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José E. D. Martins and Martin Wills
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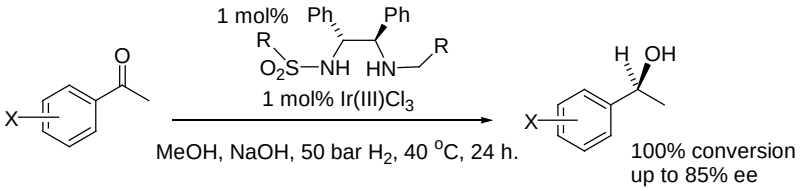

Pergamon

TETRAHEDRON

Ir(III) complexes of diamine ligands for asymmetric ketone hydrogenation

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Abstract—The use of a combination of $IrCl_3$ with a series of ligands derived from the C2-symmetric diamine diphenylethanediamine (DPEN) forms a catalyst capable of the asymmetric hydrogenation of ketones in up to 85% ee.

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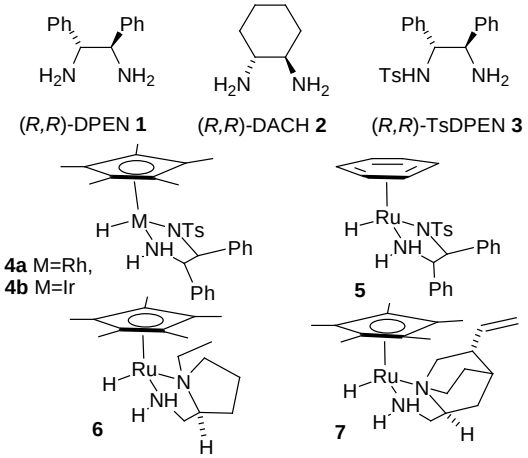
Introduction

Relatively few organometallic complexes derived from amine ligands have been reported to be effective at the control of asymmetric hydrogenation reactions,[1-10] particularly in comparison to the large numbers of diphosphine[11,12] and mixed amine/phosphine[13,14] ligands which have been reported.

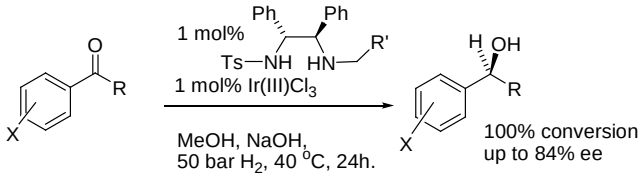
In principle, amine-based ligands possess a potential advantage over phosphorus because they are relatively simple to prepare and less prone to decomposition reactions and oxidation. Of the diamine-containing systems which have been reported, a number have been applied to the catalysis of the reduction of ketones in high ee. In most cases, the complexes are of ruthenium, rhodium or iridium metals, whilst the ligands are frequently derived from the C2-symmetric 1,2-diphenylethylene-1,2-diamine **1** (*R,R*- or *S,S*-DPEN) or 1,2-diaminocyclohexane **2** (*R,R*- or *S,S*-DACH).

An iridium-diamine complex has been prepared in situ through the combination of *N,N'*-dimethyl-DPEN (DiMeDPEN) with $[Ir(COD)_2]BF_4$. This gave products in up to 80% ee in hydrogenations of α-keto esters and 68% ee for acetophenone.[1b.c] Water soluble DiMeDPEN complexes of Ir(I) salts gave better results than Ru or Rh and 84% ee for the reduction of PhCOtBu.[2] Complexes of *R,R*-DACH **2** and DiMeDPEN with $[Ir(COD)_2]BF_4$ have been used in the hydrogenation of α-keto esters.[1a] (up to 72% and 31% ee respectively). The combination of (*R,R*)-*N*-tosyl-DPEN **3** (*R,R*-TsDPEN) and $[Ir(cod)Cl]_2$ in MeOH/toluene has been reported to be effective in the reduction of β-keto esters.[3]



A number of amine-containing isolated complexes for ketone hydrogenation have been reported.[5-10] The pentamethylcyclopentadienyl rhodium (III) and iridium (III) catalysts **4a** and **4b** respectively, derived from TsDPEN **3** have given excellent results.[5] A closely related Ru(II)/arene complex **5** has also been reported to be highly effective.[6] Ruthenium complexes **6** and **7** have also proved to be very enantioselective catalysts in ketone hydrogenation.[7,8]

