R)-9 with atom labelling (CCDC 923077). See the .cif file for full details.

CCDC 923077 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The asymmetric unit contains the Ru tethered complex. There are 4 complexes in the unit cell. There seems to be an offset π stacking between the tosyl and one of the phenyls of the diamine. The π stacking is characterised by angle between the mean planes through the interacting π systems and closest atomic contact. There is a short contact perhaps of interest between a CH on the dimethoxy ring and the oxygen of a neighbouring sulphonamide (though not the hydrogen you would expect to CH- π to
the incoming ketone). The Flack parameter refined to 0.004(10) (Shelxl). The Hooft y parameter refined to 0.009(4) (Olex2)

**Crystal Data.** C_{32}H_{35}ClN_{2}O_{4}RuS, M = 680.20, Orthorhombic, space group P2(1)2(1)2(1), a = 7.58370(10), b = 10.22300(10), c = 38.6764(3) Å, α = 90 deg., β = 90 deg., γ = 90 deg., U = 2998.51(5) Å³ (by least squares refinement on 12912 reflection positions), T =150(2) K, λ = 1.54178 Å, Z = 4, D(cal) = 1.507 Mg/m³, F(000) = 1400. μ(Mo-Kα) = 6.026 mm⁻¹. Crystal character: orange plate. Crystal dimensions 0.40 x 0.10 x 0.01 mm,

**Data Collection and Processing.** Oxford Diffraction Gemini four-circle system with Ruby CCD area detector. The crystal was held at 150(2) K with the Oxford Cryosystem Cryostream Cobra. Maximum theta was 78.06 °. The hkl ranges were -9/ 6, -12/ 12, -46/ 48. 22323 reflections measured, 6321 unique [R(int) = 0.0454]. Absorption correction by Semi-empirical from equivalents; minimum and maximum transmission factors: 0.55; 1.00. No crystal decay.

**Structure Analysis and Refinement.** Systematic absences indicated space group P2(1)2(1)2(1) and shown to be correct by successful refinement. The structure was solved by direct methods using SHELXS (Sheldrick, 1990) (TREF) with additional light atoms found by Fourier methods. Hydrogen atoms were added at calculated positions and refined using a riding model with freely rotating methyl groups. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl hydrogen atoms) times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached. The absolute structure of the individual crystal chosen was checked by refinement of a delta-f" multiplier. Absolute structure parameter x = 0.004(10). R1[for 6243 reflections with I>2sigma(I)] = 0.0393, wR2 = 0.0997. Data / restraints / parameters 6321/ 0/ 373. Largest difference Fourier peak and hole 2.655 and -0.744 e.Å⁻³.

**For both structures:**

Refinement used SHELXL 97 (Sheldrick, 1997). Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and the remaining bond lengths and angles. The Oxford Diffraction Gemini XRD system was obtained through the Science City Advanced Materials project: Creating and Characterising Next Generation Advanced Materials, with support from Advantage West Midlands (AWM) and part funded by the European Regional Development Fund (ERDF)

**References (both structures).**

For relevant information for the SHELXTL suite of programmes used to solve, refine and produce the files for this structure, please refer to "A Short History of Shelx, G. M. Sheldrick, Acta Cryst. 2008, 64, 112-122". Use Mercury (Free from CCDC at www.ccdc.cam.ac.uk/products/mercury) to view the structure.
1H and 13C-NMR Spectra.

$^1$H-NMR of (ethyl benzoate)ruthenium(II) chloride dimer.

$^{13}$C-NMR of (ethyl benzoate)ruthenium(II) chloride dimer.
$^1$H-NMR of $N$-[[1(R),2(R)]-1,2-Diphenyl-2-(3-phenylpropylamino)ethyl]-4-methylbenzenesulfonamide 6a.

$^{13}$C-NMR of $N$-[[1(R),2(R)]-1,2-Diphenyl-2-(3-phenylpropylamino)ethyl]-4-methylbenzenesulfonamide 6a.
$^1$H-NMR of \(N\-[(1R,2R\)-1,2-Diphenyl-2\-{(3-phenylpropylamino)ethyl}\]-4-methylbenzenesulfonamide\) ruthenium chloride 2 (n=1).
$^1$H-NMR of $N$-$\{(1R,2R)$-$2$-$[3$-$(4$-\text{Methoxyphenyl}$)propylamino]$-$1,2$-$diphenylethyl]$-$4$-$methylbenzenesulfonamide 6b.

$^{13}$C-NMR of $N$-$\{(1R,2R)$-$2$-$[3$-$(4$-\text{Methoxyphenyl}$)propylamino]$-$1,2$-$diphenylethyl]$-$4$-$methylbenzenesulfonamide 6b.
$^1$H-NMR of {N-[(1R,2R)-2-[3-(4-Methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride 4.

