Research paper

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Chiral C_2-Symmetric η^6-*p*-cymene-Ru(II)-phosphinite Complexes: Synthesis, and Catalytic Activity in Asymmetric Reduction of Aromatic, Methyl Alkyl and Alkyl/Aryl Ketones

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Abstract

Chiral C_2-symmetric bis(phosphinite) ligands and their binuclear ruthenium(II) complexes have been synthesized and used as catalysts in the ruthenium-catalyzed asymmetric transfer hydrogenation of aromatic, methyl alkyl and alkyl/aryl ketones using 2-propanol as both the hydrogen source and solvent in the presence of KOH. Under optimized conditions, all complexes showed high catalytic activity as catalysts in the reduction of various ketones to corresponding chiral secondary alcohols. Products were obtained with high conversions (99%) and moderate to good enantioselectivities (82% *ee*). Furthermore, C_2-symmetric bis(phosphinite) ligands and their binuclear ruthenium(II) complexes were characterized by multinuclear NMR spectroscopy, FT-IR spectroscopy, LC/MS-MS and elemental analysis.

Keywords: Ruthenium(II), C_2-symmetry, phosphinite, asymmetric transfer hydrogenation, ketones.

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1. Introduction

After many decades of intensive investigations, the preparation and study of the coordination chemistry of the optically pure phosphorus based ligands such as phosphine[1], phosphinite[2-4] and phosphite[5] have received renewed attention due to their unique catalytic performances. Phosphorus based ligands are highly versatile ligands with applications ranging from cluster chemistry[6], bioinorganic chemistry[7], and homogeneous asymmetric catalysis[8, 9] to materials sciences[10]. Among chiral ligands, C_2-symmetric ligands have been dominated in asymmetric catalysis for a long time[11]. Many improved C_2-symmetric phosphinite ligands have important applications in organometallic chemistry and asymmetric catalysis[11, 12], giving selective catalysts for asymmetric transfer hydrogenation reactions [4, 13-17]. Phosphinites can be used to fine tune the metal reactivity and selectivity, so use of phosphinites are widespread in organometallic chemistry and in homogeneous catalysis.

Metal-catalyzed asymmetric transfer hydrogenations without doubt represent a powerful and practical method for the reduction of pro-chiral ketones to produce the corresponding optically pure secondary alcohols, which are important class of intermediates for the fine chemicals especially pharmaceutical[18], agrochemical[19], cosmetic, food and flavour industries[20, 21]. A number of transition metal complexes are known to be used in asymmetric transfer hydrogenation (ATH) reactions as catalysts [22]. Over the last two decades, a considerable amount of effort has been devoted to the design and synthesis of new chiral ligands bearing Ni(II)[22], Fe[23], Ru(II)[17], Rh(I)[13, 24] and Ir(III)[14, 25] complexes. Among the well-known transition metals used in homogeneous catalysis ruthenium is the most prominent one. The choice of ruthenium among other metals in hydrogenation catalysis is due to its superior performances in terms of selectivity and activity. In particular chiral C_2-symmetric structures represent an important class of ligands used in homogeneous asymmetric catalysis with transition metals[11].

Recently, our research group has been attracted by the obvious advantages and aesthetics of C_2- symmetry. Previously, we have reported that the novel half-sandwich complexes based on the ligands with C_2-symmetric P-O backbone are active catalysts in the reduction of pro-chiral aromatic, methyl alkyl and alkyl/aryl ketones [25, 26]. In this context, herein we present the synthesis and characterization of new chiral C_2-symmetric bis(phosphinite) ligands and their half sandwich η^6-*p*-cymene-Ru(II)-phosphinite complexes as well as their activities explored as catalysts for the asymmetric transfer hydrogenation of aromatic, alkyl methyl or alkyl/aryl ketones.

