Pergamon

Tetrahedron 54 (1998) 14617–14634

TETRAHEDRON

Asymmetric Ethylmagnesiation of Alkenes Using a Novel Zirconium Catalyst

Louise Bell, Daniel C. Brookings, Graham J. Dawson, Richard J. Whitby*

Department of Chemistry, Southampton University, Southampton, HANTS, S017 1BJ, U.K.

Raymond V. H. Jones and Michael C. H. Standen

Zeneca Process Technology, Earls Road, Grangemouth, Stirlingshire, FK3 8XG, U.K.

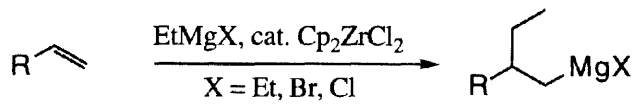
Received 6 August 1998; revised 16 September 1998; accepted 1 October 1998

Abstract: The novel C_1-symmetric zirconocene CpCp*$ZrCl_2$ (Cp=C_5H_5, Cp*= 1-neomenthyl-4, 5, 6, 7-tetrahydroindenyl) is a cheap, active, and effective catalyst for the asymmetric ethylmagnesiation of unactivated terminal alkenes.

INTRODUCTION

The zirconium catalysed ethylmagnesiation of unactivated alkenes (Eq 1), originally reported by Dzhemilev,[1] has been extensively investigated.[2,3,4] It is one of a substantial class of zirconium catalysed reactions of organomagnesium or aluminium reagents described recently.[5,6] The induction of asymmetry in transition metal catalysed reactions through the use of chiral metal complexes is an important goal in organic synthesis. Herein we report our efforts to induce asymmetry into the zirconium catalysed ethylmagnesiation reaction culminating in the design and synthesis of novel chiral metallocenes which give useful enantioinductions.[7]

Eq. 1



RESULTS AND DISCUSSION

The most widely used[8] chiral zirconocene is the C_2-symmetric ethylenebis(tetrahydroindenyl)zirconium dichloride **1a** first reported by Brintzinger.[9] The racemic complex was prepared by a literature method,[9] and kinetically resolved[10] with *R*-(BINOL) to give the chiral complex **1b**. Complex **1b** can be converted into **1a**, but since they were equally active as catalysts for the ethylmagnesiation reaction it was convenient to store and use **1b**. Since completing this work much improved methods for the synthesis and resolution of **1a** have been reported.[11] Catalysis of the ethylmagnesiation reaction of allyl alcohol, *N*-allylaniline, and *N*-methyl-*N*-allylaniline with **1b** was carried out. At least 10 mol% of **1b** was needed for reasonable conversion of substrate

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00920-X

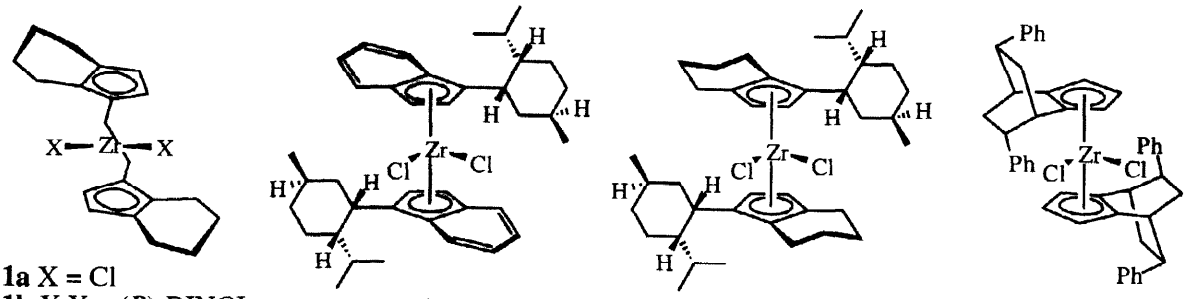
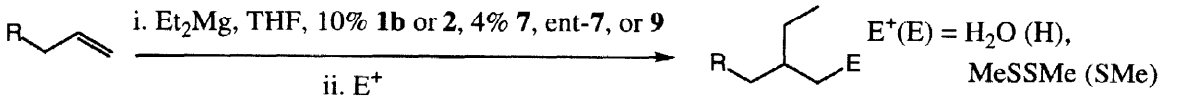


Table 1. Asymmetric ethylmagnesiation of terminal alkenes with various catalysts



		Zirconium complex									
		1b		**2**		**7**		**ent-7**		**9**	
R	E	Yield/%	e.e./%	Yield/%	e.e./%	Yield/%	e.e./%	Yield/%	e.e./%	Yield/%	e.e./%
NHPh	SMe	39	26 (*R*)	18	26 (*R*)	95	75 (*R*)	52	79 (*S*)	73	36 (*S*)
NMePh	SMe	34	26 (*R*)	5	16 (*R*)	61	52 (*R*)			65	29 (*S*)
OH	H	35	27 (*R*)	10	20 (*R*)	75	56 (*R*)			43	28 (*S*)

(c.f. 2% of Cp_2ZrCl_2, Cp = C_5H_5) and the enantiomeric excesses (e.e.'s) obtained were consistently around 27% (Table 1). Hoveyda has used **1b** for the carbomagnesiation of terminal alkenes with a chiral allylic hydroxyl or ether group.[4c] The diastereomeric ratios observed are dominated by the hydroxyl/ether group, but the additional influence of the catalyst chirality (matched / mismatched pairs) is consistent with our ≈30% e.e's.

The high cost of the synthesis of **1**, its low activity, and poor enantioselectivity led us to investigate alternatives. The known chiral zirconocenes **2**, **3**[12] and **4**[13] were synthesised and applied to the ethylmagnesiation reaction, however **3** and **4** were inactive and **2** gave very poor conversions and enantioinductions (Table 1). It became clear that we faced a general problem in asymmetric induction - a trade-off between enantioselectivity and catalytic activity - and a new design of chiral zirconocene was needed.

Although the benefits of C_2-symmetry in chiral catalysts have been described,[14] there are also disadvantages in that all aspects of the structure need to be duplicated which limits variability and tends to increase steric hindrance. In a C_2-symmetric complex such as **1** the substrate alkene may approach from either side of the proposed zirconacyclopropane intermediate in the ethylmagnesiation reaction (Fig. 1A). Steric clash of the alkene substituent with the tetrahydroindenyl ring favours the orientations shown, and hence asymmetric induction occurs. An alternative C_1-symmetric design is shown schematically in Fig. 1B where the chiral

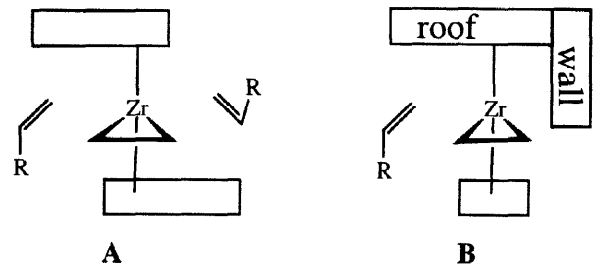
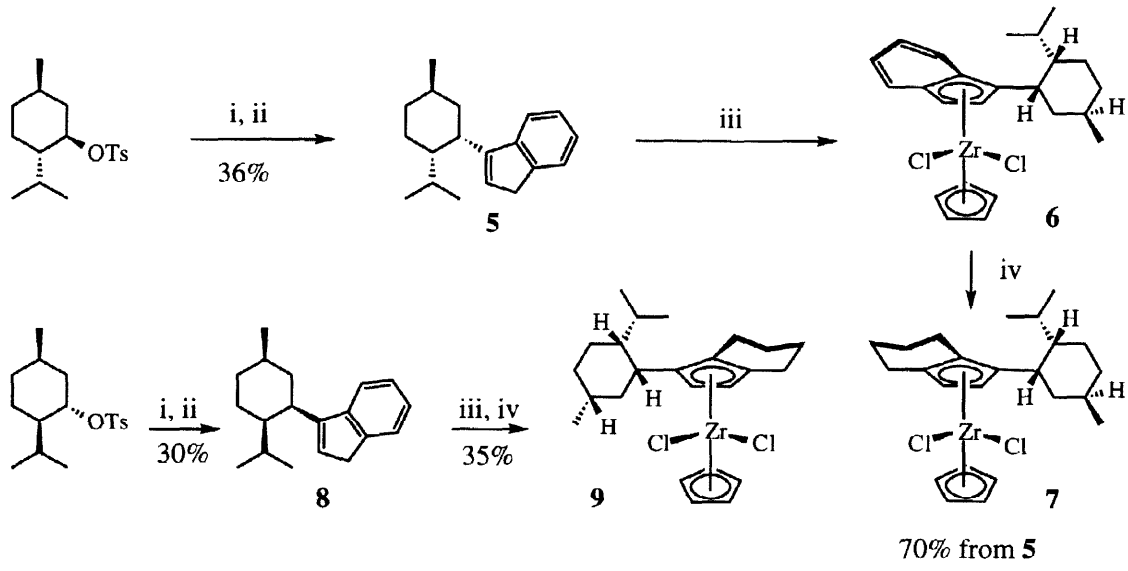


Fig. 1. C_2- and C_1-symmetric models for enantioinduction

cyclopentadiene must provide both a 'wall' to prevent approach of the substrate from one side, and a 'roof' to orientate the alkene substituent.

Efficient transfer of chirality from a metal complex to substrate is more likely if the chiral information is close to the metal centre. In **1** the planar chirality of the non-symmetrically substituted cyclopentadiene bound to the metal seems ideal, a feature we felt it important to retain. To avoid a resolution step in the synthesis of chiral complexes the planar chirality should ideally be induced from a chiral substituent. The 3-neomenthylindene ligand **5** reported by Erker[12] is an important advance since in the lowest energy rotamer about the indenyl-neomenthyl bond in Li-**5** the isopropyl substituent partially blocks one enantioface of the indene leading to face-selective metallation. The side chain chirality thus induces planar chirality on complexation. Related face-directed metallation of cyclopentadienyl ligands has also been achieved through fusion of a bicyclic chiral skeleton to the cyclopentadiene.[15] *Ansa*-metallocenes related to **1** where chiral substituents are used to direct metallation of the indenyl rings leading to predominant formation of one enantiomer of the *rac*-form have also been described.[16]

A zirconocene consisting of the ligand **5**, and an unsubstituted cyclopentadiene would satisfy the design ideas outlined above and was readily prepared (Scheme 1). The required ligand **5** was synthesised on a large scale from menthol tosylate and indenyl lithium. Optimum conditions were found to be at reflux in hexane for 48 h in the dark. Purification by filtration through silica to remove unreacted tosylate, and distillation at reduced pressure gave pure ligand **5** as a pale yellow solid. The indene **5** was lithiated by reaction with n-butyllithium in THF at -78 °C followed by 2 h at room temperature. $CpZrCl_3.2THF$ was dissolved in cold THF in the dark, then cooled to -78 °C and Li-**5** added. After stirring at room temperature for several hours solvent was removed from the bright yellow solution to give (1-neomenthylindenyl)(cyclopentadienyl)zirconium dichloride **6** as a yellow solid which was washed with several portions of cold hexane. The solid was dissolved in dichloromethane and hydrogenated over Adams catalyst (PtO_2) at 1 atmosphere hydrogen pressure until the yellow colour had disappeared (2 - 16 h) to give the required complex **7** as a colourless air and moisture stable solid (65 - 70% yield) after extraction into, and crystallisation from, toluene / hexane. The complex **7** was isolated as a single diastereoisomer, although the indenyl complex **6** contained 10 -15% of the isomer resulting from metallation of the opposite enantioface of the indene. The excellent overall yield proved critically dependent on the source of the '$CpZrCl_3$' fragment. $CpZrCl_3.DME$ prepared from $ZrCl_4.2SMe_2$ and $C_5H_5SiMe_3$ according to Livinghouse[17] was difficult to obtain completely pure due its poor solubility, and in complexations using it the