$^{13}$C-NMR of {N-[(1R,2R)-2-[3-(4-Methoxyphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride 4.
$^1$H-NMR of $N$-{(1$R$,2$R$)-2-[3-(3,5-Dimethoxyphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6c.

$^{13}$C-NMR of $N$-{(1$R$,2$R$)-2-[3-(3,5-Dimethoxyphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6c.
$^1$H-NMR of \( N\cdot[(1R,2R)-2\cdot[3\cdot3,5\text{-Dimethoxyphenyl}]\text{propylamino}]\cdot1,2\cdot\text{diphenylethyl}]\cdot4\cdot\text{methylbenzenesulfonamide} \) ruthenium chloride 9.

$^{13}$C-NMR of \( N\cdot[(1R,2R)-2\cdot[3\cdot3,5\text{-Dimethoxyphenyl}]\text{propylamino}]\cdot1,2\cdot\text{diphenylethyl}]\cdot4\cdot\text{methylbenzenesulfonamide} \) ruthenium chloride 9.
$^1$H-NMR of $N'$-{(1R,2R)-2-[3-(Biphenyl-4-yl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6d.

$^{13}$C-NMR of $N'$-{(1R,2R)-2-[3-(Biphenyl-4-yl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6d.
$^1$H-NMR of $\{N-[(1R,2R)-2-[3-(biphenyl-4-yl)-propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide\}$ ruthenium chloride 10.

$^{13}$C-NMR of $\{N-[(1R,2R)-2-[3-(biphenyl-4-yl)-propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide\}$ ruthenium chloride 10.
$^1$H-NMR of $N$-{{1$R$,2$R$}-2-[3-(4-isopropylphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6e.

$^{13}$C-NMR of $N$-{{1$R$,2$R$}-2-[3-(4-isopropylphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6e.
$^1$H-NMR of \( N-[(1R,2R)-2-[3-(4-isopropylphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide \) ruthenium chloride 11.

$^{13}$C-NMR of \( N-[(1R,2R)-2-[3-(4-isopropylphenyl)propylamino]-1,2-diphenylethyl]-4-methylbenzenesulfonamide \) ruthenium chloride 11.
$^1$H-NMR of $N$-{$(1R,2R)$-2-[3-(4-tert-butylphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6f.

$^{13}$C-NMR of $N$-{$(1R,2R)$-2-[3-(4-tert-butylphenyl)propylamino]-1,2-diphenylethyl}-4-methylbenzenesulfonamide 6f.
$^1$H-NMR of \( N-[(1R,2R)-2-[3-(4$-\text{tert-butylphenyl)propylamino]-1,2$-$\text{diphenylethyl}-4$-$\text{methylbenzenesulfonamide} \) ruthenium chloride 12.

$^{13}$C-NMR of \( N-[(1R,2R)-2-[3-(4$-\text{tert-butylphenyl)propylamino]-1,2$-$\text{diphenylethyl}-4$-$\text{methylbenzenesulfonamide} \) ruthenium chloride 12.
$^1$H-NMR of complex 5 for intramolecular reaction.

$^{13}$C-NMR of complex 5 for intramolecular reaction.
Chiral GC and HPLC data.

Reduction of 13; Racemic 1-phenylethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 110 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of acetophenone 13 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 110 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 13; Racemic 1-phenylethanol: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.

| Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] |
|-------------------|-------------|-------------|----------|------------|-----------|
| 1                 | 10.140      | 19.711      | 4.453    | 4.0        | 11.5      | 0.07      |
| 2                 | 15.423      | 238.862     | 18.737   | 48.4       | 48.2      | 0.20      |
| 3                 | 16.407      | 230.101     | 12.090   | 47.0       | 40.4      | 0.23      |
| Total             | 493.674     | 38.880      | 100.0    | 100.0      |           |           |

APH of acetophenone 13 using 4-methoxy catalyst 4: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.

| Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] |
|-------------------|-------------|-------------|----------|------------|-----------|
| 1                 | 9.663       | 1.253       | 0.316    | 0.1        | 0.6       | 0.06      |
| 2                 | 14.270      | 1225.604    | 51.317   | 96.9       | 95.5      | 0.38      |
| 3                 | 15.763      | 37.968      | 2.092    | 3.0        | 3.0       | 0.28      |
| Total             | 1264.630    | 53.725      | 100.0    | 100.0      |           |           |
Reduction of 14; Racemic 1-phenyl propanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 115 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of propiophenone 14 using 4-methoxy catalyst 4: GC analysis CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 115 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 14; Racemic 1-phenyl propanol: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15 psi H₂, det = FID 220°C, inj = 220°C.