2. Experimental

2.1. Materials and Methods

Unless otherwise mentioned, all reactions were carried out under an atmosphere of argon using conventional Schlenk glassware, Solvents were dried using established procedures and distilled under argon just prior to use. The starting materials D-phenyl alaninol, D-phenyl glycinol, (R)-(−)-1-Amino-2-propanol, (*R*)-(-)-2-amino-1-butanol, PPh_2Cl, Et_3N and $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-}Cl)Cl]_2$ were purchased from Fluka and used as received. 2,6-bis-(bromomethyl)pyridine or 1,3-bis(bromomethyl)benzene, chiral C_2-symmetric amino alcohols (**1**-**6**) [27] and bis(phosphinite) ligands (**9**-**12**) [12] were synthesized according to the literature procedures. ^1H (at 400.1 MHz), ^{13}C (at 100.6 MHz) and $^{31}P\text{-}\{^1H\}$ NMR (at 162.0 MHz) spectra were recorded on a Bruker AV 400 spectrometer, with TMS (tetramethylsilane) as an internal reference for ^1H NMR and ^{13}C NMR or 85% H_3PO_4 as an external reference for $^{31}P\text{-}\{^1H\}$ NMR, respectively. FTIR-ATR spectra were recorded with a Perkin Elmer Spectrum 100 spectrometer. Mass analyses were recorded with Shimadzu LC/MS 8040 spectrometer. Specific rotations were taken on a Perkin-Elmer 341 model polarimeter. Elemental analysis was carried out on a Costech ECS 4010 instrument. Melting points were recorded by a Gallenkamp Model apparatus with

open capillaries. GC analyses were performed on a Shimadzu GC 2010 Plus Gas Chromatograph equipped with a cyclodex-B (Agilent) capillary column (30 m x 0.32 mm I.D. x 0.25μm film thickness). Racemic samples of alcohols were obtained by reduction of the corresponding ketones with $NaBH_4$ and used as the authentic samples for %*ee* determination. The GC parameters for asymmetric transfer hydrogenation of ketones were as follows; initial temperature, 50 ºC; initial time 1.1 min; solvent delay, 4.48 min; temperature ramp 1.3 ºC/min; final temperature, 150 ºC; initial time 2.2 min; temperature ramp 2.15 ºC/min; final temperature, 250 ºC; initial time 3.3 min; final time, 44.33 min; injector port temperature, 200 ºC; detector temperature, 200 ºC, injection volume, 1.0 μL.

2.2. Synthesis

2.2.1. General procedure for the preparation of the chiral C_2-symmetric amino alcohols (7,8)

Corresponding chiral amino alcohol (30 mmol), 1,3-bis(bromomethyl)benzene (15 mmol, 3.96 g), sodium carbonate (46 mmol, 4.86 g) and KI (0.050 g) in EtOH (50 mL) were stirred at 100 ^oC for 12 h under argon. The mixture was allowed to cool room temperature and $CHCl_3$ (100 mL) was then added to the mixture and refluxed for another 2 h. The solution was filtered, solvent was removed in vacuo and $CHCl_3$ (50 mL) was added to the residue. The solution was washed with water and brine (50 mL) twice. The aqueous solution was extracted with $CHCl_3$ (2x50 mL). The combined $CHCl_3$ phases were dried over anhydrous Na_2SO_4.

2.2.1.1. (2R)-2-[benzyl({[3-({benzyl[(2R)-1-hydroxybutane-2-yl]amino} methyl) phenyl] methyl}) amino]- butane-1-ol (7)

Prepared from (2*R*)-2-(benzylamino)-butan-1-ol (30 mmol, 5.38 g) to the general procedure **2.2.1.** The crude product **7** was obtained as yellow oil (6.0 g, 87%) ^oC; $[\alpha]_D^{20}$: -56.5 (c:1, CH_2Cl_2); Anal.Calcd. for $C_{30}H_{40}O_2N_2$: C: 78.22; H: 8.75; N: 6.08. Found: C: 78.01; H: 8.54; N: 5.92; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.33-7.17 (m, 14H, $C_6\underline{H}_5$); 3.84 (m, 4H, -$C\underline{H}_2$N-); 3.53-3.87 (m,