Scheme 1. *Reagents and conditions:* i. Indenyllithium, hexane, 69 °C, 48 h; ii. H_2O; iii. BuLi, THF, -78°C - room temp. then add to $CpZrCl_3.2THF$ in THF at -78°C before stirring at room temp. for 12 h; iv. H_2 (1 atm.), PtO_2 (5%), CH_2Cl_2, room temp., 2 - 16h.

hydrogenation step was unreliable probably due to sulphur containing impurities. $CpZrCl_3$ produced by chlorination of Cp_2ZrCl_2 according to Erker[18] gave reliable reactions, provided the dissolution in THF was carried out at low temperatures, but was difficult to produce in the required quantities. The best source proved to be $CpZrCl_3.2THF$ produced by a variation to the Livinghouse method where THF is added to the initially formed $CpZrCl_3.2SMe_2$ rather than DME. Recrystallisation from THF produced material of excellent quality, which could be assayed by NMR due to its good solubility in $CDCl_3$. The material was unstable to moisture and light, but could be stored at -20 °C under argon for months. Partially decomposed samples could be recrystallised from THF to give good material. It was also important that the reaction of $CpZrCl_3.2THF$ with Li-**5** was carried out in the dark, otherwise a brown rather than yellow solution was obtained, the hydrogenation more problematic, and overall yields around 35%. Using the optimised conditions 5 g batches of the complex **7** were readily synthesised making it commercially practical. The enantiomer of **7**, ent-**7** was also readily prepared from (+)-menthol. *X*-Ray crystallography confirmed the structure and absolute stereochemistry of ent-**7** (Fig. 2). The structure also shows how the 'roof and wall' model described above (Fig. 1B) has been realised, the 6-member ring of the neomenthyl substituent providing the 'wall' and the tetrahydroindene the 'roof'. The required orientation of the chiral ligand about the metal-cyclopentadiene centroid axis is maintained by steric interactions with the unsubstituted cyclopentadiene. Pictures of **7** shown below are reflections of the structure of ent-**7** (used to make correlation with **1** easier). In the same way isoneomenthylindene **8** (from (+)-isomenthol tosylate) gave complex **9** in 35% (unoptimised) yield. **9** is the 'pseudo enantiomer' of **7** since metallation is directed to the opposite enantioface of the indene.

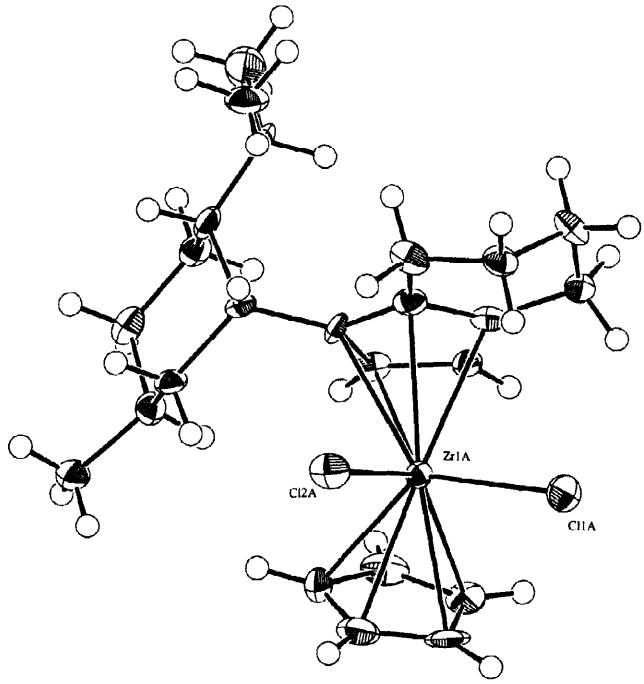


Fig. 2. X-Ray structure of ent-**7**.

The complexes **7**, ent-**7**, and **9** were used in the same ethylmagnesiation reactions as **1b** and **2**, with the results described in Table 1. To our delight the complex **7** gave much higher enantioselectivities than **1**, and was more active. Just 2 mol% of **7** gave complete ethylmagnesiation of *N*-allylaniline after 16h at room temperature. An additional advantage of complex **7** was that it was efficiently recoverable after work-up of reactions with hydrochloric acid. For example, ethylmagnesiation of 1.3 g of *N*-allylaniline using 4 mol% **7** and

ethylmagnesium chloride in ether was complete after 16 h at room temperature. Addition of 10M hydrochloric acid allowed the catalyst **7** to be extracted into toluene (89% recovery). Basification of the aqueous layer and extractive work-up gave (*R*)-*N*-(2-methylbutyl)aniline (1.2 g, 74%, 79% e.e.).

The absolute stereochemistries of the ethylmagnesiation products obtained with **1**, **7**, ent-**7**, and **9** are fully in accord with the model for addition of the alkene to intermediate η^2-ethylene complexes indicated schematically in Fig. 1A and 1B, taken with the 3D-structures of the dichlorides shown in Fig. 3. The higher enantioselectivity obtained for ethylmagnesiation of terminal alkenes with **7** compared with **1** may be rationalised from the position of the reduced indenyl rings - the 'roofs'. Viewing the structures of **7** (reflection of ent-**7**) and **1a** from 'above' (Fig. 4) suggests that the more 'forward pointing' reduced indenyl ring of the latter is better placed to interact with the substituent of a terminal alkene. The poorer result obtained with **9** compared to **7** / ent-**7** may also be rationalised based on 3D structures. The indenyl substituent on the isoneomenthyl ring in **9** lies in an equatorial position,[12] unlike the axial orientation found in **7** leading to a less effective 'wall', as can be seen in side views of the complexes ent-**7** and **9** (Fig. 4).

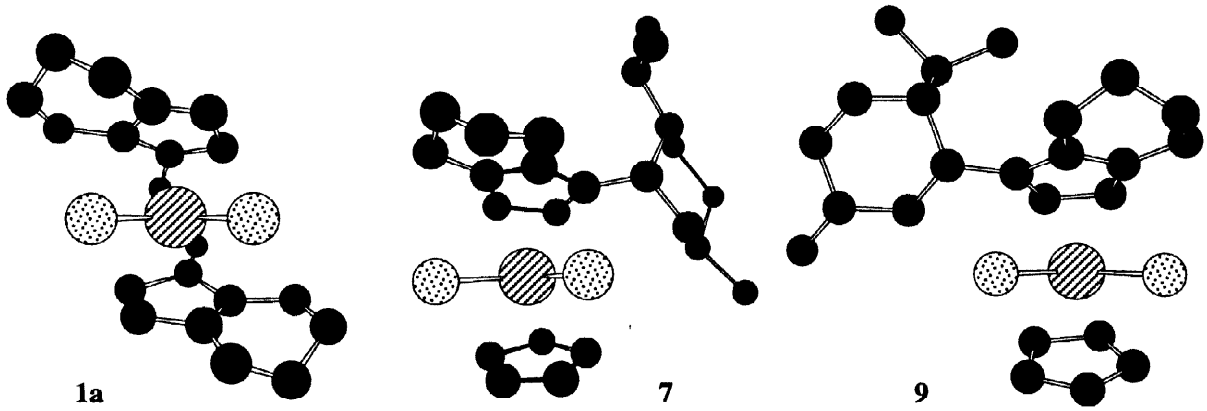


Figure 3. 3D structures of **1a** [ref. 9], **7** (from x-ray of ent-**7**), and **9** (model based on X-ray of bis(isoneomenthyl-4,5,6,7-tetrahydroindenyl)zirconium dichloride [ref. 12]).

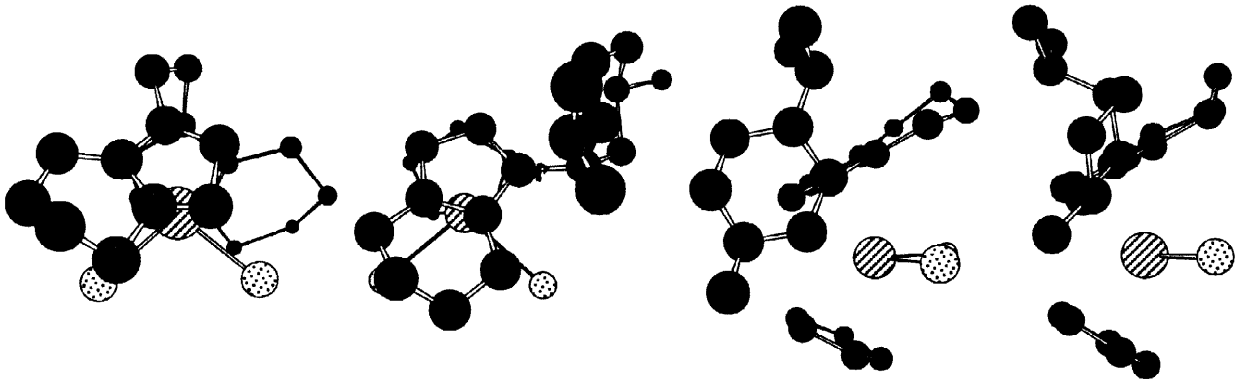
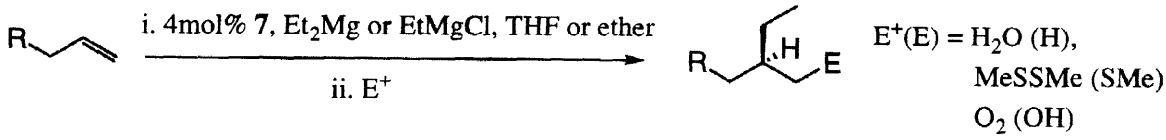
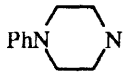
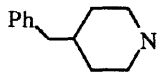


Fig. 4. Comparison of tetrahydroindenyl ring orientation in **1a** and **7**, and cyclohexyl ring orientation in **ent-7** and **9** (calculated).

The initial experiments demonstrated that complex **7** (and ent-**7**) was an effective asymmetric catalyst so a more detailed study of enantioinduction with a wider range of alkene substrates, and with variation in the solvent and organomagnesium reagent was carried out (Table 2). Good yields and moderate to good enantioselectivities were obtained in all cases except with 4-phenyl-1-butene (entry 12). In general there was little difference

Table 2. Asymmetric ethylmagnesiation of terminal alkenes with **7** as the catalyst, varying solvent and organomagnesium reagents.