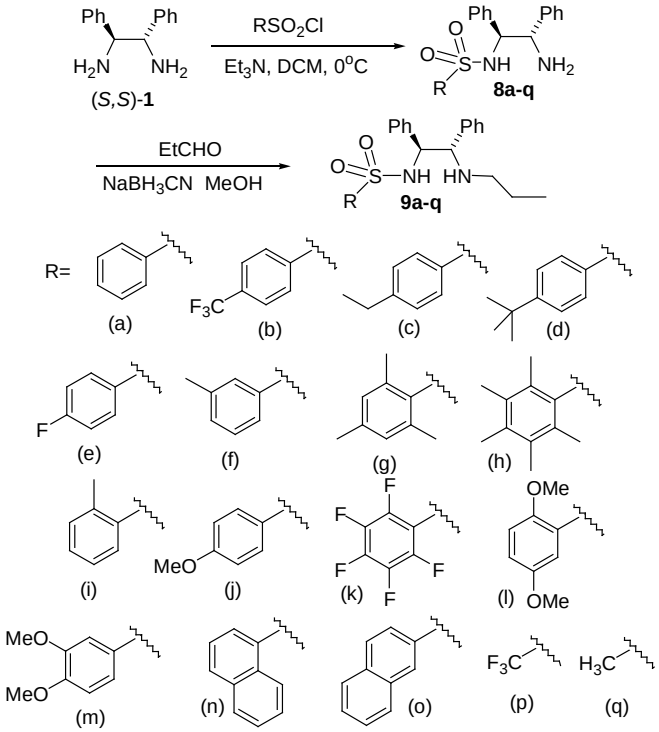
In recently reported preliminary studies, we reported that N'-alkylated derivatives of TsDPEN **3** can be combined with $IrCl_3$ to form a competent catalyst for the reduction of acetophenone derivatives in ees of up to 84% (Scheme 1).[15] Although the activity of these catalysts is lower than that of phosphine-derived catalysts, their ease of preparation from stable materials and a simple Ir(III) complex makes them attractive as a simple system for the reduction of selected ketones. The use of iridium was also shown to be important; ruthenium or rhodium complexes formed catalysts which also reduced the arene ring of the substrate. In this paper, we report the synthesis and screening of a diverse series of TsDPEN derived ligands in ketone hydrogenation.



Scheme 1: Asymmetric ketone reduction using a combination of $IrCl_3$ and a diamine ligand.[15]

Results and Discussion

In previous studies,[15] we had examined only the tosylated derivatives of DPEN **1**. In order to understand the importance of the structure of the sulfonamide part, a series of sulfonamides were selected for further studies.



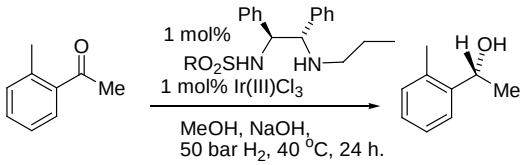
Scheme 2: Preparation of ligands **9a- 9q**.

The ligands were prepared (Scheme 2) by the reaction of (*S,S*)-DPEN **1** with the appropriate sulfonylhalide in DCM

at 0°C, using triethylamine as a base, to give sulfonamides **8a-8q**. Reductive amination of each with propanal resulted in formation of ligands **9a-9q** in good isolated yields. The incorporation of a N'-propyl group was selected as this had given the highest selectivity when used in the tosylated catalyst series.[15] In each case the (*S*,*S*) enantiomers of diamines were prepared.

Each of the ligands was employed in the asymmetric hydrogenation of 2-methylacetophenone, using the conditions previously reported for the reduction.[15] The results are summarized in Table 1. 2-Methylacetophenone was selected for study because it had given particularly promising results in preliminary results, and because ortho-substituted substrates can be challenging substrates to reduce in high ee.[16]

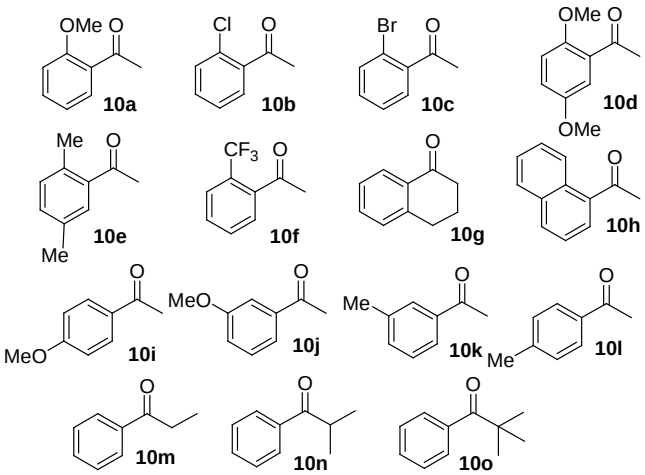
Table 1: Asymmetric hydrogenation of 2-methylacetophenone using $IrCl_3$ with diamine ligands **9a-9q**.[a]