2H, -C<u>H</u>$_2$OH (b)); 3.40-3.47 (m, 2H, -C<u>H</u>$_2$OH (a)+4H, -C<u>H</u>$_2$Ph); 3.22 (br, 2H, O<u>H</u>); 2.75-2.72 (m, 2H, N-C<u>H</u>); 1.77-1.87 (m, 2H, -C<u>H</u>$_2$CH$_3$ (a)); 1.23-1.31 (m, 2H, -C<u>H</u>$_2$CH$_3$ (b)) 0.93 (t, 6H, *J*=7.50 Hz -CH$_2$C<u>H</u>$_3$). ^{13}C-NMR (δ ppm, $CDCl_3$): 139.70, 139.37, (*i*-<u>C</u>$_6$H$_5$); 127.20, 127.89, 128.48, 128.64, 129.03, 129.65 (<u>C</u>$_6$H$_5$); 60.95 (-N<u>C</u>H-); 60.56 (-<u>C</u>H$_2$OH); 53.20, 53.42(-<u>C</u>H$_2$Ph, -<u>C</u>H$_2$N-); 17.99 (-<u>C</u>H$_2$CH$_3$); 11.99 (-CH$_2$<u>C</u>H$_3$); IR (KBr pellet, cm^{-1}) υ(OH): 3426; υ(CH): 3060, 3027, 2960, 2930; υ(C=C): 1494, 1452, 1421.

2.2.1.2. (2R)-2-[benzyl({[3-({benzyl[(1R)-2-hydroxy-1-phenylethyl]amino}methyl)phenyl]methyl}) amino]-2-phenyl ethane-1-ol (8)

Prepared from (2*R*)-2-(benzylamino)-2-phenylethane-1-ol (30 mmol, 6.81 g) according to the general procedure **2.2.1.** The crude product **8** was obtained as yellow oil (8.0 g, 96 %); $[\alpha]_D^{20}$: -153.5 (c 1, CH_2Cl_2); Anal.Calcd. for $C_{38}H_{40}O_2N_2$: C: 81.98; H: 7.24; N: 5.03. Found: C: 81.67; H: 7.03; N: 4.91; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.25-7.48 (m, 24H, C$_6$<u>H</u>$_5$); 4.15-4.20 (m, 2H, C<u>H</u>$_2$OH (b)); 3.93-4.00 (m, 4H, -C<u>H</u>$_2$Ph+2H, C<u>H</u>Ph); 3.65 (m, 2H, -C<u>H</u>$_2$OH (a)); 3.22-3.17 (m, 4H, -NC<u>H</u>$_2$); 3.08 (br, 2H, -CH$_2$O<u>H</u>).^{13}C-NMR (δ ppm, $CDCl_3$): 135.23, 139.15, 139.60 (*i*-<u>C</u>$_6$H$_5$); 127.26, 127.89, 128.03, 128.28, 128.41, 128.59, 128.74, 128.95, 129.37 (<u>C</u>$_6$H$_5$); 63.31 (-<u>C</u>HPh); 60.62 (-<u>C</u>H$_2$OH); 53.56, 53.77 (-<u>C</u>H$_2$N+(-<u>C</u>H$_2$Ph); IR (KBr pellet, cm^{-1}) υ(OH): 3419; υ(CH): 3060, 3027, 2834; υ(C=C): 1493, 1451, 1420.

