Indian Journal of Chemistry
Vol. 46B, September 2007, pp. 1475-1482

Synthesis of a new series of chiral tri- and tetradentate ligands and their application in titanium-catalyzed pinacol coupling reaction

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Received 27 December 2006; accepted (revised) 8 June 2007

A variety of chiral tridentate and tetradentate ligands, related to each other through stereoelectronic relationship have been synthesized. Homochiral diols and amino alcohols have been used for this purpose. Titanium complexes of these ligands have been prepared and examined for enantioselective pinacol coupling reaction.

Keywords: Asymmetric catalysis, chiral ligands, resolution, titanium complex, pinacol coupling

The most important aspect of asymmetric catalysis lies in the design of a proper complex, which consists of two parts — a metal atom and a chiral ligand. Fulfilling all the basic criteria of a "stable" complex does not always serve the demand of a successful catalyst. A rational design relies more on the ligand framework than on anything else[1]. In fact, ligands are the only means to transmit information from a chiral to a prochiral center. The role of the coordinating atoms for the effective functioning of a catalyst is note-worthy. Firstly, a good chelation inhibits aggregation, a very common phenomenon encountered in organometallics. Secondly, the coordinating atom tunes the Lewis acidity of a central metal atom. Thus, the reactivity of a complex changes on changing the coordinating atoms, that is, control of electronic factors. The sterics of a ligand can be controlled by the position and nature of the substituents. Crowding in the vicinity of a chiral center does not always prove better[2]. Thus, a proper balance of both steric and electronic factors may lead to an effective catalyst. To verify all the above facts, one needs a series of ligands, which will be related to each other through defined stereoelectronic relationships (**Figure 1**).

A class of tetradentate ligands (**L7**) had been utilized earlier for enantioselective pinacol coupling reaction[3]. In continuation of the study on low valent chiral titanium complexes, several new chiral ligands (L1-L6) have now been prepared. The present manuscript describes the synthesis of these ligands and their titanium complexes.

Results and Discussion

A series of homochiral ligands with rational variation of steric and electronic properties have been prepared as shown in **Figure 2**.

To prepare the [O,O,O] and [O,O,O,O] coordinating ligands, three homochiral diols **1-3** were chosen. The diols **1** and **3** were prepared according to literature procedure[4,5]. The diol **2** and the aminoalcohol **5** were obtained through chemical resolution described elsewhere[6]. As an alkylating agent, a protected benzyl chloride **7** was prepared in three steps from salicylaldehyde and used for alkylation of the diols (**Scheme I**).

Alkylation of **1** with **7** required prior protection of the primary OH group as THP ether. Monoalkylation of **3** was possible under phase transfer condition at RT. Dialkylation was achieved under more rigorous condition as described in **Scheme II**.

Three homochiral amino alcohols **4-6** were chosen to prepare the [O,N,O] tridentate hemi-SALEN ligands. Amino alcohol **4** was prepared according to the literature procedure[7]. Although **6** has been obtained earlier through the conversion of homochiral *erythro* isomer[8], the *threo* isomer we resolved using *S*-(+)-pyroglutamic acid. These amino alcohols were then reacted with salicylaldehyde to obtain the corresponding Schiff bases. A series of hemi SALEN and SALEN-type ligands **8-16** were thus obtained (**Figure 3**).

Preparation of the corresponding titanium complexes required slightly different procedures for each class of ligands. For ligands **8-13**, an azeotropic

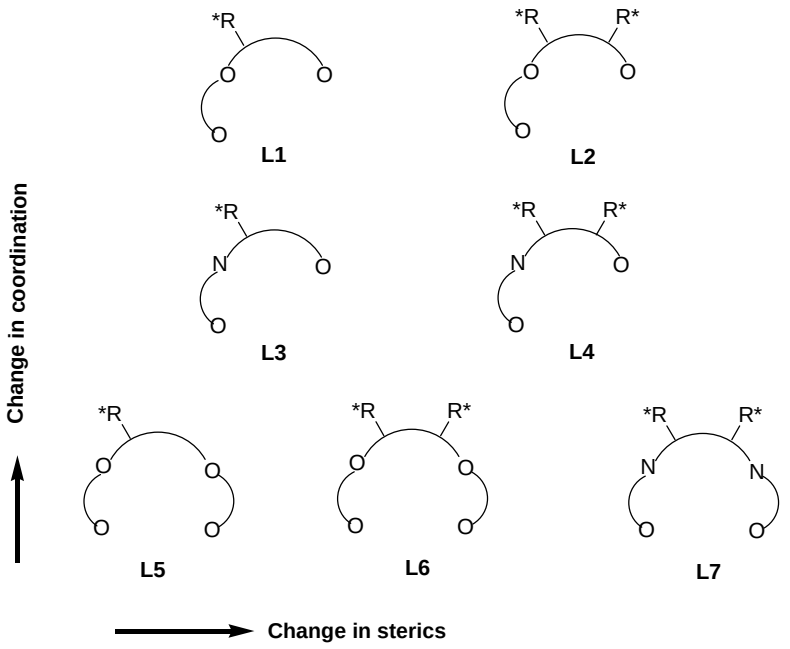


Figure 1 — Logic of the designed ligands.