			EtMgCl, Et_2O		EtMgCl, THF		Et_2Mg, Et_2O		Et_2Mg, THF		
	R	E	Yield/%	e.e./%	Yield/%	e.e./%	Yield/%	e.e./%	Yield/%	e.e./%	(*R*/*S*)
1	NHPh	SMe	90	81	92	61	92	80	95	75	(*R*)
2	NHCy	SMe	87	83	88	61	57	89	-		(*R*)
3	NHtBu	SMe	40	70	38	73	26	64	-		-
4	$NHCH_2Ph$	SMe	64	44	65	30	76	54	-		(*R*)
5	$NHCHPh_2$	SMe	87	39	84	28	-		-		-
6	NMePh	SMe	27	20	47	46	-		61	52	(*R*)
7		OH	45	61	47	58	-		50	42	(*R*)
8		OH	43	63	48	60	-		37	52	(*R*)
9	OH	H	34	55	30	60	23	60	75	56	(*R*)
10	OCH_2Ph	OH	41	83	42	65	-		-		(*S*)
11	SPh	H	84	33	80	46	63	33	-		(*R*)
12	CH_2Ph	OH	30	10	-		-				-

between using diethylmagnesium, and the more readily available ethylmagnesium halides, but substantial solvent effects were observed.

The highest enantioselectivities were obtained with secondary amines which can be attributed to the formation of a bulky magnesium aggregate on the amine giving larger interaction with the catalyst . The low values for the *N*-benzyl amine (entry 4) may indicate the importance of an α-branch on the amine, although the equally low value for the *N*-benzhydryl substrate might indicate additional 'aromatic' interactions with the cyclopentadiene favouring the 'wrong' enantiomer. Tertiary amines gave lower enantioexcesses (entries 6 - 8). There was a strong solvent effect with secondary amines giving significantly higher enantioexcess in diethyl ether, than in THF supporting the idea that aggregates are involved. With tertiary amines the solvent had little effect.

Allyl alcohol gave a moderate enantioexcess and little solvent effect. Allyl benzyl ether gave a surprisingly high enantioexcess (83%) in diethyl ether (much lower in THF) again suggesting that complexation with magnesium was assisting asymmetric induction. Unfortunately with this substrate the elimination of benzyl alcohol is a side reaction leading to lower yields, and we cannot rule-out an effect on the enantioexcesses. The substrate 4-phenyl-1-butene, lacking a coordinating group, gave very poor yields and enantioexcess.

Enantiomeric excesses were determined by chiral HPLC, chiral GC, or by NMR of the derived Mosher's ester as detailed in the experimental section. Absolute configurations were determined from water quenched products by comparison of optical rotations with the literature, or samples prepared from (*S*)-2-methyl-1-butanol (see experimental section). In all cases the sense of asymmetric induction is that predicted on the basis of the model proposed in Fig 1B, and the *X*-ray structure.

CONCLUSION

We have designed and synthesised some C_1-symmetric chiral zirconocenes where the planar chirality of a bound indenyl ligand is induced from a neomenthyl or isoneomenthyl substituent. The complexes are cheap to make, are substantially more active catalysts for the ethylmagnesiation reaction than other chiral zirconocenes tried, gave higher enantiomeric excesses, and are efficiently recoverable. The compounds (*R*)-1-benzyloxy-2-methylbutane,[19] (*S*)-1-benzyloxymethyl-butan-1-ol,[20] (*R*)-1-phenylthio-2-methylbutane[21] and (*R*)-2-methyl-1-butanol,[19] described above have all been recently used in total synthesis, and required multi-step synthetic routes for their preparation.

The design features of incorporating both chiral elements needed for asymmetric induction ('roof' and 'wall') into one cyclopentadienyl ligand, and the use of induced planar chirality on complexation, are currently being developed in a wide range of ligands, and *mono*- and *bis*-cyclopentadienyl metal complexes.

EXPERIMENTAL

General Techniques

^1H and ^{13}C NMR spectra were recorded on Jeol JNM-GX270, Bruker AM300 or Bruker AM360 spectrometers. The chemical shifts in proton spectra are reported as values in p.p.m. relative to internal tetramethylsilane standard, or residual solvent. The following abbreviations are used to denote multiplicity and shape of signal and may be compounded: s = singlet, d =doublet, t = triplet, q = quartet, m = multiplet, br = broad, fs = fine splitting. Coupling constants *J* are reported in Hz. Carbon-13 spectra were proton decoupled and referenced to the $CDCl_3$ triplet at 77.2 p.p.m. and signals reported as s, d, t, q depending on the number of directly attached protons (0, 1, 2, 3 respectively), this being determined by DEPT experiments. Spectra recorded in deuteriobenzene were referenced to the solvent signals at 7.18 (proton) and 128.7 (carbon). Electron impact (EI) mass spectra, including accurate masses, were recorded on a VG Analytical 70-250-SE double focusing mass spectrometer at 70 eV. Electrospray (ES^+) spectra were recorded on a VG Platform spectrometer in acetonitrile. M/z signals are reported as values in atomic mass units followed by the peak intensity relative to the base peak. ES spectra generally gave MH^+ as the only significant peak. Infra-red spectra were recorded on a Perkin Elmer 1600 FT-IR spectrometer as films, solutions or nujol mulls between sodium chloride plates. Peaks are described as s (strong), m (medium), w (weak), and/or br (broad). Optical rotations were measured in an AA-100 Polarimeter (Optical Activity Limited) and are uncorrected. Ultraviolet spectra were recorded on a Unicam SP800 ultraviolet spectrophotometer as solutions in benzene free absolute alcohol. Elemental analyses were performed by the University College London Microanalysis Service. Melting points were measured on a Gallenkamp type apparatus and are uncorrected. Organometallic reactions were performed under an argon atmosphere using standard Schlenk, syringe and vacuum line techniques. Column chromatography was performed on silica (230-400 mesh), under slight positive pressure. Solvent ratios are described as volumes before mixing.

Chiral gas chromatography was carried out on a Hewlett Packard 6900 machine using helium as the carrier gas, a flame ionisation detector, and the columns, flow rates and temperatures as described below. Chiral HPLC was carried out on an HP 1050 instrument using 250 mm x 4.6 mm i.d. Chiralcel OD-H, OB-H, or Bakerbond Chiralpak AD columns. Peak size analysis was carried out using HP ChemStation software. The retention times generally lengthened as the columns aged, but separations remained constant. Amide derivatives for HPLC analysis were prepared by the addition of 1 equivalent of naphthoyl chloride or benzoyl chloride to the amine and triethylamine in CH_2Cl_2.

Unless otherwise indicated materials were obtained from commercial sources and used without further purification. Ethylmagnesium chloride was purchased from Aldrich as a 2 M solution in diethyl ether or THF, and titrated for total base before use.[22] Diethylmagnesium was prepared from ethylmagnesium bromide in diethyl ether by precipitation of the 1,4-dioxane complex of magnesium bromide (centrifuge) thus displacing the Schlenk equilibrium.[23] The ≈ 1-2 M ethereal solution of diethylmagnesium so formed was titrated for total base

content as above, and for Mg^{2+} content with ethylenediaminetetraacetic acid (EDTA) using Eriochrome Black T as the indicator.[24] Solutions of diethylmagnesium in THF were prepared by removal of diethyl ether from the above under vacuum, addition of THF, removal of the THF (and residual diethyl ether) under vacuum, and finally making up the solution in THF. Butyllithium (2.5 M in hexanes) was purchased from Aldrich and titrated prior to use against 1,3-diphenylacetone 4-methylbenzenesulphonyl hydrazone.[25] Zirconium tetrachloride (99.6%) was purchased from Strem, and handled under nitrogen. Diethyl ether, THF, benzene, and hexane were freshly distilled from sodium/benzophenone, the later containing added tetraethyleneglycol dimethyl ether. Chlorinated solvents were distilled from calcium hydride. Petrol refers to the petroleum fraction b.p. 40 - 60 °C and was distilled through a Vigreux column before use.

Trimethylsilylcyclopentadiene was prepared according to Brandsma[26] and freshly distilled before use. The complexes **1b**[9,10] **2** and **3**[12] were prepared according to the literature. The complex **4**, previously reported as a mixture of *rac*- and *meso*-isomers by Vollhardt,[13] was prepared by extensive variation on the published route.[27]

N-Allyl-*N*-phenylamine, *N*-allyl-*N*-cyclohexylamine, allyl benzyl ether, allyl phenyl sulphide, and 4-phenyl-1-butene were obtained from commercial sources, and were distilled before use. *N*-Allyl-*N*-methyl-*N*-phenylamine,[28] *N*-allyl-*N*-benzylamine,[29] *N*-allyl-*N*-*tert*-butylamine,[30] and *N*-allyl-*N*-benzhydrylamine[29] were prepared from the amine and allyl bromide, and had spectral properties consistent with those previously reported.

Preparation of Metal Complexes

(η^5-Cyclopentadienyl)trichlorozirconium *bis*(tetrahydrofuran) complex.

Zirconium tetrachloride (23.3 g, 0.1 mol, handled in an inert atmosphere) was suspended in freshly distilled dichloromethane (200 mL) under argon at 0 °C. Dimethylsulphide (15 mL, 0.2 mol, 2 eq) was added dropwise at -10 °C, then the mixture stirred at room temperature for 15 min. to give a colourless solution. The solution was cooled to -10 °C, freshly distilled trimethylsilylcyclopentadiene (25 mL, 0.15 M, 1.5 eq) added dropwise by syringe, and the resulting yellow solution stirred for 3 hrs at room temperature with the exclusion of light, during which time a white precipitate formed. Freshly distilled THF (80 mL) was cooled to 0 °C and added slowly to the reaction mixture, which was then stirred at room temperature for one hour. The solution was concentrated by vacuum transfer to one quarter of the original volume giving a white solid and yellow solution. Dry hexane (100 mL) was added *via* cannula and the white solid allowed to settle. The supernatant was removed *via* cannula and the white residual solid washed with hexanes (3 x 150 mL) in the same way. The resulting solid was dried at 1 torr for 16 h at room temperature to give the *title complex* (34.9 g, 86 %, >95% pure). The purity of the product was determined by NMR using tribromobenzene as an internal standard.

δ_H (300 MHz, $CDCl_3$) 6.7 (s, 5H, Cp), 3.9 (s br, 8H, THF), 1.9 (s br, 8H, THF) ppm.

(η^5-Cyclopentadienyl)(η^5-{1-[(1*S*, 2*S*, 5*R*)-2-isopropyl-5-methylcyclohexyl]-4,5,6,7-tetrahydroindenyl})zirconium dichloride 7.

To (+)-3-[(1*S*, 2*S*, 5*R*)-2-isopropyl-5-methylcyclohexyl]lindene **5** (3.45 g, 13.6 mmol) [prepared from (-)-menthol][12] in THF (40 mL) at -78 °C was added dropwise n-butyllithium (5.5 mL of 2.5 M solution in hexanes, 13.6 mmol, 1 eq) and the mixture warmed to room temperature to give an orange solution. With the exclusion of light $CpZrCl_3.2THF$ (6.63 g, 16.3 mmol, 1.2 eq) was dissolved in THF (60 mL, pre-cooled to 0 °C) and the anion solution prepared above added by cannula to give a bright yellow solution. After stirring overnight at room temperature the solvent was removed *in vacuo* to give a bright yellow solid. The residue was dissolved in dichloromethane (100 mL), platinum oxide (90 mg, 0.4 mmol) added, and the mixture stirred under an atmosphere of hydrogen gas (1 bar) overnight. The colourless solution was filtered through celite and the solvent removed to give the *title complex* as a white solid (4.55 g, 69%). The product can be recrystallised from hot toluene to give colourless block crystals. Mp 237 - 238 °C.