APH of propiophenone 14 using 4-methoxy catalyst 4: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15 psi H₂, det = FID 220°C, inj = 220°C.
Reduction of 15; Racemic 1-(2'-methoxyphenyl)ethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 2'-methoxy-acetophenone 15 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 16; Racemic 1-(2-furyl)ethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 70 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 1-acetylfuran 16 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 70 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 17; Racemic 1-phenyl-1,2-ethanediol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 140 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 2-hydroxyacetophenone 17 using 4-Methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 140 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas
Reduction of 17: Racemic 1-phenyl-1,2-ethanediol: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 155°C, P = 18 psi He, det = FID 220°C, inj = 220°C.

APH of 2-hydroxy acetophenone 17 using 4-methoxy catalyst 4: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 155°C, P = 18 psi He, det = FID 220°C, inj = 220°C.
Reduction of 18; Racemic 1-phenyl-2-chloroethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 2-chloro acetophenone 18 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 19; Racemic 3-hydroxy-3-phenylpropionitrile: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of benzoylacetonitrile 19 using catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
**Reduction of 20; Racemic 1-(1-naphthyl)ethanol:** GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

**ATH of 1-acetonaphthone 20 using catalyst 4:** GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 21; Racemic 1-(2-naphthyl)ethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 2-acetonaphthone 21 using catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 150 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
Reduction of 22; Racemic 4-chromanol: HPLC analysis on ChiralPak IB Column: 0.46 cm x 25 cm, hexane:IPA 95:0.50, 1.0mL/min, 210 nM, 28°C.

ATH of 4-chromanone 22 using 4-methoxy catalyst 4: HPLC analysis on ChiralPak IB Column: 0.46 cm x 25 cm, hexane:IPA 95:0.50, 1.0mL/min, 210 nM, 28°C.
Reduction of 22; Racemic 4-chromanol : HPLC analysis on IB column, 0.46 x 25 cm, 1 mL/min, 95:5 Hexane:2-propanol.

| Reten. Time | Area [mV.s] | Height [mV] | Area [%] | Height [%] | WOS [min] | Compound Name |
|-------------|-------------|-------------|----------|------------|-----------|---------------|
| 1           | 8.928       | 1422.072    | 46.6     | 42.4       | 0.16      |               |
| 2           | 9.044       | 1484.376    | 50.0     | 47.5       | 0.18      |               |
| Total       | 2966.455    | 291.998     | 100.0    | 100.0      |           |               |

APH of 4-chromanone 22 using 4-methoxy catalyst 4: HPLC analysis on IB column, 0.46 x 25 cm, 1 mL/min, 95:5 Hexane:2-propanol.

| Reten. Time | Area [mV.s] | Height [mV] | Area [%] | Height [%] | WOS [min] | Compound Name |
|-------------|-------------|-------------|----------|------------|-----------|---------------|
| 1           | 6.532       | 625.591     | 33.0     | 52.1       | 0.15      |               |
| 2           | 8.436       | 2.349       | 0.1      | 0.1        | 0.30      |               |
| 3           | 9.136       | 1270.957    | 66.9     | 47.8       | 0.34      |               |
| Total       | 1900.308    | 121.721     | 100.0    | 100.0      |           |               |
Reduction of 23; Racemic 1-tetralol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 120 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

ATH of 1-tetralone 23 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 120 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
APH of 1-tetralone 23 using 4-methoxy catalyst: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 120°C, P = 18 psi He, det = FID 220°C, inj = 220°C.

| Reten. Time (min) | Area [mV.s] | Height [mV] | Area [%] | Height [%] | WOS [min] | Compound Name |
|-------------------|-------------|-------------|----------|------------|-----------|---------------|
| 1                 | 24.660      | 0.436       | 0.035    | 0.4        | 0.15      |               |
| 2                 | 44.592      | 0.698       | 0.038    | 0.7        | 0.30      |               |
| 3                 | 45.616      | 97.413      | 1.072    | 90.0       | 1.43      |               |
| Total             | 98.547      | 1.145       | 100.0    | 100.0      |           |               |

Reduction of 24; Racemic 1-(4-cyanophenyl)ethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25μm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

| Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | WOS [min] | Compound Name |
|-------------------|-------------|-------------|----------|------------|-----------|---------------|
| 1                 | 3646.824    | 986.287     | 97.3     | 99.5       | 0.06      |               |
| 2                 | 51.171      | 2.553       | 1.4      | 0.3        | 0.32      |               |
| 3                 | 59.843      | 2.067       | 1.4      | 0.2        | 0.40      |               |
| Total             | 3748.838    | 990.906     | 100.0    | 100.0      |           |               |
ATH of 4-acetylbenzonitrile 24 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 160 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

Reduction of 25; Racemic 1-(2-hydroxyphenyl)ethanol: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 170 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.
ATH of 2-hydroxy acetophenone 25 using 4-methoxy catalyst 4: GC analysis on CP-Chirasil-DEX CB 25m x 0.25mm x 0.25µm, Oven Temp = 170 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 18 psi, He gas.