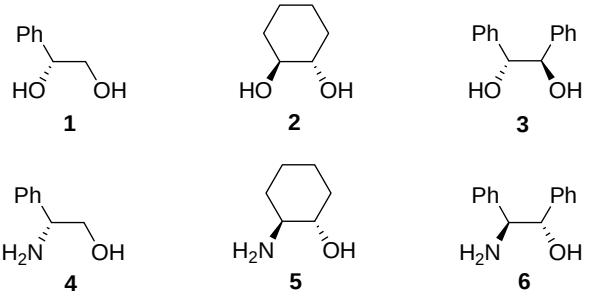
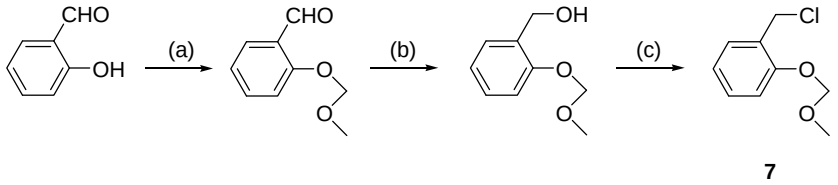


Figure 2 — Various diols and amino alcohols used to prepare the ligands

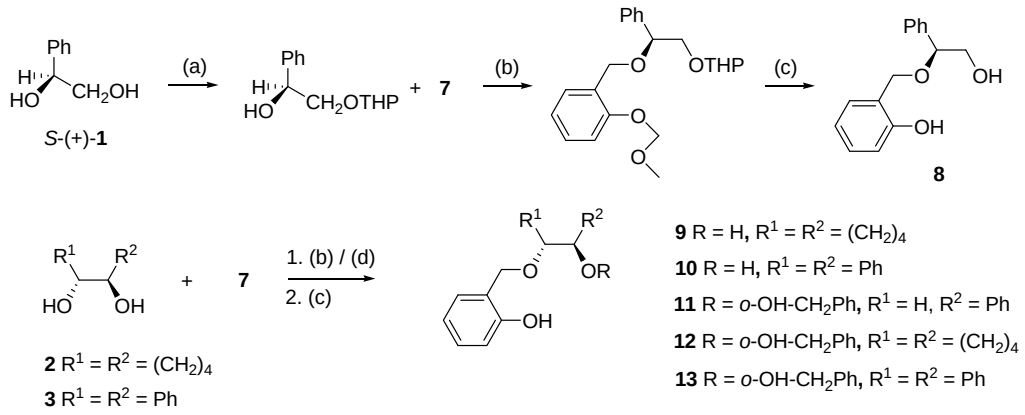


Scheme I — Reagents and conditions: (a) NaH, THF/DMF, MOMCl; (b) $NaBH_4$, H_2O; (c) PPh_3, CCl_4.

removal of isopropanol was required prior to the treatment with trimethylsilylchloride. The Ti-complexes were yellow to red in colour and the stability increased from **8** to **13**. Quantitative yields were obtained in most cases (**Table I**).

The above-described complexes were evaluated for enantioselective pinacol coupling reaction using benzaldehyde as the model substrate, zinc as the co-reductant, trimethylsilylchloride as the catalyst-regenerator and acetonitrile as the solvent. The reactions were carried out with 10 mol% catalyst loading at RT. As can be seen from the results depicted in **Table II**, poor diastereoslectivity was realized for all the catalysts. Surprisingly, the only catalyst that functioned for this reaction, was the one derived from 1,2-diamino- cyclohexane[3].

It is believed from the present results that pinacol coupling with the system involves two ketyl radicals attached to two different titanium centers. Such an arrangement will require a monomeric complex with



Scheme II — Reagents and conditions: (a) DHP, PPTS, DCM; (b) NaH, TBAI (cat.) THF; (c) ^{i}PrOH/THF (1:1), conc. HCl (cat.); (d) i) NaOH/K_2CO_3, TBABr (cat.).