Anal. Calcd for $C_{24}H_{34}Cl_2Zr$: C, 59.48; H, 7.07%. Found: C, 59.33; H, 6.95%. $[\alpha]_D^{21}$ -4.7 (c 2.9, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ 6.46 (1H, d, J = 2.9 Hz), 6.44 (5H, s), 5.58 (1H, d, J = 2.9 Hz),

3.22 (1H, m), 3.08 (1H, q, J = 4.7 Hz), 2.85 (2H, dt, J = 16.7, 5.2 Hz), 2.57 (1H, m), 2.50 (1H, dt, J = 16.8, 6.1 Hz), 1.45 - 2.01 (10H, m), 1.34 (1H, m), 1.22 (1H, ddd, J = 13.9, 10.1, 4.9 Hz), 1.05 (1H, m), 0.96 (3H, d, J = 6.6 Hz), 0.73 (3H, d, J = 6.9 Hz), 0.38 (3H, d, J = 6.9 Hz) ppm. ^{13}C NMR (75 MHz; $CDCl_3$): δ 137.8 (s), 137.2 (s), 131.7 (s), 114.8 (d), 110.0 (d), 102.9 (d), 47.6 (d), 39.4 (t), 36.4 (d), 33.6 (t), 29.0 (d), 28.9 (d), 24.9 (t), 24.5 (t), 24.1 (q), 22.5 (t), 22.2 (t), 22.1 (t), 21.9 (q), 18.5 (q). IR (nujol mull): 2922s, 1549s, 1302w, 1154w, 1015w cm^{-1}. MS (EI): *m/z* 482 (M^+, 16%), 450 (55), 446 (100), 419 (18), 403 (22), 335 (8), 257 (8), 225 (13), 117 (7), 91 (8), 69 (8).

(η^5-Cyclopentadienyl)(η^5-{1-[(1*S*, 2*S*, 5*R*)-2-isopropyl-5-methylcyclohexyl]-4,5,6,7-tetrahydroindenyl})zirconium dichloride (ent-7) and *X*-ray structure determination.

The complex **ent-7** was prepared as for **7**, and gave identical physical properties except the sign of the optical rotation. Crystals suitable for *X*-ray structure determination were grown by slow cooling of a hot toluene solution. A transparent plate 0.1 x 0.45 x 0.48 mm^3 was mounted in air on a glass fibre and the data collection carried out at -120 °C on a Seimens P4/Ra diffractometer using graphite-monochromated CuKα radiation (λ = 1.54178 Å). The complex crystallised in the monoclinic space group $P2_1$ with lattice parameters a = 10.069(2), b = 18.033(2), c = 12.762(2) Å, β = 105.15(2)° and a unit cell volume of 2236.7(6) Å^3. 5455 independent reflections were collected [I≥2σ(I)] and the structure was solved by the heavy atom method using Seimens SHELXTL IRIS, the refinement converging to give R(F) = 6.2% and Rw(F^2) = 8.1%. Maximum and minimum heights in the final difference map were 1.50 and –2.02 e$^-$/Å^3. Hydrogens were placed in calculated positions. There were four molecules per unit cell and two independent molecules per symmetric unit cell. The only significant difference between the two independent molecules in the unit cell is in the conformation of the saturated portion of the tetrahydroindenyl ring. The zirconium atoms are co-ordinated in a distorted tetrahedral fashion by the two chlorine atoms and the two cyclopentadiene rings. The angle between vectors drawn from the metal to the centres of the cyclopentadiene rings is about 130° and the distance to the rings is about 2.2 Å. The *X*-ray structure has been deposited at the Cambridge Crystallographic Data Centre, or may be viewed at http://www.soton.ac.uk/~rjw1/ZenCpPro/JlrXray.pdb

(η^5-Cyclopentadienyl)(η^5-{1-[(1*R*, 2*R*, 5*R*)-2-isopropyl-5-methylcyclohexyl]-4,5,6,7-tetrahydroindenyl})zirconium dichloride 9.

Prepared from 3-[(1*R*, 2*R*, 5*R*)-2-isopropyl-5-methyl]indene[12] as for complex **7** and then recrystallised from hot toluene to give the product as a white solid (641 mg, 33%). Mp 209 - 212 °C.

HRMS (EI): $C_{24}H_{34}Cl_2Zr$ requires *m/z* 482.1084; found 482.1094. $[\alpha]_D^{20}$ +3.2 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.42 (5H, s), 6.13 (1H, d, J = 2.6 Hz), 5.63 (1H, d, J = 2.8 Hz), 2.73-3.00 (3H, m), 2.51 (2H, m), 1.10 - 1.65 (13H, m), 0.94 (3H, d, J = 6.1 Hz), 0.85 (3H, d, J = 6.6 Hz), 0.31 (3H, d, J = 6.2 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.9(s), 138.5 (s), 129.9 (s), 114.8 (d), 106.6 (d), 102.3 (d), 41.7 (d), 40.6 (d), 35.3 (t), 32.6 (d), 30.7 (t), 29.4 (q), 25.6 (d), 24.9 (t), 24.4 (q), 23.8 (t), 23.2 (t), 22.6 (t), 21.8 (t), 21.7 (q) ppm. IR (solution in CCl_4): 2947m, 2360w, 1549s, 1458w, 1252m, 1217m, 1068w, 1005m, 978m cm^{-1}. MS (EI): *m/z* 482 (M^+, 17%) 446 (100), 419 (15), 403 (30), 335 (8), 305 (6), 257 (6), 227 (19), 129 (7), 91 (9), 55 (8).

Preparation of starting alkenes.

1-Allyl-4-benzylpiperidine

Allyl bromide (8.5 g, 70 mmol, 1.5 eq) was slowly added to triethylamine (9.8 mL, 7.1 g, 70 mmol, 1.5eq) and 4-benzylpiperidine (8.2 g, 47 mmol, 1eq) in diethyl ether (50 mL) and the reaction stirred overnight at room temperature. Sodium hydroxide (100 mL of a 2 M aqueous soln.) was added, the organic layer removed, and the aqueous layer extracted into diethyl ether (3 x 60 mL). The combined organic layers were dried over $MgSO_4$, solvent removed, and the residue chromatographed on silica (5-10% diethyl ether in petrol).

Removal of solvent from relevant fractions and Kugelrohr distillation (135 °C, 1.0 mbar) gave the *title compound* as a pale yellow oil (8.5 g, 84%).

^{1}H NMR (300MHz, $CDCl_3$): δ 7.1-7.3 (5H, m), 5.89 (1H, ddt, *J* = 17.3, 10.3, 6.8 Hz), 5.1-5.2 (2H, m), 2.97 (2H, d+fs, *J* = 6.6 Hz), 2.91 (2H, d+fs, *J* = 11.8 Hz), 2.55 (2H, d, *J* = 7.0 Hz), 1.86 (2H, td, *J* = 11.8, 2 Hz), 1.65 (2H, d + fs, *J* = 12.9 Hz), 1.53 (1H, m), 1.32 (2H, qd, *J* = ≈12, 3.8 Hz) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 140.9 (s), 137.5 (d), 129.3 (d), 128.3 (d), 125.9 (d), 117.7 (t), 62.4 (t), 54.0 (t), 43.3 (t), 38.0 (d), 32.4 (t) ppm. IR (liq. film): 3062m, 3025m, 2918s, 2847s, 2787s, 1603m, 1584w, 1495m, 1465m, 992m, 918s cm^{-1}. MS (ES$^+$): *m/z* 202.2 (MH$^+$).

1-Allyl-4-phenylpiperazine

By the same method as for 1-allyl-4-benzylpiperidine (Kugelrohr distillation at 75-80 °C, 1.0 mbar, lit[31] b.p. 110-114 °C, 0.8 mbar) the *title compound* was prepared as a pale yellow oil which solidified in the fridge (91%).

HRMS (EI): $C_{13}H_{18}N_2$ requires *m/z* 202.1469; found 202.1462. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (2H, t, *J* = 7.5 Hz), 6.95 (2H, d, *J* = 8.0 Hz), 6.86 (1H, t, *J* = 7.5 Hz), 5.92 (1H, ddt, *J* = 16.9, 10.1, 6.6 Hz), 5.2 - 5.3 (2H, m), 3.23 (4H, t, *J* = 5.1 Hz), 3.07 (1H, dt, *J* = 6.6, 1.3 Hz), 2.63 (4H, t, *J* = 5.1 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.5 (s), 135.1 (d), 129.3 (d), 119.8 (d), 118.4 (t), 116.2 (d), 62.0 (t), 53.3 (t), 49.3 (t) ppm. IR (liq. film): 3063w, 3036w, 2938m, 2817s, 1599s, 1502s, 1451m, 1383m, 1011m, 926m cm^{-1}. MS (ES$^+$): *m/z* 215.2 (MH$^+$).

Zirconium catalysed ethylmagnesiation reactions.

General procedures (1 mmol scale).

To the zirconium catalyst under argon at room temperature was added a solution of the substrate (1 mmol) in diethyl ether or THF (2 mL) followed by a solution of the organomagnesium species in diethyl ether or THF (5 mmol, 1 - 2 M soln.). After stirring for 16 - 72 h at room temperature the reaction was complete (except with catalyst **1b** and **2** where incomplete reaction was typical) to give the desired organomagnesium reagent.

For catalysts **1b** and **2**, 10 mol% was used, for **7**, **ent-7**, and **9**, 4 mol%, and for zirconocene dichloride (used to prepare racemic samples of all the compounds) 2 mol%.

For all of the compounds below the name (major enantiomer), optical rotation, and major peak in chiral GC or HPLC is given for the enantiomer resulting from the use of **7** as the catalyst.

For protonation, reactions were quenched by the addition of NH_4Cl aq.

For conversion to the SMe derivative, the reaction mixture was diluted with THF (5 mL), cooled to 0 °C, and Me_2S_2 (1 mL) added dropwise, followed by stirring at room temperature for 3 hours. Removal of solvent under vacuum was followed by an aqueous work-up.

For oxygenation, the reaction mixture was diluted with THF (5 mL), cooled to 0 °C, then stirred under an oxygen atmosphere (balloon, oxygen dried by passage through a column of 4Å molecular seives) for 5 hours at 0 °C before aqueous work-up. On larger scale the initial reaction could be strongly exothermic.

For non amines, extraction of the organic products into diethyl ether (3 x 20 mL), drying ($MgSO_4$), and removal of solvent gave the crude products.

For amines the reactions were quenched with HCl aq (6 M, 20 mL), the organic phase discarded, and the aqueous phase washed with diethyl ether (20 mL). The aqueous phase was then rendered strongly basic by the addition of saturated NaOH aq, and the amine extracted into diethyl ether (3 x 20 mL). Drying ($MgSO_4$) and removal of solvent gave the crude product.