Entry	Ligand	Conv./%	Ee/% (*R*/*S*)
1	**9a**	100	79 (*R*) 90:10
2	**9b**	100	55 (*R*)
3	**9c**	100	79 (*R*) 90:10
4	**9d**	100	81 (*R*) 90:10
5	**9e**	99	62 (*R*)
6	**9f**	100	82 (*R*)
7	**9g**	100	40 (*R*)
8	**9h**	100	55 (*R*)
9	**9i**	100	73 (*R*)
10	**9j**	100	77 (*R*)
11	**9k**	93	65 (*R*)
12	**9l**	100	81 (*R*)
13	**9m**	100	80 (*R*)
14	**9n**	100	76 (*R*)
15	**9o**	100	83 (*R*)
16	**9p**	29	4 (*R*)
17	**9q**	81	61 (*R*)

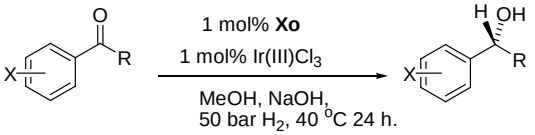
a. Conditions: 1M 2-methylacetophenone in methanol (1 mL); 1% catalyst, 50 bar hydrogen, NaOH:catalyst = 30:1, 40 °C, 24 h.

Of the ligands tested, the best results were obtained using those with relatively unhindered aromatic rings containing electron withdrawing groups (entries 3, 4, 6, 12, 13, 15). With the exception of ligand **9l**, diamines containing substituents at the ortho-position(s) gave lower asymmetric inductions (entries 7-9), and those with two ortho-substituents were particularly poor, possibly for steric reasons. Electron-withdrawing groups on the aromatic ring provided a reduction in the activity and the enantioselectivity, whilst both non-aromatic rings gave incomplete conversions and correspondingly reduced ees. Of the ligands examined, the best was the 2-naphthalene sulfonyl derivative **9o**, therefore this was selected for further tests on a series of ketones **10a-10o** (Table 2).



The enantioselectivities of the reductions using ligand **9o** are reasonably similar to those obtained with the N-tosyl derivative, although in some cases a marginally improved result was obtained (e.g. entries 2, 3, 5, 6, 8, 10, 14). In the case of tetralone **10g** and 2,5-dimethoxyacetophenone **10d**, ligand **9o** was somewhat inferior.

Table 2: Asymmetric hydrogenation of ketones using $IrCl_3$ with diamine ligand **9o**, **9d** and **9f**.[a]



Entry	Ligand	Ketone	Conv./%	Ee/% (*R*/*S*)
1	**9o**	**10a**	100	71 (*R*)
2	**9o**	**10b**	100	70 (*R*)
3	**9o**	**10c**	99	54 (*R*)
4	**9o**	**10d**	100	67 (*R*)
5	**9o**	**10e**	100	85 (*R*)
6	**9o**	**10f**	100	75 (*R*)
7	**9o**	**10g**	100	52 (*R*)
8	**9o**	**10h**	100	72 (*R*)
9	**9o**	**10i**	100	67 (*R*)
10	**9o**	**10j**	100	61 (*R*)
11	**9o**	**10k**	100	65 (*R*)
12	**9o**	**10l**	100	61 (*R*)
13	**9o**	**10m**	100	62 (*R*)
14	**9o**	**10n**	100	71 (*R*)
15	**9o**	**10o**	100	72 (*R*)
16	**9d**	**10e**	100	84 (*R*)
17	**9d**	**10d**	100	71 (*R*)
18	**9d**	**10g**	90	45 (*R*)
19	**9f**	**10e**	98	80 (*R*)
20	**9f**	**10d**	100	60 (*R*)
21	**9f**	**10g**	99	53 (*R*)

a. Conditions: 1M ketone in methanol (1 mL); 1% catalyst, 50 bar hydrogen, NaOH:catalyst = 30:1, 40 °C, 24 h.

Some of the best results were obtained with relatively hindered ortho-substituted ketones (e.g. **10a, 10b, 10e** and **10f**). To complete this series of tests, ligands **9d** and **9f** were also tested against the more challenging ketones (also shown in Table 2). Competitive, but not sharply improved, results were obtained with these ligands.