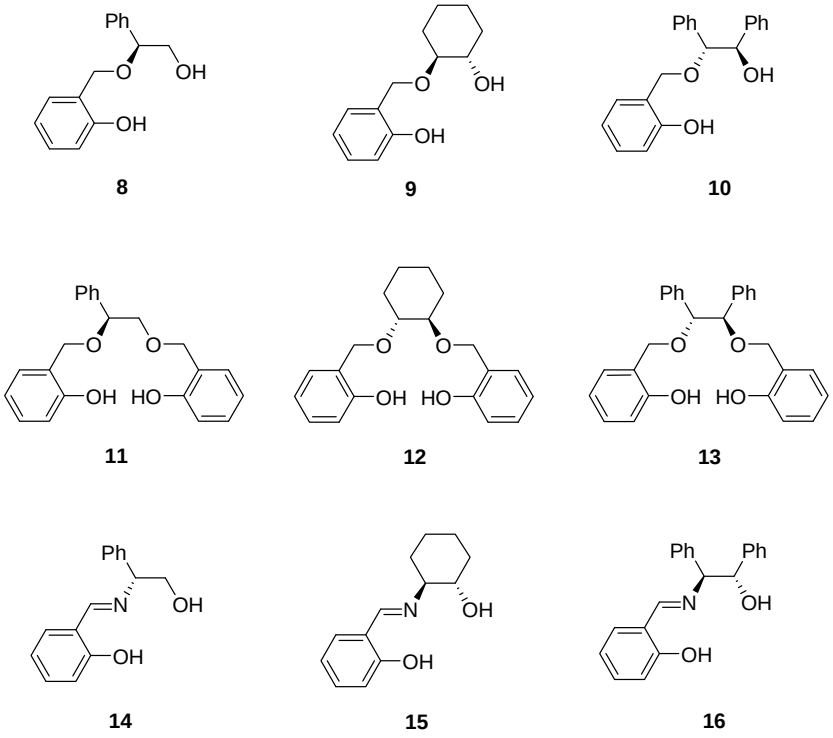


Figure 3 — Family of tri- and tetradentate ligands.

minimum steric hindrance around the reaction site (**Figure 4**). Such is the case with entry 9 (**Table II**), where best diastereoslection was realized. However, the factors responsible for enantioselection will require further investigations.

Experimental Section

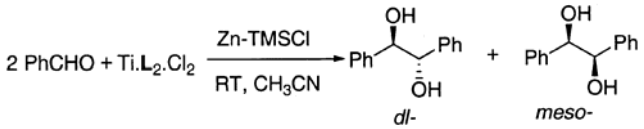
^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and the chemical shift values were reported in ppm downfield to TMS ($\delta = 0$) for ^{1}H and relative to the central $CDCl_3$ resonance ($\delta = 77$) for ^{13}C NMR on AC 200 or DRX 500 MHz spectrometer. The abbreviations s, bs, d, t, q and m refer to the singlet, broad singlet, doublet, triplet, quartet and multiplet respectively. Melting points were determined on Yamaco micro melting point apparatus and are uncorrected. Optical rotations were measured with a Bellingham and Stanley ADP220 digital polarimeter using a sodium lamp ($\lambda = 589$ nm) at 24°C. IR spectra were recorded in Shimadzu FTIR-8400 spectrometer with NaCl optics. Thin layer chromatography (TLC) were run on 0.25 mm aluminium backed E-Merck silica gel plates ($60F_{254}$) and UV light/I_2/anisaldehyde

Table I — Synthesis of titanium complexes and their characterization

Entry	Ti-complex	m.p., °C	$[\alpha]_D$ (°)
1	Ti-**8**	200-240	–33.3 (c 0.2, $CHCl_3$)
2	Ti-**9**	>300	+7.5 (c 0.15, $CHCl_3$)
3	Ti-**10**	220-280	+142.9 (c 0.21, $CHCl_3$)
4	Ti-**11**	a	b
5	Ti-**12**	c	c
6	Ti-**13**	200-220	+90 (c 0.2, $CHCl_3$)
7	Ti-**14**	235-238	+228.5 (c 0.07, $CHCl_3$)
8	Ti-**15**	230-235	+168.7 (c 0.15, $CHCl_3$)
9	Ti-**16**	225-230	–159 (c 0.2, $CHCl_3$)

(a) Did not melt, but decomposed at 280°C; (b) Too dark coloured to measure rotation; (c) Very hygroscopic, melts in range (100-200°C).

Table II — Pinacol coupling reaction with benzaldehyde



Entry	Ligand	Yield[a], %	*dl:meso*[b]
1	**8**	65	44:55
2	**9**	94	52:48
3	**10**	76	60:40
5	**11**	76	50:50
6	**12**	91	53:47
7	**13**	71	50:50
8	**14**	65	46:64
9	**15**	86	91:9[c]
10	**16**	76	50:50

[a]Isolated and purified; [b] Determined by ^{1}H NMR; [c] Racemic product.

were used for visualization. All solvents and reagents were purified and dried according to procedures given in D. D. Perin's *Purification of Laboratory Reagents*. All reactions were carried out under argon atmosphere using freshly distilled solvents under anhydrous conditions, unless otherwise specified. Yields refer to isolated product, purified by chromatography or distillation.