(*R*)-*N*-(2-Methylbutyl)-*N*-phenylamine. Example of larger scale reaction, with recovery of catalyst.

To catalyst **7** (194 mg, 4 mol %) under argon was added a solution of *N*-allyl-*N*-phenylamine (1.33 g, 10 mmol, 1 eq) in diethyl ether (20 mL). The solution was cooled to 0 °C and ethylmagnesium chloride (25 mL,

2.0M in diethyl ether, 50 mmol, 5.0 eq) added dropwise forming a yellow / brown solution which was stirred for 16 h at room temperature.

A small aliquot (ca. 2 mL) was worked up with dimethyldisulphide to afford (*R*)-*N*-{2-[(methylsulphanyl)methyl]butyl}-*N*-phenylamine (see below). HPLC analysis on a Chiralcel OD-H column 2% isopropanol / hexane 1 mL / minute gave a 79 % e.e, retention times 11.3 (major enantiomer) and 12.4 minutes.

The rest of the reaction mixture was cautiously added to a rapidly stirred mixture of ice (300 g) and concentrated HCl aq (100 mL). The aqueous layer was extracted with toluene (3 x 30 mL) and the solvents removed *in vacuo* to give the recovered chiral zirconocene **7** as a crude yellow brown solid (173 mg, 89 % recovery by nmr against 1,3,5 tribromobenzene internal standard). Recrystallisation from chloroform / hexanes at - 20 °C gave pure **7** as white crystals (123 mg, 63%).

The aqueous layer was made strongly basic (pH = 14) with excess saturated NaOH solution, extracted with diethyl ether (3 x 100 mL) and the organic extracts dried over $MgSO_4$. The solvents were removed *in vacuo* to give a yellow oil which was purified by column chromatography (100 % petrol) and Kugelrohr distillation (105 °C, 0.5 mm Hg. lit[32] 142 °C, 25 mbar) to afford (*R*)-*N*-(2-methylbutyl)-*N*-phenylamine as a colourless oil (1.214g, 74 %).

$[\alpha]_D^{20}$ -12.3 (c 2.6, EtOH) for a sample of 79% e.e. as determined above. $[\alpha]_D^{20}$ +15.8 (c 0.52, EtOH) for a sample prepared from (*S*)-2-methyl-1-butanol as detailed below. HRMS (EI): $C_{11}H_{17}N$ requires *m/z* 163.1361; found 163.1364. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20 (2H, dd, *J* = 7.7, 8.4 Hz), 6.71 (1H, tt, *J* = 7.4, 1.1 Hz), 6.63 (2H, dd, *J* = 7.7, 1.1 Hz), 3.70 (1H, br s), 3.09 (1H, dd, *J* = 12.1, 6.1 Hz), 2.92 (1H, dd, *J* = 12.1, 7.0 Hz), 1.71 (1H, octet, *J* = 6.6 Hz), 1.54 (1H, ddq, *J* = 13.9, 5.1, 7.4 Hz), 1.25 (1H, ddq, *J* = 13.6, 6.3, 7.5 Hz), 1.00 (3H, d, *J* = 7.0 Hz), 0.97 (1H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.7 (s), 129.3 (d), 116.9 (d), 112.7 (d), 50.0 (t), 34.6 (d), 27.4 (t), 17.6 (q), 11.5 (q) ppm. IR (film): 3416m, 2957s, 2923s, 2871s, 1601s, 1504s, 1461s, 1429m, 1378m, 1318s, 1257s, 736s, 672s cm^{-1}. MS (EI): *m/z* 163 (M^+, 23%), 106 (100), 77 (13).

(*R*)-*N*-{2-[(Methylsulphanyl)methyl]butyl}-*N*-phenylamine

By the general procedure, with Me_2S_2 quench followed by column chromatography (2% diethyl ether in petrol) and Kugelrohr distillation (145 - 150 °C, 0.1 mbar) the *title compound* was prepared as a colourless oil.

Anal.: Calcd for $C_{12}H_{19}NS$: C, 68.87; H, 9.15; N, 6.69%. Found: C, 68.66; H, 9.32; N, 6.64%. HRMS (EI): $C_{12}H_{19}NS$ requires *m/z* 209.1238; found 209.1241. $[\alpha]_D^{30}$ -10.1 (c 6.5, $CHCl_3$) for a sample of 50% e.e. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22 (2H, m), 6.70 (3H, m), 3.88 (1H, br s), 3.23 (1H, dd, *J* = 13.0, 6.5 Hz), 3.17 (1H, dd, *J* = 13.0, 6.0 Hz), 2.63 (1H, dd, *J* = 12.9, 5.7 Hz), 2.58 (1H, dd, *J* = 12.7, 6.5 Hz), 2.13 (3H, s), 1.87 (1H, sept., *J* = 6.2 Hz), 1.52 (2H, m), 0.99 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.5 (s), 129.4 (d), 117.3 (d), 112.8 (d), 46.8 (t), 39.2 (d), 37.4 (t), 24.7 (t), 16.6 (q), 11.2 (q) ppm. IR (film): 3412s, 2959s, 2911s, 1600s, 1505s, 1317s, 1259s, 749s, 692s cm^{-1} . MS (EI): *m/z* 209 (M^+, 32%), 107 (10), 106 (100), 77 (10). Enantiomeric excess detemined by HPLC on a Chiralcel OD-H column, 1ml/min, 2% isopropanol in hexane, retention times 9.5 (major) and 10.2 minutes.

(*R*)-*N*-Cyclohexyl-*N*-(2-methylbutyl)amine

Using the general method (EtMgCl in diethyl ether, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (10% diethyl ether in petrol) and Kugelrohr distillation (110 °C, 1 mbar) *N*-allyl-*N*-cyclohexylamine (139 mg, 1 mmol) gave the *title compound* (87 mg, 52%) as a colourless oil.

HRMS (EI): $C_{11}H_{23}N$ requires *m/z* 169.1830; found 169.1831. $[\alpha]_D^{21}$ -13.0 (c 0.8, EtOH) for a sample of 78% e.e. $[\alpha]_D^{21}$ +18.1 (c 0.8, EtOH) for a sample prepared from (*S*)-2-methyl-1-butanol as detailed below. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.54 (1H, ddd, *J* = 11.4, 5.9, 2.6 Hz), 2.32 (2H, m), 1.9-0.8 (20H, m) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.11 (d), 53.30 (t), 35.12 (d), 33.85 (t), 33.76 (t), 27.71 (t), 26.35 (t), 25.27 (t), 25.16 (t), 17.86 (q), 11.42 (q) ppm. IR (CH_2Cl_2 solution): 3615w, 2980s, 2873s, 1460s, 1380s, 1200m, 1097s cm^{-1}. MS (ES^+): *m/z* 170 (MH^+).

(*R*)-*N*-Cyclohexyl-{2-[(methylsulphanyl)methyl]butyl}amine

By the general procedure, with Me_2S_2 quench followed by column chromatography (10% diethyl ether in petrol) and Kugelrohr distillation (65 °C, 0.1 mbar) *N*-allyl-*N*-cyclohexylamine gave the *title compound* as a colourless oil.

HRMS (EI) $C_{12}H_{25}NS$ requires *m/z* 215.1708; found 215.1692. $[\alpha]_D^{30}$ -3.5 (c 6.1, $CHCl_3$) for a sample of 59% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 2.62 (2H, dd, *J* = 5.9, 3 Hz), 2.53 (2H, d, *J* = 5.9 Hz), 2.37 (1H, ddd, *J* = 14, 7.4, 3.7 Hz), 1.90 (1H, bs), 1.73 - 1.57 (4H, m), 1.42 (2H, pentet, *J* = 7.4 Hz), 1.3 - 1.0 (6H, m), 0.9 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 57.0 (d), 49.5 (t), 39.9 (d), 37.5 (t), 33.6 (t), 33.6 (t), 26.2 (t), 25.1 (t), 24.5 (t), 24.1 (t), 16.3 (q), 10.9 (q) ppm. IR (film): 3297w, 2857s, 2851s, 1445s, 1128m, 736m cm^{-1}. MS (ES^+): *m/z* 216.2 (MH^+).

Enantiomeric excess determined by HPLC analysis of the 1-naphthoyl amide derivative on a Chiralcel OD-H column, 1ml/min, 10% isopropanol in hexane, retention times: 7.85 (major) and 9.37 minutes.

***N*-tert-Butyl-{2-[(methylsulphanyl)methyl]butyl}amine**

By the general procedure, with Me_2S_2 quench followed by column chromatography (10% diethyl ether in petrol), *N*-allyl-*N*-*tert*-butylamine gave the *title compound* as a colourless oil.

HRMS (EI) $C_{10}H_{23}NS$ requires *m/z* 189.1551; found 189.1535 $[\alpha]_D^{30}$ -3.0 (c 3.5, $CHCl_3$) for a sample of 70% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 2.54 (4H, m), 2.09 (3H, s), 1.59 (1H, septet, *J* = 6.3 Hz), 1.80 (1H, br s), 1.42 (2H, m), 1.15 (9H, s), 0.90 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.2 (s), 44.8 (t), 40.4 (d), 37.5 (t), 29.0 (q), 24.4 (t), 16.3 (q), 10.9 (q) ppm. IR (film): 3290 w, 2861 s, 2799 s, 1443 s, 694 s cm^{-1}. MS (ES^+): *m/z* 190.1 (MH^+). Enantiomeric excess determined by HPLC analysis of the benzoyl amide derivative on a Chiralcel OD-H column, 1ml/min, 2% isopropanol in hexane, retention times: 10.1 and 11.0 (major) minutes.

(*R*)-*N*-Benzyl-*N*-(2-methylbutyl)amine

Using the general method (EtMgCl in diethyl ether, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (5 - 10% diethyl ether in petrol) and Kugelrohr distillation (82 °C, 0.7 mbar), *N*-allyl-*N*-benzylamine (147 mg, 1 mmol) gave the *title compound* (120 mg, 68%) as a colourless oil.

HRMS (EI) $C_{12}H_{19}N$ requires *m/z* 177.1517; found 177.1522. $[\alpha]_D^{20}$ -6.3 (c 0.79, EtOH) for a sample of 40% e.e. $[\alpha]_D^{21}$ +14.2 (c 1.2, EtOH) for a sample prepared from (*S*)-2-methyl-1-butanol as detailed below. ^1H NMR (300 MHz, $CDCl_3$): δ 7.3 (5H, m), 3.79 (2H, s), 2.57 (1H, dd, *J* = 11.7, 5.9 Hz), 2.43 (1H, dd, *J* = 11.8, 7.1 Hz), 1.57 (1H, octet, *J* = 6.8 Hz), 1.44 (2H, m), 1.19 (1H, m), 0.921 (3H, d, *J* 6.6 Hz), 0.898 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7 (s), 128.4 (d), 128.1 (d), 126.8 (d), 56.0 (t), 54.1 (t), 34.8 (d), 27.5 (t), 17.6 (q), 11.3 (q) ppm. IR (film): 3348w, 2958s, 2872s, 1601w, 1452s, 1362m, 1176m, 968m, 733s cm^{-1}. MS (ES^+): *m/z* 178 1 (MH^+).