Conclusions

In conclusion, a series of N'-alkyl–N-sulphonylated derivatives of the readily available and inexpensive diamine DPEN have been prepared and tested in asymmetric ketone hydrogenation reactions. In some cases, notably those of relatively sterically congested ketones (ortho-substituted arenas, tBu-substituted), the ees are high. Whilst not competitive with the best hydrogenation systems in terms of activity and ee, the simplicity of this hydrogenation system (i.e. it is compatible with the simple salt $IrCl_3$) may in some cases provide an attractive alternative. The novel ligands and intermediates to them may find application in other asymmetric catalytic processes, including asymmetric transfer hydrogenation reactions.[17]

Experimental section

General experimental details, and the procedure for the hydrogenation reaction, have been described in a previous publication.[15]

General procedure for synthesis of sulfonated DPEN derivatives: Compounds **8a – 8q** were obtained by reaction between (*S,S*)-DPEN **1** and the correspondent sulfonylchloride (1:1) in DCM and Et_3N overnight. With the exception of **8p** all reactions were performed at 0^oC. Although some of the monotosylated ligands have been described in the literature, only a few references contain experimental data, hence most were fully characterized. Below is a representative example; the other ligands are described in the Supporting Information.

Naphthalene-2-sulfonic acid (2-amino-1,2-diphenyl-ethyl)-amide 8o: (*S,S*)-DPEN **1** (0.3g, 1.4 mmol) was dissolved in DCM (20 cm^3) and cooled to 0^oC, then Et_3N (0.21 cm^3, 1.5 mmol) was added followed by a solution of 2-Naphthalenesulfonyl chloride (0.31 g, 1.4 mmol) in DCM (5 cm^3) . The system was allowed to stay at rt and it was stirred overnight. The mixture was washed with water (10 cm^3) and then the organic phase was separated, dried over dried $MgSO_4$ and evaporated under reduced pressure to afford the crude product which was purified by silica gel chromatography (0 → 5 % v/v Methanol/DCM) to afford **8o** as a white solid (0.47 g, 1.1 mmol, 84%). mp 199 – 201^oC; $[\alpha]_D^{27}$ = – 34 (*c* 0.55, CH_3OH); ν_{max}(neat)/cm^{-1}: 3386, 3330, 3059, 3029, 1589, 1495, 1455, 1417, 1311, 1151, 1129, 875, 853, 750, 696, 662. δ_H (300 MHz; $CDCl_3$)/ppm: 8.00 – 6.90 (17H, m, Ar-H), 6.20 (1H, br s, NH), 4.46 (1H, d, *J* 5.0, $PhCHNHSO_2R$), 4.13 (1H, d, *J* 5.0, $PhCHNH_2$), 1.44 (2H, br s, NH_2). δ_C (75 MHz; $CDCl_3$)/ppm: 141.1, 139.1, 136.8, 134.4, 131.8, 129.1, 128.8, 128.3, 128.2, 128.1, 128.0, 127.6, 127.4, 126.8, 126.2 (Ar-C), 63.2 (CH), 60.3 (CH). HRMS calcd for $C_{24}H_{23}N_2O_2S$ $[M + H]^+$ 403.1472, found 403.1488.

General procedure for N'-propyl-N-sulphonylDPEN derivatives: The N-propyl derivatives **9a – 9q** were obtained by reductive amination of the mono sulfonylated derivative **8a – 8q** with propanal. Below is a representative example; the other ligands are described in the Supporting Information.

Naphthalene-2-sulfonic acid (1,2-diphenyl-2-propylamino-ethyl)-amide 9o: To a stirred solution of **8o** (0.20 g, 0.5 mmol) and molecular sieves (0.7 g) in dried methanol (10 cm^3), was added propanal (0.035 cm^3, 0.50 mmol) followed by 2 drops of glacial acetic acid. The reaction was followed by TLC until the imine was formed (3 hours) and then sodium cyanoborohydride (0.13 g, 2.0 mmol) was added and the reaction left to stir overnight at rt. The molecular sieves were filtered through filter paper and the solution was concentrated under reduced pressure. The residue was dissolved in chloroform (30 mL), washed with saturated $NaHCO_3$ solution (20 mL) and then dried over anhydrous $MgSO_4$. The solvent was removed to give a crude product which was purified by silica gel column chromatography (0 → 30 % v/v ethyl acetate/hexane) to afford **9o** as a white solid (0.12 g, 0.27 mmol, 57 %). mp 148 – 151^oC. $[\alpha]_D^{27}$ = – 4 (*c* 0.37, CH_3OH); ν_{max}(neat)/cm^{-1}: 3291, 3058, 2953, 2928, 2807, 2325, 1593, 1494, 1453, 1330, 1158, 1149, 1072, 1053, 1021, 8914, 839, 744, 697, 665. δ_H (300 MHz; $CDCl_3$)/ppm: 8.00 – 6.85 (17H, m, Ar-H), 4.32 (1H, d, *J* 8.0, $PhCHNHSO_2R$), 3.61 (1H, d, *J* 8.0, PhCHNHpropyl), 2.30 (2H, m, CH_2), 1.35 (3H, m, CH_2 and NH), 0.81 (3H, t, *J* 7.3, CH_3). δ_C (75 MHz; $CDCl_3$)/ppm: 139.2, 137.9, 136.8, 134.4, 131.8, 129.1, 128.7, 128.5, 128.3, 128.1, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2, 126.9, 122.3 (Ar-C), 67.6 (CH), 63.1 (CH), 48.9 (CH_2), 23.1 (CH_2), 11.5 (CH_3). HRMS calcd for $C_{27}H_{29}N_2O_2S$ $[M + H]^+$ 445.1940, found 445.1944.