Preparation of 1-chloromethyl-2-methoxymethoxy-benzene, 7

A. Preparation of (2-methoxymethoxy-phenyl)-methanol: To a suspension of NaH (4.8 g, 110 mmol) in a mixture of THF/DMF (50 mL each) under argon atmosphere was added salicylaldehyde (10.6 mL, 100 mmol) dropwise at 0°C. Immediately, a vigorous reaction started and the evolution of the H_2 gas was monitored through a bubbler. When the rate slowed

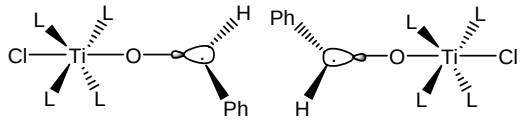


Figure 4 — Possible mode of coupling

down, the reaction mixture was brought to RT and stirred for half an hour. Methoxymethylenechloride (8.3 mL, 110 mmol) was added to it dropwise at 0°C. The reaction mixture was stirred at RT for another half an hour till the completion of the reaction (TLC). Water (10 mL) was added to the reaction mixture cautiously, keeping the heterogeneous reaction mixture in an ice-bath. $NaBH_4$ (4.8 g, 120 mmol) was added portionwise while the colour of the reaction mixture changed from yellow to white. After 15 min when the TLC showed the disappearance of the aldehyde, water (~200 mL) was added to the reaction mixture, and the reaction mass was extracted with ether (3×50 mL). The combined organic layer was washed with brine (1×20 mL) and kept over anhydrous Na_2SO_4. On evaporation of the solvent (2-methoxymethoxy-phenyl)-methanol was obtained as a colourless liquid (17.5 g, quantitative); IR (neat): 3407, 1458 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3H, OCH_3), 4.70 (s, 2H, CH_2Ph), 5.23 (s, 2H, CH_2), 6.98-7.11 (m, 2H, H_{Ar}), 7.22-7.32 (m, 2H, H_{Ar}).

B. Chlorination of (2-methoxymethoxy-phenyl)-methanol: The above alcohol (3.36 g, 20 mmol) was placed in a single necked round bottom flask. Freshly distilled dry CCl_4 (40 mL) was introduced. PPh_3 (5.7 g, 22 mmol) was added in a single lot and the reaction mixture was stirred at RT. After dissolution of the solid material, dry pyridine (2 mL, 25 mmol) was added to the reaction mixture and stirring was continued for 8 hr at RT. When the starting material disappeared (TLC), petroleum ether (100 mL) was added and the solid material was triturated. After allowing the solid to settle down, the supernant solvent was decanted off slowly. This procedure was repeated three more times. The combined organic layer was conentrated on a rotary evaporator. The resulting liquid (some solid may appear) was distilled in a kugelrohr to obtain a colourless liquid. This liquid was further purified by chromatography using 100-200 mesh neutral silica gel and petroleum ether as an eluent to obtain **8** (2.52 g, 68%) as a colourless liquid; b.p. 160°C at 4 mm of Hg; IR (neat): 2956, 2850, 1492 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.49 (s, 3H, OCH_3), 4.66 (s, 2H, CH_2Ph), 5.23 (s, 2H, CH_2), 6.96-

7.11 (m, 2H, H_{Ar}), 7.25-7.33 (m, 2H, H_{Ar}); ^{13}C NMR ($CDCl_3$): δ 41.6, 56.1, 94.0, 114.1, 121.7, 126.4, 129.9, 130.5, 154.8. Anal. Calcd. for $C_9H_{11}O_2Cl$: C, 57.91; H, 5.95. Found C, 58.24; H, 5.85%.

Preparation of (*S*)-2-(2-Hydroxy-1-phenylethoxymethyl)-phenol, 8

A. Mono THP diol: To a solution of (*S*)-(+)-phenylethane-1,2-diol (Ref. 4) (2.76 g, 20 mmol) and PPTS (0.5 g, 2 mmol) in freshly distilled dry DCM (20 mL) was added DHP (2.0 mL, 22 mmol) at 0°C. Stirring was continued at that temperature for 6 hr and then at RT overnight. The reaction mixture was diluted with DCM and washed with saturated bicarbonate solution (2×20 mL). It was further washed with brine (1×10 mL) and kept over anhydrous Na_2SO_4. Finally, the monoprotected alcohol was purified by column chromatography over 100-200 mesh neutral silica gel using 15% EtOAc-petroleum ether as eluent (viscous liquid, 2.85 g, 64%); $[\alpha]_D$ = + 123.2° (*c* 4.4, $CHCl_3$); IR ($CHCl_3$): 3434, 2941, 1452 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.36-1.99 (m, 6H, C*H*$_2$), 3.38-4.08 (m, 4H, C*H*$_2$), 4.43-4.66 (m, 1H, C*H*Ph), 4.72-4.98 (m, 1H, C*H*), 7.20-7.44 (m, 5H, H_{Ar}); ^{13}C NMR ($CDCl_3$): δ 20.1, 25.1, 30.8, 63.6, 73.2, 75.8, 100.4, 126.2, 127.7, 128.3, 140.3.

B. Alkylation of the protected alcohol: To a suspension of NaH (0.68 g, 14.1 mmol) in THF (30 mL) was added the mono protected diol (2.85 g, 12.8 mmol) dissolved in THF (5 mL) under argon atmosphere. After the rate of hydrogen evolution slowed down, the benzyl chloride **7** (2.62 g, 14.1 mmol) dissolved in THF (5 mL) was added. TBAI (0.46 g, 1.2 mmol) was introduced directly into the reaction mixture. The reaction flask was purged thoroughly with argon and then the reaction mass refluxed for 4 hr till the starting alcohol disappeared (TLC). Most of THF was evaporated on a rotavapor, water (50 mL) was added carefully into the reaction mixture and the desired product was extracted with diethyl ether (3×30 mL). The combined ethereal layer was washed with brine (1×20 mL), and then kept over anhydrous Na_2SO_4. On concentration, a sticky mass was obtained which was purified by passing through a small bed of celite to remove inorganic impurities. The viscous liquid thus obtained was carried forward as such for the next step.