2.2.2. General procedure for the synthesis of the chiral *C*$_2$-symmetric bis(diphenylphosphinite) ligands (13-16).

To a solution of aminoalcohol **5-8** (1.5 mmol) in dry toluene (20 mL) was added triethylamine (3.0 mmol, 0.31 g) and the mixture was stirred for 10 min under argon atmosphere. To this solution was added dropwise monochlorodiphenylphosphine, Ph_2PCl (3.0 mmol, 0.68 g). The mixture was then stirred at room temperature until the reactions were completed. A white precipitate of triethylamine hydrochloride was removed by filtration under argon and the

remaining organic phase was evaporated under reduced pressure to produce a white viscous oily product. The phosphinite ligands were observed to be stable in the ambient air.

2.2.2.1. (2*R*)-2-[benzyl({[6-{[benzyl[(1*R*)-2-[(diphenylphosphanyl)oxy]-1-phenylethyl]amino} methyl)pyridin-2-yl]methyl})amino]-2-phenylethyldiphenylphosphinite] (13)

Prepared from chiral amino alcohol **5** (1.5 mmol, 0.84 g) according to the general procedure **2.2.2.** White viscous oily product **13** (1.3 g, 94%). Anal. Calcd. for $C_{61}H_{57}N_3O_2P_2$; C 79.11; H 6,21; N 4.54, Found; C 79.01; H 6.08; N 4.42; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.20-7.39 (m, 43H, aromatic protons); 4.42 (m, 2H, -C$\underline{H}_2$OP (b)); 4.18-4.25 (m, 2H, C$\underline{H}_2$OP (a),+2H, -NC$\underline{H}$); 3.91 (m, 4H, -NC$\underline{H}_2$Py); 3.52 (m, 4H, -NC$\underline{H}_2$Ph). ^{13}C-NMR (δ ppm, $CDCl_3$): 137.29, 139.72, 141.80, 159.53, (*i*-carbons); 126.92, 127.41, 128.22, 128.30, 128.81, 128.11, 129.29, 130.20, 130.41, 130.51, 130.54, 130.73 (aromatic carbons); 69.53 (d, *J*=18,1 Hz, -$\underline{C}$H$_2$OP); 63.48 (d, *J*=8.1 Hz, -N$\underline{C}$H); 56.22 (-N$\underline{C}$H$_2$Py); 55.04 (-N$\underline{C}$H$_2$Ph); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 114.51 (s, O-$\underline{P}$(Ph)$_2$) **(Fig S1)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3058, 3025, 2934; υ(C=N): 1589; υ(C=C): 1493, 1454, 1434; υ(O-P): 1022.

2.2.2.2. (2*R*)-2-[benzyl({[6-({benzyl[(2*R*)-1-[(diphenylphosphanyl)oxy]butane-2-yl]amino} methyl)pyridin-2-yl]methyl})amino]butyldiphenylphosphinite (14)

Prepared from chiral amino alcohol **6** (1.5 mmol, 0.69 g) according to the general procedure **2.2.2.** White viscous oily product **14** (1.18 g, 95 %). Anal.Calcd. for $C_{53}H_{57}N_3O_2P_2$; C 76.70; H 6.93; N 5.06; Found; C 76.52; H 6.75; N 4.93; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.21-7.54 (m, 33H, aromatic protons); 4.04 (m, 2H, -C$\underline{H}_2$OP (a)); 3.81-3.97 (m, 4H, -NC$\underline{H}_2$Py+2H, -C$\underline{H}_2$OP (b)); 3.66 (m, 4H, -NC$\underline{H}_2$Ph); 2.86 (m, 2H, -C$\underline{H}$CH$_2$CH$_3$); 1.72 (m, 2H, -C$\underline{H}_2$CH$_3$ (a)); 1.58 (m, 2H, -C$\underline{H}_2$CH$_3$ (b)); 0.97 (t, 6H, *J*=7.2 Hz -CH$_2$C$\underline{H}_3$). ^{13}C-NMR (δ ppm, $CDCl_3$): 160.05 (*i*-pyridine); 142.02 (d, *J*=18,1 Hz, *i*-OP$\underline{C}_6$H$_5$); 136.69 (*i*-$\underline{C}_6$H$_5$); 120.30, 126.72, 128.12, 128.30, 128.36, 128.49, 128.82, 129.17, 129.65, 130.29, 130.44, 130.50, 130.65 (aromatic carbons); 69.57 (d,