Analysis of reduction products:

1-(2-methylphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 150 ^0C, P = 15 psi, ketone 10.8 min, R isomer 15.6 min., S isomer 16.3 min.); $[\alpha]_D^{32}$ = + 68.5 (c 0.54 in $CHCl_3$) 83% ee (R) (lit.[18] $[\alpha]_D^{29}$ –72.1 (c 0.53, $CHCl_3$) for 91% ee (S)). δ_H (300 MHz; $CDCl_3$)/ppm: 7.49 – 7.06 (4H, m, Ar-H), 5.05 (1H, q, *J* 6.4, PHCHOH), 2.30 (3H, s, $ArCH_3$), 1.41 (3H, d, *J* 6.4, CH_3). δ_C (75 MHz; $CDCl_3$)/ppm: 143.9, 134.2, 130.3, 127.1, 126.3, 124.5 (Ar-C), 66.7, (CH), 23.9 (CH_3), 18.9 (CH_3).

1-(2'-Methoxyphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 140 ^0C, P = 15 psi, ketone 31.3 min, S isomer 37.5 min., R isomer 39.0 min.); $[\alpha]_D^{33}$ = + 37 (c 0.67 in toluene) 71% ee (R) (lit.[19] $[\alpha]_D^{23}$ -63.0 (c 1.10 in toluene) > 99% ee (S)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.34 (1H, dd, *J* 7.4 and 1.6, Ar-H),

7.25 (1H, td, *J* 7.8 and 1.8, Ar-H), 6.96 (1H, t, *J* 7.4, Ar-H), 6.88 (1H, d, *J* 8.3, Ar-H), 5.09 (1H, q, *J* 6.5, $PhCHCH_3$), 3.86 (3H, s, OCH_3), 2.72 (1H, br s, OH), 1.50 (3H, d, *J* 6.5, CH_3); δ_C (100.6 MHz; $CDCl_3$)/ppm: 156.6 (next to OCH_3) 133.4, 128.3, 126.1, 120.8, 110.4 (Ar-C), 66.6 (CH), 55.3 (OCH_3), 22.9 (CH_3).

1-(2'-Chlorophenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 150 ^{0}C, P = 15 psi, ketone 13.7 min, R isomer 20.7 min., S isomer 22.4 min.); $[\alpha]_D^{33}$ = + 44.5 (c 0.7 in $CHCl_3$) 70% ee (R) (lit.[20] $[\alpha]_D^{20}$ +41 (c 1.0 in $CHCl_3$) 67% ee (R)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.56 (1H, dd, *J* 7.8 and 1.8, Ar-H), 7.32-7.25 (2H, m, Ar-H), 7.18 (1H, td, *J* 7.7 and 1.8, Ar-H), 5.26 (1H, dq, *J* 6.3 and 2.8, $PhCHCH_3$), 2.33 (1H, br d, *J* 3.0, OH), 1.46 (3H, d, *J* 6.5, CH_3); δ_C (100.6 MHz; $CDCl_3$)/ppm: 143.1, 131.6, 129.4, 128.4, 127.2, 126.4 (Ar-C), 66.9 (CH),23.5 (CH_3).