C. Deprotection of the MOM group: The above product (3.6 g) was dissolved in a mixed solvent of ^{i}PrOH-THF (20 mL, 1:1) and few drops of concentrated HCl was added to it. After 48 hr when the reaction went to completion (TLC), the reaction mixture was worked up in the usual way. The resulting diol **8** was purified by flash chromatography using 15% EtOAc-petroleum ether as eluent. It was further purified by crystallization from a mixture of petroleum ether and ethylacetate. White needles (1.3 g, 26% overall); m.p. 98-100°C; $[\alpha]_D$ = + 102° (*c* 1, EtOH); IR ($CHCl_3$): 3384, 2918, 1585 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.61 (bs, 1H, O*H*), 3.66-3.87 (m, 2H, C*H*$_2$), 4.47-4.79 (m, 3H, C*H*Ph), 6.78-7.02 (m, 3H, H_{Ar}), 7.17-7.48 (m, 6H, H_{Ar}) 7.61 (bs, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 66.9, 70.2, 82.9, 116.7, 120.0, 122.7, 127.0, 128.6, 128.8, 129.7, 137.4, 156.0. Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.74; H, 6.61. Found: C, 73.51; H, 6.58%.

Preparation of ligand (*S,S*)-2-(2-Hydroxy-cyclohexylmethyl)-phenol, 9

A. Alkylation of (*S,S*)-(+)-1,2-cyclohexanediol: Using a similar alkylation procedure as described for ligand **8**, (*S,S*)-(+)-1,2-cyclohexanediol **2** (Ref. 6) (1.16g, 10 mmol) was alkylated with benzyl chloride **7** (2.04 g, 11 mmol) at 60°C for 8 hr.

B. Deprotection of the MOM-ether: The resulting protected alcohol following the removal of inorganic impurities was dissolved in THF (14 mL) and a few drops of concentrated HCl was added to it. The homogeneous solution was stirred at RT for 24 hr till the starting material disappeared (TLC). Usual workup followed by flash chromatography using 230-400 mesh silica gel and 10% EtOAc-petroleum ether as eluent afforded the diol **9** which was further purified by crystallization from a mixture of petroleum ether–ethyl acetate. White solid (0.96 g, 64%); m.p. 130-132°C; $[\alpha]_D$ = +40.5° (*c* 1.21, $CHCl_3$); IR ($CHCl_3$): 3380, 3018, 2937, 1490 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.11-1.43 (m, 4H, C*H*$_2$), 1.59-1.81 (m, 2H, C*H*$_2$), 1.93-2.23 (m, 2H, C*H*$_2$), 2.96 (bs, 1H, O*H*), 3.17-3.36 (m, 1H, C*H*), 3.44-3.60 (m, 1H. C*H*), 4.68 (d, *J* = 11.2 Hz, 1H, C*H*$_2$Ph), 4.80 (d, *J* = 11.2 Hz, 1H, C*H*$_2$Ph), 6.77-6.95 (m, 2H, H_{Ar}), 7.01-7.28 (m, 2H, H_{Ar}), 7.96 (bs, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 23.9, 24.1, 29.7, 33.0, 70.7, 74.0, 84.0, 116.5, 119.8, 123.4, 129.0, 129.5, 156.0. Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.23; H, 8.18. Found: C, 69.82; H, 8.21%.

Preparation of ligand (*R,R*)-2-(2-Hydroxy-1,2-diphenyl-ethoxymethyl)-phenol, 10

A mixture of (*R,R*)-(+)-stilbene diol **3** (Ref. 5) (1.07 g, 5 mmol), NaOH (1 g, 25 mmol), K_2CO_3 (13.8 g, 100 mmol) and TBABr (0.34 g, 1 mmol) was crushed finely in a motar pestle. The fine powder was placed in a 50 mL round bottom flask and 25 mL DCM was added to it. Benzyl chloride **7** (1.3 g,

7 mmol) was introduced into the vigorously stirred suspension and stirring was continued till the diol disappeared on TLC (after 4 hr). The reaction mixture was diluted with DCM (20 mL) and then filtered. The organic layer was washed with brine (1×10 mL) and then kept over anhydrous Na_2SO_4. On evaporation of the solvent, a pasty mass (1.6 g) was obtained which was passed through a short bed of celite to remove inorganic impurities. The viscous liquid obtained was used as such for the next step.