J=17,1 Hz, -$\underline{C}H_2OP$); 60.88 (d, *J*=9.1 Hz-$\underline{C}HCH_2CH_3$); 56.09 (-$N\underline{C}H_2Py$); 55.09 (-$N\underline{C}H_2Ph$); 21.11 (-$\underline{C}H_2CH_3$); 11.88 (-$CH_2\underline{C}H_3$); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 115.02 (s, O-$\underline{P}(Ph)_2$) **(Fig S2)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3034, 3022, 2944; υ(C=N): 1575; υ(C=C): 1483, 1444, 1424; υ(O-P): 1026.

2.2.2.3. (2*R*)-2-[benzyl({[3-({benzyl[(2*R*)-1-[(diphenylphosphanyl)oxy]butane-2-yl]amino} methyl) phenyl]methyl})amino]butyldiphenylphosphinite (15)

Prepared from chiral amino alcohol **7** (1.5 mmol, 0.69 g) according to the general procedure **2.2.2.** White viscous oily product **15** (1.15 g, 93 %). Anal.Calcd. for $C_{54}H_{58}N_2O_2P_2$; C 78.24; H 7.06; N 3.38; Found; C 78.08; H 6.94; N 3.18; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.24-7.59 (m, 34H, aromatic protons); 4.01 (m, 4H, -$C\underline{H}_2OP$); 3.87 (m, 4H, -$NC\underline{H}_2Py$); 3.70 (m, 4H, -$NC\underline{H}_2Ph$); 2.87 (m, 2H, -$C\underline{H}CH_2CH_3$); 1.66 (m, 2H, -$C\underline{H}_2CH_3$ (b)); 1.57 (m, 2H, -$C\underline{H}_2CH_3$ (a)); 0.98 (t, 6H, *J*= 7.2 Hz -$CH_2C\underline{H}_3$). ^{13}C-NMR (δ ppm, $CDCl_3$): 140.41, 140.71, 142.05, 142.23 (*i*-carbons); 126.67, 127.34, 128.13, 128.34, 128.41, 128.81, 129.32, 129.42, 130.33, 130.48, 130.54, 130.70 (aromatic carbons); 69.51(d, *J*=17,1 Hz, -$\underline{C}H_2OP$); 59.74 (d, *J*= 8.1 Hz-$\underline{C}HCH_2CH_3$); 54.37 (-$N\underline{C}H_2Py$); 54.27 (-$N\underline{C}H_2Ph$); 21.83 (-$\underline{C}H_2CH_3$); 11.76 (-$CH_2\underline{C}H_3$); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 114.17 (s, O-$\underline{P}(Ph)_2$) **(Fig S3)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3377, 3057, 2961; υ(C=C): 1493, 1452, 1438; υ(O-P): 1027.

2.2.2.4. (2R)-2-[benzyl({[3-({benzyl[(1R)-2-[(diphenylphosphanyl)oxy]-1-phenylethyl]amino} methyl)phenyl]methyl}) amino]-2-phenylethyldiphenylphosphinite (16)

Prepared from chiral amino alcohol **8** (1.5 mmol, 0.69 g) according to the general procedure **2.2.2.** White viscous oily product **16** (1.28g, 92 %); Anal.Calcd. for $C_{62}H_{58}N_2O_2P_2$; C 80.50; H 6.33; N 3.03; found; C 80.40; H 6.21; N 2.94; ^{1}H-NMR (δ ppm, $CDCl_3$): 7.23-7.47 (m, 44H, aromatic protons); 4.43 (m, 2H, -$C\underline{H}_2OP$ (b)); 4.31 (m, 2H, -$C\underline{H}_2OP$ (a)); 4.19 (m, 2H, -$NC\underline{H}$); 3.83 (m, 4H, -$NC\underline{H}_2Py$); 3.45 (m, 4H, -$NC\underline{H}_2Ph$); ^{13}C-NMR (δ ppm, $CDCl_3$): 137.88, 139.89,