(*R*)-*N*-Benzyl-{2-[(methylsulphanyl)methyl]butyl}amine

By the general procedure, with Me_2S_2 quench followed by column chromatography (30% diethyl ether in petrol) and Kugelrohr distillation (70 °C, 0.2 mbar) *N*-allyl-*N*-benzylamine gave the *title compound* as a colourless oil.

HRMS (EI): $C_{13}H_{21}NS$ requires *m/z* 223.1394; found 223.1414. $[\alpha]_D^{30}$ -8.0 (c 0.85, $CHCl_3$) for a sample of 54% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (5H, m), 3.80 (2H, s), 2.66 (2H, d, *J* = 5.9 Hz), 2.57 (2H, dd, *J* = 6.6 Hz, 5.2 Hz), 2.10 (3H, s), 1.72 (1H, septet, *J* = 6.6 Hz), 1.47 (3H, m), 0.91 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.9 (s), 128.6 (d), 128.3 (d), 127.1 (d), 54.4 (t), 52.0 (t), 39.9 (d), 37.7 (t), 24.6 (t), 16.5 (q), 11.2 (q) ppm. IR (film): 3024 w, 2958 s, 2913 s, 1602 w, 1493 s, 1453 s cm^{-1}. MS (ES^+): *m/z* 224.2 (MH^+).

Enantiomeric excess determined by HPLC analysis of the 1-naphthoyl amide derivative on a Chiralcel OD-H column, 1ml/min, 8% isopropanol in hexane, retention times: 12.1 (major) and 13.4 minutes.

N-Benzhydryl-N-{2-[(methylsulphanyl)methyl]butyl}amine

By the general procedure, with Me_2S_2 quench followed by column chromatography (10% diethyl ether in petrol) and Kugelrohr distillation (135 °C, 0.2 mbar) *N*-allyl-*N*-benzhydrylamine gave the *title compound* as a colourless oil.

HRMS (EI): $C_{16}H_{26}NS$ requires *m/z* 300.1786; found 300.1792. $[\alpha]_D^{20}$ -3.8 (c 1.5, $CHCl_3$) for a sample of 39% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 7.20 - 7.45 (10H, m), 4.82 (1H, s), 2.52 -2.68 (4H, m), 2.11 (3H, s), 1.70 (1H, septet, *J* = 5.8 Hz), 1.57 (1H, br s), 1.50 (2H, m), 0.89 (3H, t, *J* = 7.8 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4 (s), 128.5 (d), 127.3 (d), 126.9 (d), 67.8 (d), 50.6 (t), 40.0 (d), 37.7 (t), 24.4 (t), 16.3 (q), 11.1 (q). IR (film): 3057 w, 2958 s, 2913 s, 1597 m, 1491 s, 1452 s, 1262 m, 1108 s, 1076 m, 1028 s cm^{-1}. MS (ES^+): *m/z* 300.3 (MH^+). Enantiomeric excess determined by HPLC analysis of the benzoyl amide derivative on a Chiralcel OD-H column 1ml/min 2% isopropanol in hexane, retention times: 12.8 (major) and 13.9 minutes.

(*R*)-N-Methyl-N-(2-methylbutyl)-N-phenylamine

Using the general method (EtMgCl in THF, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (petrol) and Kugelrohr distillation (85 °C, 0.7 mbar, lit[33] b.p. 131-2, 16 mbar) *N*-allyl-*N*-methyl-*N*-phenylamine (147 mg, 1 mmol) gave the *title compound* (113 mg, 64%) as a colourless oil.

Anal.: Calcd for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90%. Found: C, 81.29; H, 10.97; N, 7.76%. HRMS (EI): $C_{12}H_{19}N$ requires m/z 177.1517; found 177.1514. $[\alpha]_D^{20}$ -4.1 (c 4.2, EtOH) for a sample of 37% e.e. (*S*)-Enantiomer has a reported[33] rotation of $[\alpha]_D^{15}$ +11.06 (neat). ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (2H, m), 6.75 (3H, m), 3.43 (1H, dd, *J* = 14.6, 6.8 Hz), 3.02 (3H, s), 1.91 (1H, m), 1.54 (1H, m), 1.20 (1H, m), 1.00 (3H, t, *J* = 7.4 Hz), 0.97 (3H, d, *J* = 6.6 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.8 (s), 129 2 (d), 115.7 (d), 111.9 (d), 59.7 (t), 39.5 (q), 34.0 (d), 27.4 (t), 17.3 (q), 11.6 (q) ppm. IR (film):2955s, 2870s, 1598s, 1506s, 1461m, 1371m, 1242m, 1087m, 990m, 746s, 691s cm^{-1}. MS (EI): *m/z* 177 (M^+, 8%) , 149 (8), 120 (100).

(*R*)-N-Methyl-N-{2-[(methylsulphanyl)methyl]butyl}-N-phenylamine

By the general procedure, with Me_2S_2 quench followed by column chromatography (2% diethyl ether in petrol) and Kugelrohr distillation (150 °C, 0.2 mbar) *N*-allyl-*N*-methyl-*N*-phenylamine gave the *title compound* as a colourless oil.

HRMS (EI): $C_{13}H_{21}NS$ requires m/z 223.1394; found 223.1396. $[\alpha]_D^{30}$ -4.5 (c 2.8, $CHCl_3$) for a sample of 20% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (2H, m), 6.76 (2H, d, *J* = 9.0 Hz), 6.70 (1H, tt, *J* = 7.2, 1.2 Hz), 3.43 (1H, dd, *J* = 14.7, 7.8 Hz), 3.23 (1H, dd, *J* = 14.7, 6.9 Hz), 2.99 (3H, s), 2.57 (2H, d, *J* = 5.7 Hz), 2.11 (3H, s), 2.04 (1H, m), 1.49 (2H, m), 0.98 (3H, t, *J* = 7.2 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.8 (s), 129.3 (d), 116.1 (d), 112.2 (d), 56.4 (t), 39.6 (d), 38.6 (d), 37.0 (t), 24.2 (t), 16.7 (q), 11.2 (q) ppm. IR (film): 2959 (s), 2873 (s), 1598 (s), 1504 (s), 1462 (m), 1373 (m), 1277 (m), 1213 (m), 1034 (m), 992 (m) cm^{-1}. MS (EI): *m/z* 223 (M^+, 24%), 121 (15), 120 (100), 105 (5), 104 (5), 77 (9). Enantiomeric excess determined by HPLC on Chiralcel OD-H column, 1ml/min 2% isopropanol in hexane, retention times 6.0 and 6.5 (major) minutes, and on a Chiralcel OB-H column, 1ml/min 2% isopropanol in hexane, retention times 7.8 (major) and 9.4 minutes.

(*R*)-4-Benzyl-1-(2-methylbutyl) piperidine

Using the general method (EtMgCl in diethyl ether, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (50% diethyl ether in petrol) and Kugelrohr distillation (135 °C, 1 mbar) 1-allyl-4- benzylpiperidine (215 mg, 1 mmol) gave the *title compound* (197 mg, 83%) as a colourless oil.

HRMS (FAB): $C_{17}H_{28}N$ (MH^+) requires *m/z* 246.2221; found 246.2216. $[\alpha]_D^{21}$ -5.1 (c 1.6, EtOH) for a sample of 60% e.e. $[\alpha]_D^{21}$ +8.5 (c 3.3, EtOH) for a sample prepared from (*S*)-2-methyl-1-butanol as detailed below. ^1H NMR (300 MHz, $CDCl_3$): δ 7.31 (2H, t, *J* = 6.8 Hz), 7.20 (3H, m), 2.85 (2H, m), 2.56 (2H, d, *J* = 6.8 Hz), 2.14 (1H, dd, *J* = 11.9, 6.6 Hz), 2.05 (1H, dd, *J* = 12.1, 7.5 Hz), 1.82 (2H, dq, *J* = 11.9, 2.2

Hz), 1.57 (2H, m), 1.35 (6H, m,), 1.05 (3H, d, *J* 6.5 Hz), 0.91 (3H, t, *J* = 6.9 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1 (s), 129.3 (d), 128.3 (d), 125.8 (d), 66.1 (t), 54.9 (t), 54.4 (t), 43.5 (t), 38.3 (d), 32.5 (d), 29.1 (t), 18.1 (q), 11.6 (q) ppm. IR (film): 3062m, 3026m, 2955s, 2918s, 1604w, 1495m, 1463m, 1453s cm^{-1}. MS (EI): *m/z* 245 (M^+, 5%), 188 (100), 91 (12), 44 (7).

(*R*)-2-[(4-Benzylpiperidino)methyl]-1-butanol

By the general procedure, with oxygen quench followed by column chromatography (diethyl ether) and Kugelrohr distillation (200 °C, 1 mbar) 1-allyl-4-benzylpiperidine gave the *title compound* as a colourless oil

Anal: Calcd for $C_{17}H_{27}NO$: C, 78.11; H, 10.41; N, 5.36%. Found: C, 78.06; H, 10.55; N, 5.26%. HRMS (EI) $C_{17}H_{27}NO$ requires *m/z* 261.2092; found 261.2096. $[\alpha]_D^{20}$ -20.4 (c 2.5, EtOH) for a sample of 63% e.e. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (2H, tt, *J* = 6.8, 1.3 Hz), 7.17 (3H, m), 3.77 (1H, dt, *J* = 10.5, 3.0 Hz), 3.47 (1H, t, *J* = 10.3 Hz), 3.19 (1H, d, *J* = 11.4 Hz), 2.84 (1H, d, *J* = 11.4 Hz), 2.52 (2H, d, *J* = 7.0 Hz), 2.44 (1H, t, *J* = 2.7 Hz), 2.36 (1H, t, *J* = 12.5 Hz), 2.06 (2H, td, *J* = 11.6, 2.2 Hz), 1.87 (1H, m), 1.68 (2H, m), 1.53 (1H, m), 1.27 (2H, m), 1.08 (2H, q, *J* = 6.8 Hz), 0.89 (3H, t, *J* = 7.7 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7 (s), 129.3 (d), 128.4 (d), 126.0 (d), 69.8 (t), 65.8 (t), 56.3 (t), 53.0 (t), 43.2 (t), 38.0 (d), 37.4 (d), 32.7 (t), 32.1 (t), 23.1 (t), 12.0 (q). IR (film): 3268m, 3083m, 3025m, 2918s, 1603w, 1494m, 1377m, 1128m cm^{-1}. MS (EI): *m/z* 261 (M^+, 5%), 189 (22), 188 (100), 91 (12). Enantiomeric excess determined by HPLC on Chiralpak AD column, 1ml/min, 10% ethanol in hexane, retention times 5.4 (major) and 9.4 minutes.

(*R*)-1-(2-Methylbutyl)-4-phenylpiperazine

Using the general method (EtMgCl in diethyl ether, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (50% diethyl ether in petrol) and Kugelrohr distillation (190 °C, 1.0 mbar) 1-allyl-4- phenylpiperazine (202 mg, 1 mmol) gave the *title compound* (195 mg, 84%) as a colourless oil.