Deprotection of MOM group was carried out as described above to obtain **10** as a viscous liquid, which solidified after keeping under vacuum for 1hr. The diol was purified by recrystallization from a mixture of petroleum ether-EtOAc to obtain a white solid (1.15 g, 72% overall); m.p. 121-123°C; $[\alpha]_D$ = –22.4° (*c* 2, EtOH); IR ($CHCl_3$): 3390, 1454, 1066 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.1 (bs, 1H, O*H*), 4.47 (d, *J* = 8.1 Hz, 1H, C*H*Ph), 4.55 (d, *J* = 11.5 Hz, 1H, CH_2), 4.62 (d, *J* = 11.5 Hz, 1H, CH_2), 4.82 (d, *J* = 8.1 Hz, 1H, C*H*Ph), 6.81-6.96 (m, 3H, H_{Ar}), 7.03-7.09 (m, 4H, H_{Ar}), 7.16-7.26 (m, 7H, H_{Ar}), 7.55 (bs, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 70.6, 78.5, 87.6, 116.7, 119.9, 122.9, 127.2, 127.7, 128.0, 128.1, 128.2, 128.9, 129.7, 136.9, 139.3, 156.1. Anal. Calcd. for $C_{21}H_{20}O_3$: C, 78.71; H, 6.30. Found: C, 78.19; H, 6.35%.

Preparation of *O,O'*-bis(2-hydroxyphenylmethyl)-phenyl-ethane diol, 11

To a suspension of NaH (0.58 g, 12 mmol) in THF (10 mL) was added (*S*)-(+)-1-phenyl-1,2-ethanediol **1** (Ref. 4) (1.07 g, 5 mmol) dissolved in 10 mL THF dropwise under argon atmosphere. The reaction mass was stirred for 1 hr. When the evolution of H_2 ceased, benzyl chloride **7** (2.23 g, 12 mmol) was introduced followed by TBAI (0.18 g, 0.5 mmol). The reaction flask was purged thoroughly with argon and then the reaction mass refluxed till the alcohol disappeared (TLC, 4 hr). After cooling, most of the THF was evaporated in rotavapour and 20 mL of water was added cautiously. The desired compound was extracted with ether (3×30 mL). The combined organic layer was washed with brine (1×20 mL) and then kept over anhydrous Na_2SO_4. After evaporating the organic solvent, a viscous liquid was obtained which was passed through a short pad of celite to remove inorganic impurities and the viscous liquid obtained was used as such for the next step.

Deprotection of the MOM group was carried out as described above. The resulting diol **11** was obtained as a colourless liquid after flash chromatography using 10% EtOAc - petroleum ether as eluent (1.35 g, 77% overall); $[\alpha]_D$ = + 53.3° (*c* 2.2, $CHCl_3$); IR ($CHCl_3$): 3382, 1490 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.60-3.64 (m, 1H, CH_2), 3.69-3.75 (m, 1H, CH_2), 4.50-4.83 (m, 5H, C*H*Ph), 6.78-7.04 (m, 6H, H_{Ar}), 7.11 (bs, 1H, O*H*), 7.18-7.41 (m, 7H, H_{Ar}), 7.59 (bs, 1H, –O*H*); ^{13}C NMR ($CDCl_3$): δ 70.1, 72.2, 74.0, 80.3, 116.7, 117.0, 120.0, 120.1, 122.1, 122.3, 127.0, 128.6, 128.8, 129.7, 129.8, 136.9, 155.9, 156.1. Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.40; H, 6.34. Found: C, 74.89; H, 6.42%.

Preparation of ligand *O,O'*-bis(2-hydroxyphenylmethyl)-1,2-cyclohexanediol, 12

According to the general procedure described for ligand **11**, (*R*,*R*)-(-)-1,2-cyclohexane diol **2** (0.81 g, 7 mmol) and benzyl chloride **7** (3.2 g, 17 mmol) after 12 hr of reflux followed by the deprotection in THF afforded ligand **12**. The ligand was further purified by recrystallization from a mixture of petroleum ether-diethyl ether to obtain a white solid (1.5 g, 65% overall); m.p. 74-76°C; $[\alpha]_D$ = –7.01° (*c* 1.14, $CHCl_3$); IR ($CHCl_3$): 3353, 2933, 1492 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.10-1.45 (m, 4H, CH_2) 1.61-1.74 (m, 2H, CH_2), 2.04-2.17 (m, 2H, CH_2), 3.35-3.47 (m, 2H, C*H*), 4.77 (s, 4H, CH_2Ph), 6.77-7.27 (m, 8H, H_{Ar}), 7.63 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$): δ 23.5, 29.7, 70.5, 81.6, 116.7, 119.9, 122.9, 128.4, 129.5, 156.0. Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.13; H, 7.38. Found: C, 73.30; H, 7.32%.