Reduction of 26; Racemic 1-cyclohexylethanol : GC analysis of acetate derivative on Chrompac cyclodextrin-β-236M-19 50m x 0.25mm x 0.25µm, Oven Temp = 115 °C, Det .Temp = 220 °C, Inj. Temp = 220 °C, P = 15 psi, H₂ gas.
ATH of cyclohexyl methyl ketone 26 using 3,5-dimethoxy catalyst 9: GC analysis of acetate derivative on Chrompac cyclodextrin-β-236M-19 50m x 0.25mm x 0.25µm, Oven Temp = 115°C, Det.Temp = 220°C, Inj. Temp = 220°C, P = 15 psi, H₂ gas.

Reduction of 26; Racemic cyclohexyl ethanol: GC analysis of acetate derivative on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 µm, T = 100°C, P = 18psi He, det = TCD 100°C, inj = 220°C.
APH of cyclohexyl methyl ketone 26 using 3,5-dimethoxy catalyst 9: GC analysis of acetate derivative on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 100°C, P = 18psi He, det = TCD 100°C, inj = 220°C.

| Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] | Compound Name |
|-------------------|-------------|-------------|----------|------------|-----------|--------------|
| 1                 | 9.064       | 1.034       | 0.080    | 52.6       | 0.21      |              |
| 2                 | 14.068      | 0.846       | 0.057    | 43.0       | 0.24      |              |
| 3                 | 18.580      | 0.687       | 0.000    | 4.4        | 0.15      |              |
| Total             |             |             | 1.967    | 0.146      | 100.0     |              |

Reduction of 27; Racemic 2,3-dihydro-1H-inden-1-ol : GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 100°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.

| Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] |
|-------------------|-------------|-------------|----------|------------|-----------|
| 1                 | 79.577      | 115.661     | 1.478    | 44.7       | 1.38      |
| 2                 | 81.663      | 143.012     | 1.317    | 55.3       | 1.67      |
| Total             |             |             | 258.674  | 2.796      | 100.0     | 100.0     |
APH of 1-indanone 27 using 4-methoxy catalyst 4: GC analysis on Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 100°C, P = 15 psi H₂, det = FID 220°C, inj = 220°C.

Reduction of 28; Racemic 1-(4'-methoxyphenyl)ethanol: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 130°C, P = 18 psi He, det = FID 220°C, inj = 220°C.
APH of 4’-methoxy acetophenone 28 using 4-methoxy catalyst 4: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 130°C, P = 18psi He, det = FID 220°C, inj = 220°C.

Reduction of 29; Racemic 1-(4’-trifluoromethylphenyl)ethanol: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 130°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.
APH of 4’-trifluoromethyl-acetophenone 29 using 4-methoxy catalyst 4: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 130°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.

Reduction of 30; Racemic 1-(3’,5’-Bis(trifluoromethyl)phenyl)ethanol Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 120°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.
APH of 3',5'-bis(trifluoromethyl)-acetophenone 30 using 4-methoxy catalyst 4: GC analysis on Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 120°C, P = 15psi H₂, det = FID 220°C, inj = 220°C.

Reduction of 31; Racemic 1-phenyl-2,2-dimethyl-1-propanol: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 125°C, P = 18psi He, det = TCD 100°C, inj = 220°C.
APH of 2,2-dimethyl-propiophenone 31 using 4-methoxy catalyst 4: GC analysis on CP-ChiraSil-DEX CB 25 m x 0.25 mm x 0.25 μm, T = 125°C, P = 18 psi He, det = TCD 100°C, inj = 220°C.

Reduction of 32; Racemic 2-phenoxy-1-phenylethanol: HPLC analysis on IB column, 0.46 x 25 cm, 0.7 mL/min, 95:5 hexane:2-propanol.
APH of 2-phenoxy acetophenone 32 using 4-methoxy catalyst 4: HPLA analysis on IB column, 0.46 x 25 cm, 0.7 mL/min, 95:5 hexane:2-propanol.

Reduction of 33; Racemic Salsolidine: GC analysis on Chrompak cyclodextrin-β-236M-19 50m x 0.25mm x 0.25µm, Oven Temp = 170 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 15 psi, H₂ gas.
ATH of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline 33 using 3.5-dimethoxy catalyst 9: GC analysis on Chropak cyclodextrin-β-236M-19 50m x 0.25mm x 0.25µm, Oven Temp = 170 °C, Det. Temp = 220 °C, Inj. Temp = 220 °C, P = 15 psi, H₂ gas.