HRMS (EI): $C_{15}H_{24}N_2$ requires *m/z* 232.1939; found 232.1945. $[\alpha]_D^{25}$ -4.8 (c 1.5, EtOH) for a sample of 61% e.e. $[\alpha]_D^{21}$ +7.6 (c 2.5, EtOH) for a sample prepared from (*S*)-2-methyl-1-butanol as detailed below. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (2H, t, *J* = 9.1 Hz), 6.94 (2H, dd + fs, *J* = 7.7, 1.1 Hz), 6.85 (1H, tt, *J* = 7.2 Hz), 3.20 (4H, t, *J* = 5.1 Hz), 2.57 (2H, apparent d, *J* = 4.4 Hz), 2.56 (2H, apparent d, *J* = 4.6 Hz), 2.23 (1H, dd, *J* = 12.1, 6.8 Hz), 2.13 (1H, dd, *J* = 11.9, 7.7 Hz), 1.61 (1H, br s), 1.49 (1H, m), 1.15 (1H, m), 0.92 (3H, d, *J* = 6.6 Hz), 0.91 (3H, t, *J* = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.7 (s), 129.3 (d), 119.7 (d), 116.2 (d), 65.6 (d), 53.8 (t), 49.4 (t), 32.1 (d), 28.0 (t), 18.1 (q), 11.6 (q) ppm. IR (liq. film): 3036w, 2956s, 2813s, 1600s, 1502s, 1453m, 1378m, 1232s cm^{-1}. MS (EI): *m/z* 232 (M^+, 28%), 176 (18), 175 (100), 132 (22),105 (8), 77 (7), 70 (23).

(*R*)-2-[(4-Phenylpiperazino)methyl]-1-butanol

By the general procedure, with oxygen quench followed by column chromatography (50 - 100% diethyl ether in petrol) and Kugelrohr distillation (129 - 130 °C, 1 mbar) 1-allyl-4-phenylpiperazine gave the *title compound* as a white solid. The racemic compound had m.p. 70 – 71 °C (recrystallised from diethyl ether).

Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.53; H, 9.75; N, 11.28%. Found: C, 72.13; H, 9.84; N, 11.14%. HRMS (EI): $C_{15}H_{24}N_2O$ requires *m/z* 248.1888; found 248.1891. $[\alpha]_D^{20}$ -22.2 (c 2.1, EtOH) for a sample of 61% e.e. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (2H, t, *J* = 8.5 Hz), 6.89 (3H, m), 3.79 (1H, dt, *J* = 10.5, 2.4 Hz), 3.53 (1H, t, *J* = 10.3 Hz), 3.20 (4H, m), 2.87 (2H, m), 2.54 (4H, m), 1.94 (1H, m), 1.14 (2H, quin., *J* = 6.8 Hz), 0.93 (3H, t, *J* = 7.0 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.2 (s), 129.3 (d), 120.1 (d), 116.4 (d), 69.7 (t), 65.4 (t), 53.9 (t), 49.4 (t), 37.4 (d), 23.0 (t), 12.0 (q) ppm. IR (film): 3404s, 2960s, 2874s, 1600s, 1495m, 1453s, 1364m , 1206m, 1098s , 1045s cm^{-1}. MS (EI): *m/z* 248 (M^+, 25%) , 176 (15) , 175 (100) , 132 (14) , 70 (15). Enantiomeric excess determined by HPLC on a Chiralcel OD-H column, 1ml/min 10% ethanol in hexane, retention times 11.6 (major) and 12.6 minutes.

(*R*)-2-Methylbutan-1-ol and (*R*)-2-methylbutyl (4-methylbenzene)sulphonate

(*R*)-2-Methylbutan-1-ol was prepared from allyl alcohol by the general procedure described above with protic quench, except that solvent was removed from the crude product by atmospheric pressure distillation. Kugelrohr distillation at atmospheric pressure gave the title alcohol contaminated with small amounts of solvent. Enantiomeric excess determination was carried out by formation of the (α-methoxy, α-trifluoromethyl)phenyl esters (Mosher's esters).[34] To obtain a pure product the alcohol was derivatised as the 4-methylbenzenesulphonate *in situ:*

To a solution of allylalcohol (580 mg, 10 mmol, 1.0 eq) and the zirconium catalyst **7** (194 mg, 4 mol %) in diethyl ether (20 mL) under argon, was added ethylmagnesium chloride (2.0 M in diethyl ether, 30 mL, 60 mmol, 6.0 eq) dropwise at 0 °C. The resultant dark yellow suspension was allowed to stir at room temperature overnight. The reaction mixture was cooled to 0 °C and water (20 mL) followed by 2 M HCl (20 mL) cautiously added. The aqueous layer was extracted with diethyl ether (3 x 30 mL) and the combined organic phases washed with brine (2 x 50 mL) and dried over $MgSO_4$. The solution was filtered, and concentrated to ca 50 mL by distillation through a vacuum jacketed Dufton column. The resulting solution of 2-methyl-butanol was cooled to 0 °C and pyridine (20 mL) added followed by portionwise addition of 4-methylbenzene sulphonylchloride (5.72 g, 30 mmol, 3.0 eq). The pale yellow solution was allowed to warm to room temperature and stirred overnight before pouring into 2 M HCl (100 mL) and diethyl ether (50 mL). The organic phase was separated and washed with 2 M HCl (50 mL), saturated sodium bicarbonate solution (3 x 50 mL), water (3 x 100 mL) and brine (3 x 100 mL). The solvent was removed *in vacuo* and the crude residue redissolved in THF (30 mL) and *N,N*-dimethyl-ethyldiamine (3.52 g, 40 mmol) added in order to react with the excess toluene sulphonylchloride. The mixture was stirred for 1 h before diethyl ether (50 mL) was added and the organic phase washed with 6 M HCl (5 x 30 mL), dried over $MgSO_4$ and the solvents removed *in vacuo* to give a crude yellow oil. Purification by column chromatography (15 % EtOAc, petrol) afforded (2*R*)-2-methylbutyl (4-methylbenzene)sulphonate as a colourless oil (1.32 g, 80 %). Data consistent with the literature.[19] $[\alpha]_D^{22}$ -2.5 (c 3.35, $CHCl_3$) for a sample of 54% e.e. (from Mosher's ester analysis of alcohol). Literature[19] $[\alpha]_D^{21}$ -4.7 (c 1.06, $CHCl_3$) for pure (*R*)-enantiomer.

(*R*)-1-[(2-Methylbutoxy)methyl]benzene

Using the general method (EtMgCl in diethyl ether, 4 mol% **7** as catalyst), quenching with water, followed by column chromatography (5% diethyl ether in petrol) and Kugelrohr distillation (120 °C, 50 mbar) allyl benzyl ether (148 mg, 1 mmol) gave the *title compound* (96 mg, 54%) as a colourless oil. Spectral data consistent with the literature.[19]

$[\alpha]_D^{21}$ -2.8 (c 2.2, $CHCl_3$) for a sample of 65% e.e. Literature[19] $[\alpha]_D^{21}$ -4.5 (c 3.23, $CHCl_3$) for (*R*)-enantiomer.

(*S*)-2-(Benzyloxymethyl)-1-butanol

By the general procedure, with oxygen quench followed by column chromatography (50% diethyl ether in petrol) and Kugelrohr distillation (130 °C, 1 mbar) allyl benzyl ether gave the *title compound* as a colourless oil. Spectral data consistent with the literature.[20]

$[\alpha]_D^{20}$ +3.3 (c 1.1, EtOH) and -11.6 (c 1.2, $CHCl_3$) for a sample of 81% e.e. Seebach reports[20] the (*R*)-enantiomer (≈ 91% e.e., but not proven) of the *title compound* has $[\alpha]_D^{RT}$ +3.2 (c 3.10, $CHCl_3$), consistent with our configuration, if not e.e. For comparison there are many reports[35] on the rotation of (*R*)-3-benzyloxy-2-methyl-1-propanol, consistently -4 in EtOH and +17 in $CHCl_3$.

Enantiomeric excess was determined by HPLC on Chiralpak AD column, 220nm detection, 1ml/min, 2% isopropanol in hexane, retention times 17.6 (major) and 18.3 minutes.

(*R*)-Phenyl(2-methylbutyl)sulphide.

Using the general method followed by column chromatography (5% diethyl ether in petrol) and Kugelrohr distillation (60 °C, 1 mbar) gave the *title compound* as a colourless oil. Spectral data consistent with the literature.[21] $[\alpha]_D^{22}$ -9.2 (c 2.5, $CHCl_3$) for a sample of 46% e.e. Literature[21] $[\alpha]_D^{22}$ -24.9 (c 1.24, $CHCl_3$) for (*R*)-enantiomer. Enantiomers separable by GC on FS-hydrodex-β-3p column (Machery-Nagel), 25 m x 0.25 mm x 0.25 μm, flow rate of 2 mL/min, at 110 °C, retention times = 27.3 (major) and 27.8 min. Injection of pure (*S*)-phenyl(2-methylbutyl)sulphide (prepared from (*S*)-2-methyl-1-butanol) confirmed the second (minor peak) as being the (*S*) enantiomer.

2-Ethyl-4-phenyl-1-butanol

By the general procedure, with oxygen quench followed by column chromatography (20% diethyl ether in petrol), 4-phenyl-1-butene gave the *title compound* as a colourless oil.

HRMS (EI): $C_{12}H_{18}O$ requires *m/z* 178.1358; found 178.1359. $[\alpha]_D^{20}$ -1.7 (c 1.8, EtOH) for a sample of 10% e.e. ^1H NMR (300 MHz, $CDCl_3$): δ 7.27(5H, m), 3.54 (2H, d, *J* = 5.1 Hz), 2.65 (2H, t, *J* = 8.1 Hz), 1.6 (3H, m), 1.48 (1H, s), 1.45(2H, m), 0.95 (3H, t, *J* = 7.3Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.9 (s), 128.5 (d), 125.8 (d), 65.1 (t), 41.7 (d), 33.3 (t), 32.5 (t), 23.4 (t), 11.4 (q). IR (film): 3404s (br), 2930s, 1603m, 1495m, 1452m, 1043m cm^{-1}. MS (EI): *m/z* 178 (M^+, 21%), 160 (15), 131 (52, 117 (24), 104 (100), 91 (84). Enantiomeric excess determined by HPLC on Chiralcel OD-H column, 210nm detection, 1ml/min, 3% isopropanol in hexane, retention times 8.4 (major) and 9.1 minutes.

Preparation of samples of known absolute stereochemistry from (S)-2-methyl-1-butanol.

4-Benzyl-1-[(2*S*)-2-methylbutyl]piperidine

To a solution of 4-benzylpiperidine (5.25 g, 30 mmol, 2.5 eq) in dry DMF (20 mL) was added (*S*)-2-methylbutyl methanesulphonate[36] (2.00 g, 12 mmol, 1.0 eq) and the mixture allowed to stir at 85 °C in a sealed flask under argon for 72 h. The reaction mixture was poured into saturated sodium bicarbonate solution (50 mL) and the aqueous phase extracted with diethyl ether (3 x 50 mL). The organic phases were combined and washed with water (4 x 100 mL) and brine (4 x 100 mL) before the organic phase was dried over $MgSO_4$ and the solvents removed *in vacuo* to give a crude yellow oil. Purification by column chromatography (20 % ethylacetate / petrol) and Kugelrohr distillation (130 °C, 0.3 mm Hg) afforded the *title compound* as a colourless oil (1.886 g, 64 %). $[\alpha]_D^{26}$ +8.5 (c = 3.32, EtOH).