140.01, 141.79, 141.97, (*i*-carbons); 126.83, 127.23, 127.41, 128.09, 128.18, 128.25, 128.32, 128.75, 129.34, 130.23, 130.48, 130.70, 130.83 (aromatic carbons); 69.36 (d, *J*=18.1 Hz, -$\underline{C}H_2OP$); 62.48 (d, *J*=8.0 Hz, -N$\underline{C}$H); 54.44 (-N$\underline{C}H_2$Py); 54.39 (-N$\underline{C}H_2$Ph). ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 114.87 (s, O-$\underline{P}(Ph)_2$); **(Fig S4)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3055, 3026, 2924; υ(C=C): 1480, 1453, 1452; υ(O-P): 1021.

2.2.3. General procedure for the synthesis of bis(phoshinite) ruthenium(II) complexes, (17-24).

[Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ (1.5 mmol, 0.92 g) and bis(phosphinite) ligands **9-16** (1.5 mmol) were dissolved in 30 mL of CH_2Cl_2 under argon atmosphere and stirred for 1 h at room temperature. The resulting solution was concentrated to 2 mL under reduced pressure, and addition of petroleum ether (15 mL) caused the precipitation of a tile-red solid. The supernatant solution was decanted, the solid was washed with hexane:diethylether (1:1) and dried in vacuum, yielding ruthenium(II) complex **17-24**.

Complex 17

Prepared from bis(phosphinite) ligand **9** (1.5 mmol, 1.43 g) according to the general procedure **2.2.3**. Yield (**17**); 0.21 2.10 g, 89%, m.p: 145-147 ^{o}C. $[\alpha]_D^{20}$ = -41.3^o (c: 0.5, CH_2Cl_2); Anal.Calcd for $C_{83}H_{89}N_3O_2P_2Ru_2Cl_4$; C 63.64; H 5.73; N 2.68; Found; C 63.40; H 5.48; N 2.55; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.08-7.93 (m, 43H, aromatic protons); 5.07 (d, 2H, *J*= 5.8 Hz *p*-cymene $\underline{C}_6H_4$); 5.01 (d, 2H, *J*= 5.8 Hz *p*-cymene $\underline{C}_6H_4$); 4.79 (d, 2H, *J*= 5.8 Hz *p*-cymene $\underline{C}_6H_4$); 4.73 (d, 2H, *J*= 5.7 Hz *p*-cymene $\underline{C}_6H_4$); 3.62-3.89 (m, 4H, -C$\underline{H}_2$Py+4H, - C$\underline{H}_2$OP + 4H, NC$\underline{H}_2$Ph); 3.17 (m, 2H, -C$\underline{H}$N); 3.01 (m, 4H, -C$\underline{H}_2$Ph); 2.55 (m, 2H C$\underline{H}(CH_3)_2$ *p*-cymene); 1.46 (s, 6H, -C$\underline{H}_3$ *p*-cymene); 1.06 (d, 12H, *J*= 8.0 Hz, CH(C$\underline{H}_3$)$_2$ *p*-cymene); ^{13}C NMR (δ ppm, $CDCl_3$): 138,09, 139.51, 139.75, 159.51 (aromatic *ipso* carbons); 127.62, 127.86, 128.20, 128.45, 128.69, 129.52, 130.70, 130.86, 131.59, 131.69, 133.38, (aromatic carbons); 98.51, 113,20 (*ipso* *p*-cymene); 88.30, 87.86, 88.43, 88.92 (*p*-cymene $\underline{C}_6H_4$); 66.10 (-$\underline{C}H_2$OP); 61.41 (d, *J*= 8.1 Hz, -