Preparation of *O,O'*-bis(2-hydroxyphenylmethyl)-1,2-diphenyl-ethanediol, 13

According to the general procedure described for ligand **11**, (*R*,*R*)-(+)-stilbene diol (1.07 g, 5 mmol) **3** and benzyl chloride **7** (2.6 g, 14 mmol) after 4 hr of reflux followed by deprotection in a mixed solvent of THF-^{i}PrOH afforded ligand **13**. The ligand was purified by recrystallization from a mixture of petroleum ether-ethyl acetate to obtain a white solid (1.6 g, 75% overall); m.p. 111-113°C; $[\alpha]_D$ = –40.0° (*c* 2, EtOH); IR ($CHCl_3$): 3388, 1454 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.52-4.67 (m, 6H, C*H*Ph), 6.79-6.88 (m, 4H, H_{Ar}), 6.94-7.03 (m, 6H, H_{Ar}), 7.16-7.24 (m, 8H, H_{Ar}), 7.64 (bs, 2H, O*H*); ^{13}C NMR ($CDCl_3$): δ 69.7, 85.6, 117.3, 120.1, 122.6, 127.8, 128.3, 128.4, 129.1, 129.8, 136.3, 156.0. Anal. Calcd. for $C_{28}H_{26}O_4$: C, 78.84; H, 6.16. Found: C, 78.72; H, 6.14%.

Preparation of (*R*)-(+)-2-[(2-Hydroxy-1-phenyl-ethylimino)-methyl]phenol, 14

To a solution of (*R*)-(-)-phenyl glycinol **4** (Ref. 7) (0.68 g, 5 mmol) in DCM (5 mL) was added salicylaldehyde (0.53 mL, 5 mmol) and $MgSO_4$ (1 g) at RT. The solution immediately turned yellow. Stirring was continued for 8 hr till the completion of the reaction (TLC). The reaction mixture was diluted with 10 mL of DCM and filtered. On concentration of the DCM layer, a yellowish solid **14** was obtained which was crystallized from a mixture of petroleum ether-ethyl acetate (1.0 g, 83%); m.p. 91-93°C; $[\alpha]_D$ = +109.24° (*c* 1.1, EtOH); IR ($CHCl_3$): 3421, 3016, 1629 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.62 (bs, 1H, O*H*), 3.90-3.96 (m, 2H, CH_2), 4.48 (t, *J* = 6.6 Hz, 1H, C*H*Ph), 6.88-6.92 (m, 1H, H_{Ar}), 6.97-6.99 (m, 1H, H_{Ar}), 7.24-7.42 (m, 7H, H_{Ar}), 8.49 (s, 1H, C*H*), 13.28 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 67.5, 75.6, 117.0, 118.7, 118.8, 127.1, 127.8, 128.8, 131.7, 132.6, 139.3, 161.0, 166.2. Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.65; H, 6.28; N, 5.81. Found: C, 75.01; H, 6.24; N, 5.76%.

Preparation of (*S,S*)-(+)-2-[(2-Hydroxycyclohexylimino)-methyl]-phenol, 15

Following a similar procedure as described for ligand **14**, (*S,S*)-(+)-2-aminocyclohexanol[6] (0.58 g, 5 mmol) and salicylaldehyde (0.53 mL, 5 mmol) after 6 hr afforded 0.95 g (87%) of ligand **15** as a yellow solid after crystallization from petroleum ether (0.95 g, 87%); m.p. 101-102°C; $[\alpha]_D$ = + 115.83° (*c* 1.2, MeOH); IR ($CHCl_3$): 3415, 2935, 1631 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.23-1.52 (m, 3H, CH_2), 1.55-1.93 (m, 4H, CH_2), 1.99-2.16 (m, 2H, CH_2, O*H*), 2.90-3.08 (m, 1H, C*H*), 3.55-3.74 (m, 1H, C*H*) 6.81-7.01 (m, 2H, H_{Ar}), 7.19-7.38 (m, 2H, H_{Ar}), 8.42 (s, 1H, C*H*), 13.30 (bs, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 24.0, 24.2, 32.6, 32.7, 73.1, 74.9, 116.9, 118.4, 118.5, 131.3, 132.2, 161.3, 165.0. Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.19; H, 7.83; N, 6.39. Found: C, 70.82; H, 7.88; N, 6.32%.

Preparation of (*S,S*)-(-)-2-[(2-Hydroxy-1,2-diphenylethyl-imino)-methyl]-phenol, 16

A Preparation of (±)-*trans*-2-amino-1,2-diphenyl-ethanol: The compound was prepared according to the reported literature procedure[8].

B. Resolution of (±)-*trans*-2-amino-1,2-diphenylethanol

i) Preparation of the diastereomeric salt: To a solution of (*S*)-(-)-Pyroglutamic acid (4.8 g, 37.2 mmol) in ethanol (30 mL) was added (±)-*trans*-2-amino-1,2-diphenylethanol (7.3 g, 34 mmol) in batches and the reaction mixture was heated to reflux for half an hour. After cooling, the crystallization commenced immediately. It was allowed to stand overnight at RT. The white crystals were collected by filtration and washed with cold EtOH (5 mL). The solid was dried in vacuum and further purified by recrystallization from the same amount of solvent (3.56 g, 31% overall); m.p. 198-20°C; $[\alpha]_D$ = –71.26° (*c* 2, H_2O).

ii) Hydrolysis of the salt: The solid (3.56 g) was dissolved in a minimum amount of water, cooled and basified with liquor NH_3. It was further stirred for half an hour before filtration. The white solid was washed with a minimum amount of cold water and then dried. Thus (*S,S*)-(-)-aminoalcohol **6** was obtained in good yield (2.1 g, 94% recovery, 29% overall); m.p. 114-115°C; (lit.[9a] 116.5-117°C); $[\alpha]_D$ = –124.2° (*c* 1.2, EtOH) [lit.[8] –124° (*c* 1.18, EtOH)].