1-(2'-Bromophenyl)ethanol: Enantiomeric excess and conversion by GC analysis through its acetate derivative (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 160 ^{0}C, P = 15 psi, Ketone 15.4 min., R isomer 21.8 min., S isomer 23.6 min.); $[\alpha]_D^{33}$ + 27 (c 0.6 in $CHCl_3$) 54 % ee (R) (lit.[21] $[\alpha]_D^{20}$ = –39.5 (c= 0.96, $CHCl_3$) 81 % ee (S); δ_H (300 MHz; $CDCl_3$)/ppm: 7.59 – 7.06 (4H, m, Ar-H), 5.20 (1H, q, *J* 6.3, CH α-OH), 1.44 (3H, d, *J* 6.3, CH_3). δ_C (75 MHz; $CDCl_3$)/ppm: 144.0, 132.0, 128.1, 127.2, 126.0, 121.0 (Ar-C), 68.5 (CH), 22.9 (CH_3).

1-(2,5-dimethoxyphenyl)ethanol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 155 ^{0}C, P = 15 psi, ketone 40.7 min., R isomer 49.6 min., S isomer 51.6 min.); $[\alpha]_D^{33}$ + 18.6 (c 0.5 in $CHCl_3$) 71% ee (R) (lit.[22] $[\alpha]_D^{25}$ = +23.8 (c 2.6 in $CHCl_3$) 91% ee (R)); δ_H (300 MHz; $CDCl_3$/ppm: 6.96 – 6.71 (3H, m, Ar-H), 5.05 (1H, m, CH α-OH), 3.81 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 1.48 (3H, d, *J* 6.5, CH_3). δ_C (75 MHz; $CDCl_3$/ppm: 153.7, 150.6, 134.6, 112.4, 112.2, 111.3 (Ar-C), 66.4 (CH), 55.8 (OCH_3), 55.7 (OCH_3), 22.9 (CH_3).

1-(2-Trifluoromethylphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 120 ^{0}C, P = 15 psi, ketone 18.1 min, R isomer 31.8 min., S isomer 34.1 min.). $[\alpha]_D^{33}$ = + 33 (c 0.16 in CH_3OH) 75 % ee (R) (lit.[19] $[\alpha]_D^{22}$ = –45.5 (c= 0.66, CH_3OH) 97 % ee (S); δ_H (400 MHz; $CDCl_3$)/ppm: 7.84 (1H, d, *J* 7.8, ArH), 7.64-7.58 (2H, m, ArH), 7.38 (1H, t, *J* 7.7, ArH), 5.34 (1H, q, *J* 6.3, $CH(OH)CH_3$), 1.98 (1H, br s, OH), 1.50 (3H, d, *J* 6.3, CH_3); δ_C (100.6MHz; $CDCl_3$)/ppm: 145.0 (F_3C), 132.4, 127.4, 127.1, 125.7, 125.4, 125.3 (Ar-C), 65.7 (CH), 25.5 (CH_3).

1-(1'-Naphthyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 170 ^{0}C, P = 10 psi, ketone 49.1 min, S isomer 70.6 min., R isomer 72.8 min.); $[\alpha]_D^{33}$ + 65 (c 0.8 in Et_2O) 72% ee (R) (lit.[23] $[\alpha]_D^{28}$ +77.2 (c 0.67 in Et_2O) 99% ee (R)); δ_H (300 MHz; $CDCl_3$)/ppm: 8.09 (1H, d, *J* 8.0, Ar-H), 7.87-7.83 (1H, m, Ar-H), 7.76 (1H, d, *J* 8.3, Ar-H), 7.65 (1H, d, *J* 7.0, Ar-H), 7.53-7.43 (3H, m, Ar-H), 5.64 (1H, q, *J* 6.4, $CH(OH)CH_3$), 2.05 (1H, br s, OH), 1.65 (3H, d, *J* 6.5, CH_3); δ_C (75 MHz; $CDCl_3$)/ppm: 141.5, 133.8, 130.3, 128.9, 127.9, 126.0, 125.6, 125.5, 123.2, 122.1 (Ar-C), 67.1 (CH), 24.4 (CH_3).

1-phenyl-2,2-dimethyl-1-propanol: Enantiomeric excess and conversion determined by GC analysis through its acetate derivative (Chrompac cyclodextrin-β- 236M-19 50m, gas He, T = 125 ^{0}C, P = 10 psi, ketone 39.6 min, R isomer (acetate) 59.7 min., S isomer (acetate) 58.2 min.); $[\alpha]_D^{33}$ + 28 (c 0.55 in acetone) 72% ee (R) (lit.[24] $[\alpha]_D^{20}$ – 30.3 (c 0.3 in acetone) 100% ee (S)); δ_H (300 MHz; $CDCl_3$)/ppm: 7.28 – 7.19 (5H, m, Ar-H), 4.33 (1H, s, PhCHOH), 0.88 (9H, s, $3CH_3$). δ_C (75 MHz; $CDCl_3$)/ppm: 141.5, 127.0, 126.9, 126.6 (Ar-C), 81.7 (CH), 35.0 (C), 25.3 ($3CH_3$).