CHCH$_2$Ph): 55.58 (-NCH$_2$Py); 54.33 (-NCH$_2$Ph); 33.49 (-CHCH$_2$Ph); 30.04 (-CH(CH$_3$)$_2$ *p*-cymene); 21.81, 21.89 (-CH(CH$_3$)$_2$ *p*-cymene); 17.24 (-CH$_3$ *p*-cymene); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 112.13 (s); **(Fig S5)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3056, 3025, 2958; υ(C=C): 1488, 1447, 1436; υ(O-P): 1025; m/z: 1567.45 [M-H$^+$] $C_{83}H_{89}N_3O_2P_2Ru_2Cl_4$ (MA: 1566.503) **(Fig S6)**.

Complex 18

Prepared from bis(phosphinite) ligand **13** (1.5 mmol, 1.39 g) according to the general procedure **2.2.3.** Yield (**18**); 2.15 g, 93%, m.p: 136-138 ^{o}C. $[\alpha]_D^{20}$ = -47.5^o (c: 0.5, CH_2Cl_2); Anal. Calcd. for $C_{81}H_{85}N_3O_2P_2Ru_2Cl_{42}$; C 63.20; H 5.57; N 2.73, Found; C 62.98; H 5.32; N 2.55; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.14-7.65 (m, 43H, aromatic protons); 4.98-5.13 (m, 8H, *p*-cymene C_6H_4); 3.93-4.31 (m, 6H, -CH$_2$OP+ -CHN); 3.77 (m, 4H, -NCH$_2$Py); 3.42 (m, 4H, -NCH$_2$Ph); 2.59 (m, 2H, -CH(CH$_3$)$_2$ *p*-cymene); 1.64 (s, 6H, -CH$_3$ *p*-cymene); 1.02 (d, 12H, *J*= 6.3 Hz, -CH(CH$_3$)$_2$ *p*-cymene); ^{13}C NMR (δ ppm, $CDCl_3$): 135.94, 136,89, 139.42, 159.52 (aromatic ipso carbons); 120.87, 126.94, 127.69, 127.79, 128.28, 128.77, 128.85, 129.21, 130.79, 132.59, 132.70 (aromatic carbons); 97.49, 111,93 (*ipso p*-cymene); 87.37, 87.69, 90.12, 90.31 (*p*-cymene C_6H_4); 67.07 (-CH$_2$OP); 61.88 (-NCH); 55.94 (-NCH$_2$Py); 54.57 (-NCH$_2$Ph); 30.08 (-CH(CH$_3$)$_2$ *p*-cymene); 21.72, 21.90 (-CH(CH$_3$)$_2$ *p*-cymene); 17.35 (-CH$_3$ *p*-cymene); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 112.27 (s); **(Fig S7)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3055, 2957, 2923; υ(C=C): 1452, 1448, 1375; υ(O-P): 1024; m/z: 1540.35 [M-H$^+$] $C_{81}H_{85}N_3O_2P_2Ru_2Cl_4$ (MA: 1538.16) **(Fig S8)**.

Complex 19

Prepared from bis(phosphinite) ligand **14** (1.5 mmol, 1.24 g) according to the general procedure **2.2.3.** Yield (**19**); 2.0 g, 92%, m.p: 125-127 ^{o}C. $[\alpha]_D^{20}$ = -41.4^o (c: 1, CH_2Cl_2); Anal.Calcd. for $C_{73}H_{85}N_3O_2P_2Ru_2Cl_4$; C 60.79; H 5.94; N 2.91; Found; C 60.40; H 5.68; N 2.55; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.18-7.93 (m, 33H, aromatic protons); 5.15 (m, 8H, *p*-cymene C_6H_4); 3.86 (d, 4H, *J*= 4.0 Hz, -CH$_2$OP); 3.80 (m, 4H, -NCH$_2$); 3.66 (s, 4H, -NCH$_2$Ph); 2.72 (m, 2H, -CHCH$_2$CH$_3$);