C. Preparation of the Schiff base, 16: The aminoalcohol (*S,S*)-(-)-*trans*-2-amino-1,2-diphenyl-ethanol **6** (1.07 g, 5 mmol) and salicylaldehyde (0.53 mL, 5 mmol) were taken in EtOH (15 mL) and the mixture was refluxed gently for 15 min. On completion of the reaction (TLC), the solvent was removed under reduced pressure. A yellowish solid was obtained which was purified by crystallization from petroleum ether-ethyl acetate (1.3 g, 82%); m.p. 138-139°C; $[\alpha]_D$ = –98.18° (*c* 1.1, EtOH); IR ($CHCl_3$): 3421, 1629 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.43 (bs, 1H, O*H*), 4.42 (d, *J* = 7.4 Hz, 1H, C*H*Ph), 5.01 (d, *J* = 7.4 Hz, 1H, C*H*Ph), 6.82-7.04 (m, 2H, H_{Ar}), 7.08-7.4 (m, 12H, H_{Ar}), 8.42 (s, 1H, C*H*), 13.30 (bs, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 78.4, 81.1, 117.0, 118.7, 118.8, 127.0, 127.6, 127.8, 128.0, 128.3, 131.8, 132.7, 139.2, 140.0, 161.0, 166.7. Anal. Calcd. for $C_{21}H_{19}NO_2$: C, 79.46; H, 6.05; N, 4.41. Found: C, 79.60; H, 6.07; N, 4.49%.

General procedure for the preparation of titanium complexes

Method-A: This procedure was used for the preparation of Ti-**8** to Ti-**13**. To a solution of titanium tetraisopropoxide (5 mL of 1 M solution in toluene, 5 mM) was added the ligand (5 mM) dissolved in dichoromethane (20 mL). The resulting homogeneous solution was stirred for 1 hr at RT. Most of the dichloromethane was then removed by distillation (bath temperature <70°C. The residue was treated dropwise with TMSCl (1.26 mL, 10 mM). After stirring for 1 hr at RT, all the solvent was stripped off under reduced pressure, and the residue was dried at 50°C for 1 hr under high vacuum.

Method-B: This procedure was adapted for T-**15**, Ti-**16** and Ti-**17**. To a solution of titanium tetraisopropoxide (5 mL of 1 M solution in toluene, 5

mM) was added the ligand (5 mM) dissolved in toluene or dichoromethane (5 mL). The resulting homogeneous solution was stirred at RT till the ligand was consumed (monitored by TLC). It was then treated dropwise with TMSCl (1.26 mL, 10 mM). The solvent was removed under reduced pressure, the residue triturated with anhydrous ether, and dried at 50°C for 1 hr under high vacuum.

Pinacol coupling: Following the procedure described earlier[3], the reaction was carried out using various titanium complexes as the catalysts.

Conclusion

In conclusion, a new series of tri and tetradentate chiral ligands with hemi-SALEN or SALEN type structures have been prepared. It is believed that these ligands and their derivatives will be useful for several metal-catalyzed enantioselective transformations.

Acknowledgements

The authors are thankful to Department of Science and Technology for financial support of the research, and A.C. is grateful to CSIR for a Research Fellowship.

References

1 (a) Tomioka K, *Synthesis* **1990**, 541; (b) Morrison J D, *Asymmetric Synthesis*, Vol 5 (Academic Press Inc., London) **1985**; (c) Seyden-Penne J, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, (John Wiley and Sons, New York) **1995**.

2 (a) Cozzi P G, *Chem Soc Rev* 33, **2004**, 410; (b) Larrow J F & Jacobsen E N, *Top Organomet Chem* 6, **2004**, 123; (c) Bandini M, Cozzi P G & Umani-Ronchi A, *Chem Commun* **2002**, 919; (d) Atwood D A & Harvey M J *Chem Rev* 101, **2001**, 37; (e) Canali L & Sherrington D C, *Chem Soc Rev* 28, **1999**, 85.

3 Chatterjee A, Bennur T H, Joshi N N, *J Org Chem* 68, **2003**, 5668.

4 King R B, Bakos J, Hoff C D & Marko L, , *J Org Chem* 44, **1979**, 1729.

5 Dietl F, Merz A & Tomahogh R, *Tetrahedron Lett* 23, **1982**, 5255.

6 Chatterjee A, Sasikumar M & Joshi N N, *Synthetic Commun* (in press).

7 McKenno M J & Meyers A I, *J Org Chem* 58, **1993**, 3568.

8 Lyle G G & Lacroix W, *J Org Chem* 28, **1963**, 900.