1-Tetralol: Enantiomeric excess and conversion determined by GC analysis through its acetate derivative (Chrompac cyclodextrin-β- 236M-19 50m, gas He, T = 140 ^{0}C, P = 15 psi, ketone 47.2 min, R isomer (acetate) 62.9 min., S isomer (acetate) 64.2 min.); $[\alpha]_D^{35}$ – 15 (c 0.37 in $CHCl_3$) 53 % ee (R) (lit.[25] $[\alpha]_D^{27}$ –32.3 (c 1.00 in $CHCl_3$) 98% ee (R)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.43-7.38 (1H, m, Ar-H), 7.21- 7.15 (2H, m, Ar-H), 7.10-7.06 (1H, m, Ar-H), 4.74 (1H, br s, CHOH), 2.85-2.66 (2H, m, CH_2 ortho to CHOH), 2.00-1.70 (5H, m, 2 × CH_2 + OH); δ_C (100.6 MHz; $CDCl_3$)/ppm: 138.9, 137.1, 129.0, 128.7, 127.6, 126.2 (Ar-C), 68.1 (CH), 32.3 (CH_2), 29.3 (CH_2), 18.9 (CH_2).

1-(4'-Methoxyphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 130 ^{0}C, P = 15 psi, ketone 65.96 min, R isomer 71.8 min., S isomer 74.3 min.); $[\alpha]_D^{32}$ + 33.8 (c 0.54 in $CHCl_3$) 67 % ee (R) (lit.[25] $[\alpha]_D^{27}$ +32.3 (c 1.00 in $CHCl_3$) 90% ee (R)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.30-7.26 (2H, m, Ar-H), 6.89-6.85 (2H, m, Ar-H), 4.83 (1H, q, *J* 6.3, $PhCHCH_3$), 3.79 (3H, s, OCH_3), 2.02 (1H, br s, OH), 1.46 (3H, d, *J* 6.3, CH_3); δ_C (100.6 MHz; $CDCl_3$)/ppm: 159.0 (next to OCH_3), 138.1, 126.7, 113.9 (Ar-C), 70.0 (CH), 55.3 (OCH_3), 25.0 (CH_3).

1-(4-methylphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 125 ^{0}C, P = 15 psi, ketone 28.3 min, R isomer 35.2 min., S isomer 38.1 min.); $[\alpha]_D^{33}$ + 38 (c 0.72 in $CHCl_3$) 61% ee (R) (lit.[18] $[\alpha]_D^{26}$ –53.0 (c 0.55, $CHCl_3$) for 92% ee (S)). δ_H (300 MHz; $CDCl_3$)/ppm: 7.22 – 7.15 (2H, m, Ar-H), 7.12 – 7.06 (2H, m, Ar-H), 4.73 (1H, q, *J* 6.4, PHCHOH), 2.30 (3H, s, CH_3), 1.38 (3H, d, *J* 6.4). δ_C (75 MHz; $CDCl_3$)/ppm: 143.0, 136.9, 129.1, 125.4 (Ar-C), 70.0 (CH), 25.1 (CH_3), 21.1 (CH_3).

1-Phenylpropan-1-ol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 115 ^{0}C, P = 15 psi, ketone 29.3 min, R isomer 45.8 min., S isomer 47.9 min.); $[\alpha]_D^{33}$ + 33 (c 1 in $CHCl_3$) 62% ee (R) (lit.[26] $[\alpha]_D^{20}$ +47.0 (c 1.4 in

$CHCl_3$) 95% ee (R)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.36-7.24 (5H, m, Ar-H), 4.57 (1H, t, *J* 6.5,PhCH(OH)CH_2), 2.00 (1H, br s, OH), 1.86-1.68 (2H, m, CH_2), 0.90 (3H, t, *J* 7.4, CH_3); δ_C (100.6 MHz; $CDCl_3$)/ppm: 144.6, 128.4, 127.5, 126.0 (Ar-C), 76.0 (CH), 31.9 (CH_2), 10.2 (CH_3).