In a similar way (*S*)-1-(2-methylbutyl)-4-phenylpiperazine ($[\alpha]_D^{21}$ +7.6 (c 2.5, EtOH)) and (*S*)-*N*-(2-methylbutyl)-*N*-phenylamine ($[\alpha]_D^{20}$ +15.8 (c 0.52, EtOH)) were prepared.

(*S*)-*N*-Benzyl-*N*-(2-methylbutyl)amine ($[\alpha]_D^{21}$ +14.2 (c 1.2, EtOH)) and (*S*)-*N*-cyclohexyl-*N*-(2-methylbutyl)amine ($[\alpha]_D^{21}$ +18.1 (c 0.8, EtOH)) were prepared by the displacement of the ammonium hexafluorophoshonate salt of (*S*)-2-methylbutan-1-ol by benzylamine and cyclohexylamine in DMF at 80 °C according to a literature method.[37]

ACKNOWLEDGEMENTS

We thank Zeneca Fine Chemicals Manufacturing Organisation, Grangemouth and the EPSRC 'Catalysts and processes initiative' (GR/K71127) and 'Asymmetric synthesis LINK program' for funding this work. We acknowledge the use of the EPSRC chemical database service at Daresbury.[38] We also thank Dr. Chris Cerrarelli (Zeneca Pharmaceuticals, Wilmington, USA) for *X*-ray analysis, Dr. John Blacker, Dr. Ben Mellor, and Caroline Trainor, (Zeneca process studies group, Huddersfield) for preparing quantities of the ligand **5**, and Dr John Langley for mass spectra.

REFERENCES AND NOTES.

1. Dzhemilev, U. M.; Vostrikova, O. S.; Sultanov, R. M. *Izv. Akad. Nauk SSSR, Ser. Kim.* **1983**, 218. Dzhemilev, U. M.; Vostrikova, O. S. *J. Organomet. Chem.* **1985**, *285*, 43.
2. Lewis, D. P.; Muller, P. M.; Whitby, R. J.; Jones, R. V. H. *Tetrahedron Lett.* **1991**, *32*, 6797. Lewis, D. P.; Whitby, R. J.; Jones, R. V. H. *Tetrahedron* **1995**, *51*, 4541.
3. Takahashi, T.; Seki, T.; Nitto, Y.; Saburi, M.; Rousset, C. J.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 6266.
   Rousset, C. J.; Negishi, E. I.; Suzuki, N.; Takahashi, T. *Tetrahedron Lett.* **1992**, *33*, 1965.
   Knight, K. S.; Waymouth, R. M. *J. Am. Chem. Soc.* **1991**, *113*, 6268.
4 (a) Hoveyda, A. H.; Xu, Z. M. *J. Am. Chem. Soc.* **1991**, *113*, 5079.
   (b) Hoveyda, A. H.; Morken, J. P.; Houri, A. F.; Xu, Z. M. *J. Am. Chem. Soc.* **1992**, *114*, 6692.
   (c) Hoveyda, A. H.; Morken, J. P. *J. Org. Chem.* **1993**, *58*, 4237.
   (d) Houri, A. F.; Didiuk, M. T.; Xu, Z. M.; Horan, N. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6614.
5. Dzhemilev, U. M. *Tetrahedron* **1995**, *51*, 4333.
   Knight, K. S.; Wang, D.; Waymouth, R. M.; Ziller, J. *J. Am. Chem. Soc.* **1994**, *116*, 1845.
   Uesaka, N.; Mori, M.; Okamura, K.; Date, T. *J. Org. Chem.* **1994**, *59*, 4542.
   Takahashi, T.; Kotora, M.; Kasai, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2693.
   Negishi, E.; Montchamp, J.; Anastasia, L.; Choueiry, D. *Tetrahedron Lett.* **1998**, 2503.
   Knight, K. S.; Waymouth, R. M. *Organometallics* **1994**, *13*, 2575.
   Takahashi, T.; Kondakov, D. Y.; Suzuki, N. *Organometallics* **1994**, *13*, 3411.
   Suzuki, N.; Kondakov, D. Y.; Takahashi, T. *J. Am. Chem. Soc.* **1993**, *115*, 8485.
   Takahashi, T.; Kondakov, D. Y.; Suzuki, N. *Chem. Lett.* **1994**, 259.
6. Asymmetric addition / elimination of alkylmagnesium halides to allylic ethers using **1a** or **b**:
   Morken, J. P.; Didiuk, M. T.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6997.
   Morken, J. P.; Didiuk, M. T.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 3123;
   Didiuk, M. T.; Johannes, C. W.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7097;
   Visser, M. S.; Hoveyda, A. H. *Tetrahedron* **1995**, *51*, 4383.
   Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 3779.
   Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291.
   Asymmetric 2-aluminoethylalumination of alkenes using **7**: Dawson, G.; Durrant, C. A.; Kirk, G. G.; Whitby, R. J.; Jones, R. V. H.; Standen, M. C. H. *Tetrahedron Lett.* **1997**, *38*, 2335.
   Asymmetric co-cyclisation of 1,n-dienes using BuMgCl and **1**: Yamaura, Y.; Hyakutake, M.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 7615.
7. Bell, L.; Whitby, R. J.; Jones, R. V. H.; Standen, M. C. H. *Tetrahedron Lett.* **1996**, *37*, 7139. Jones, R. V. H.; Standen, M. C. H.; Whitby, R. J.; Bell, J. L. International patent WO 96/25420, publication date 22.08.96.
8. Hoveyda, A. H.; Morken, J. P. *Angew. Chem., Int. Ed. Engl.* **1996**, 35, 1263.
9. Wild, F. R. W. P.; Wasiucionek, M.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1985**, *288*, 63.
   Schafer, A.; Karl, E.; Zsolnai, L.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1987**, *328*, 87.
10. Grossman, R. B.; Doyle, R. A.; Buchwald, S. L. *Organometallics* **1991**, *10*, 1501.
11. Diamond, G. M.; Rodewald, S.; Jordan, R. F. *Organometallics* **1995**, *14*, 5.
    Diamond, G. M.; Jordan, R. F.; Petersen, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 8024.
    Chin, B.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 2267.
12. Erker, G.; Aulbach, M.; Knickmeier, M.; Wingbermuhle, D.; Kruger, C.; Nolte, M.; Werner, S. *J. Am. Chem. Soc.* **1993**, *115*, 4590.

13. Halterman, R. L.; Vollhardt, K. P. C.; Welker, M. E.; Blaser, D.; Boese, R. *J. Am. Chem. Soc.* **1987**, *109*, 8105.
14. Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.
15. Paquette, L. A.; Sivik, M. R.; Bzowej, E. I.; Stanton, K. J. *Organometallics* **1995**, *14*, 4865 and references therein.
Halterman, R. L.; Tretyakov, A. *Tetrahedron* **1995**, *51*, 4371.
Halterman, R. L.; Vollhardt, K. P. C. *Tetrahedron Lett.* **1986**, *27*, 1461.
Rousset, C. J.; Iyer, S.; Negishi, E. *Tetrahedron-Asymmetry* **1997**, *8*, 3921.
16. Burk, M. J.; Colletti, S. L.; Halterman, R. L. *Organometallics* **1991**, *10*, 2998.
Rheingold, A. L.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Organometallics* **1992**, *11*, 1869.
Hollis, T. K.; Rheingold, A. L.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Organometallics* **1992**, *11*, 2812.
Chen, Z. L.; Halterman, R. L. *J. Am. Chem. Soc.* **1992**, *114*, 2276.
Chen, Z. L.; Halterman, R. L. *Organometallics* **1994**, *13*, 3932.
Halterman, R. L.; Combs, D.; Kihega, J. G.; Khan, M. A. *J. Organomet. Chem.* **1996**, *520*, 163.
17. Lund, E. C.; Livinghouse, T. *Organometallics* **1990**, *9*, 2426.
18. Erker, G.; Berg, K.; Treschanke, L.; Engel, K. *Inorg. Chem.* **1982**, *21*, 1277. This paper mentions formation of $CpZrCl_3.2THF$, but with no details. $CpZrCl_3.2THF$ has been used in the formation of mixed metallocenes (e.g. Paquette, L. A.; Moriarty, K. J.; Meunier, P.; Gautheron, B.; Sornay, C.; Rogers, R. D.; Rheingold, A. L. *Organometallics* **1989**, *8*, 2159) but we are not aware of a published procedure for its synthesis.
19. White, J. D.; Johnson, A. T. *J. Org. Chem.* **1994**, *59*, 3347.
20. Sefkow, M.; Neidlein, A.; Sommerfeld, T.; Sternfeld, F.; Maestro, M.A.; Seebach. D. *Leibigs Ann. Chem.* **1994**, 719.
21. Mori, K.; Kuwahara, S.; Ueda, H. *Tetrahedron* **1983**, *39*, 2439.
22. Skoog, D. A.; West, D. M. *Analytical Chemistry: An Introduction*; 4th ed.; Saunders College Publishing: London, 1986.
23. Anderson, R. A.; Wilkinson, G. *Inorganic Synthesis* **1979**, *19*, 262.
24. Vogel, A. I. *Quantitative Inorganic Analysis*; 3rd ed.; Longmans: London, 1961.
25. Lipton, M.F.; Sorenson, C. M.; Sadler, A. C.; Shapiro, R. H. *J. Organomet. Chem.* **1980**, *186*, 155.
26. *Preparative Polar Organometallic Chemistry 2*, L. Brandsma, Springer-Verlag, 1990.
27. Gathergood, N. G.; Whitby, R. J. paper in preparation.
28. Beholze, L. G.; Stille, J. R. *J. Org. Chem.* **1993**, *58*, 5095.
29. Lemaire-Audoire, S.; Savignac, M.; Dupuis, C.; Genet, J. P. *Bull. Chem. Soc. Fr.* **1995**, *132*, 1157.
30. Griller, D.; Nonhebel, D. C.; Walton, J. C. *J. Chem. Soc., Perkin trans 2* **1983**, 1373.
31. Prasad, R. N.; Hawkins, L. R.; Tietje, K. *J. Med. Chem.* **1968**, *11*, 1144.
32. Adler, S.; Haskelberg, L.; Bergmann, F. *J. Chem. Soc.* **1940**, 576.
33. Jones, H. O. *J. Chem. Soc.* **1905**, *87*, 135.
34. Spinella, A.; Alvarez, L. A.; Cimino, G. *Tetrahedron* **1993**, *49*, 3203.
35. Beilstein database BS9802AB, © Beilstein Chemiedaten und Software GmbH, Beilstein Institute fuer Literatur der Organischen Chemie.
36. Brookhart, M.; Liu, Y. M,; Goldman, E. W.; Timmers, D. A.; Williams, G. D. *J. Am. Chem. Soc.* **1991**, *113*, 927.
37. Castro, B.; Selve, C. *Bull. Soc. Chim. Fr.* **1971**, 4368.
38. Fletcher, D. A.; McMeeking, R. F.; Parkin, D. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 746.