1-(3-methylphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 125 ^{0}C, P = 15 psi, ketone 26.1 min, R isomer 37.7 min., S isomer 38.8 min.); $[\alpha]_D^{33}$ + 34.6 (c 0.8 in $CHCl_3$) 65% ee (R) (lit.[18] $[\alpha]_D^{26}$ –42.6(c 0.62, $CHCl_3$) for 84% ee (S)). δ_H (300 MHz; $CDCl_3$)/ppm: 7.26 – 7.4 (4H, m, Ar-H), 4.80 (1H, q, *J* 6.4, PHCHOH), 2.34 (3H, s, CH_3), 1.44 (3H, d, *J* 6.4). δ_C (75 MHz; $CDCl_3$)/ppm: 145.8, 138.1, 128.4, 128.2, 126.1, 122.4 (Ar-C), 70.3 (CH), 25.1 (CH_3), 21.4 (CH_3).

1-(3'-Methoxyphenyl)ethanol: Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 140 ^{0}C, P = 15 psi, ketone 33.4 min, R isomer 48.8 min., S isomer 51.0 min.); $[\alpha]_D^{33}$ + 21.6 (c 0.74 in MeOH) 61 % ee (R) (lit.[19] $[\alpha]_D^{22}$ –34.9 (c 0.849 in MeOH) >99% ee (S)); δ_H (400 MHz; $CDCl_3$)/ppm: 7.26 (1H, dd, $J_1 = J_2$ 8.0, Ar-H), 6.96-6.92 (2H, m, Ar-H), 6.83-6.79 (1H, m, Ar-H), 4.86 (1H, q, *J* 6.4, CH(OH)CH_3), 3.81 (3H, s, ArOCH_3), 1.94 (1H, br s, OH), 1.48 (3H, d, *J* 6.5, CH_3); δ_C (100.6 MHz; $CDCl_3$)/ppm: 159.8 (ArC-OMe), 147.6, 129.6, 117.7, 112.9, 110.9 (Ar-C), 70.4 (CH), 55.2 (OCH_3), 25.2 (CH_3).

2-Methyl-1-phenylpropan-1-ol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 115 ^{0}C, P = 10 psi, ketone 45.8 min., R isomer 90.7 min., S isomer 92.1 min.); $[\alpha]_D^{33}$ = + 33 (c 0.47 in ether) 71% ee (R) (lit.[19] $[\alpha]_D^{25}$ –49.1 (c 0.85 in ether) 99% ee (S)); δ_H (400 MHz; $CDCl_3$/ppm: 7.37 – 7.22 (5H, m, Ar-H), 4.33 (1H, d, *J* 6.9, CH α-OH), 2.00 – 1.88 (1H, m, CH), 0.99 (3H, d, *J* 6.6, CH_3), 0.78 (3H, d, *J* 6.8, CH_3). δ_C (100.6 MHz; $CDCl_3$/ppm: 143.0, 127.5, 126.8, 125.9 (Ar-C), 79.4 (CH), 34.6 (CH), 18.3 (CH_3), 17.6 (CH_3).

1-(2,5-dimethylphenyl)ethanol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, gas He, T = 140 ^{0}C, P = 15 psi, ketone 21.8 min., R isomer 36.5 min., S isomer 39.9 min.); $[\alpha]_D^{33}$ = + 64 (c 0.5 in $CHCl_3$) 85 % ee (R) (lit.[15] $[\alpha]_D^{27}$ –61.7 (c 0.6 in $CHCl_3$) 83 % ee (S)). δ_H (300 MHz; $CDCl_3$/ppm: 7.32 – 6.92 (3H, m, Ar-H), 5.03 (1H, q, *J* 6.4, CH α-OH), 2.31 (3H, s, CH_3), 2.26 (3H, s, CH_3), 1.41 (3H, d, *J* 6.4, CH_3). δ_C (75 MHz; $CDCl_3$/ppm: 143.7, 135.8, 131.0, 130.3, 127.8, 125.1 (Ar-C), 66.7 (CH), 23.9 (CH_3), 21.1 (CH_3), 18.4 (CH_3).

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Supplementary Material

Procedures for preparation of, and characterization data for, ligands not described above, and ^{1}H and ^{13}C-NMR of all new compounds.

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Captions for schemes and figures:

Scheme 1: Asymmetric ketone reduction using a combination of $IrCl_3$ and a diamine ligand.[15]

Scheme 2: Preparation of ligands **9a- 9q**.

Table 1: Asymmetric hydrogenation of 2-methylacetophenone using $IrCl_3$ with diamine ligands **9a-9q**.[a]

Table 2: Asymmetric hydrogenation of ketones using $IrCl_3$ with diamine ligand **9o**, **9d** and **9f**.[a]