2.61 (m, 2H, -C<u>H</u>$(CH_3)_2$ *p*-cymene); 1.77 (s, 6H, -C<u>H</u>$_3$ *p*-cymene); 1.60 (m, 2H, -CHC<u>H</u>$_2$CH$_3$ (a)); 1.39 (m, 2H, -CHC<u>H</u>$_2$CH$_3$ (b)); 1.06 (m, 12H, -CH(C<u>H</u>$_3$)$_2$ *p*-cymene); 0.84 (t, 6H, *J*= 7.2 Hz -CHCH$_2$C<u>H</u>$_3$); ^{13}C NMR (δ ppm, $CDCl_3$): 135.48, 140.04, 159.96 (aromatic *ipso* carbons); 120.44, 126.81, 127.80, 128.15, 128.75, 130.80, 132.20, 133.07, (aromatic carbons); 97.47, 111,73 (*i*-<u>C</u>$_6$H$_4$); 87.59, 90.17, 90,42 (*p*-cymene <u>C</u>$_6$H$_4$); 67.02 (-<u>C</u>H$_2$OP); 60.51 (-<u>C</u>HCH$_2$CH$_3$): 55.81-54.56 (-N<u>C</u>H$_2$ + -N<u>C</u>H$_2$Ph); 30.08 (<u>C</u>H$(CH_3)_2$ *p*-cymene); 21.77, 21.95 (-CH(<u>C</u>H$_3$)$_2$ *p*-cymene); 20.71 (-CH<u>C</u>H$_2$CH$_3$); 17.53 (-<u>C</u>H$_3$ *p*-cymene); 11.90(-CHCH$_2$<u>C</u>H$_3$); ^{31}P-{^{1}H}- NMR (δ ppm, $CDCl_3$): 111.88 (s); **(Fig S9)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3056, 2960, 2926; υ(C=C): 1448, 1435, 1375; υ(O-P): 1026; m/z: 1443.30 [M-H$^+$] $C_{73}H_{85}N_3O_2P_2Ru_2Cl_4$ (MA: 1442.38) **(Fig S10)**.

Complex 20

Prepared from bis(phosphinite) ligand **11** (1.5 mmol, 1.20 g) according to the general procedure **2.2.3.** Yield (**20**); 1.9 g, 90%, m.p: 126-128 ^{o}C. $[\alpha]_D^{20}$ = -30.8^o (c: 1, CH_2Cl_2); Anal.Calcd. for $C_{71}H_{81}N_3O_2P_2Ru_2Cl_4$; C 60.30; H 5.77; N 2.97; Found; C 60.09; H 5.58; N 2.75; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.23-7.90 (m, 33H, aromatic protons); 5.29 (br, 2H, *p*-cymene C$_6$<u>H</u>$_4$); 5.10 (br, 6H, *p*-cymene C$_6$<u>H</u>$_4$); 4.63 (br, 2H, -C<u>H</u>CH$_3$); 3.65 (d, 2H, *J*= 14.5 Hz, -CHC<u>H</u>$_2$ (a)); 3.56 (d, 2H, J:13.72 Hz, -NC<u>H</u>$_2$ (a)); 3.40 (d, 2H, *J*= 14.5 Hz, -CHC<u>H</u>$_2$ (b)); 3.27 (d, 2H, *J*= 13.7 Hz, -NC<u>H</u>$_2$ (b)); 2.54-2.69 (m, 4H, -NC<u>H</u>$_2$Ph(a)+-C<u>H</u>$(CH_3)_2$ *p*-cymene); 2.39 (m, 2H, -NC<u>H</u>$_2$Ph(b)); 1.81 (s, 6H, -C<u>H</u>$_3$ *p*-cymene); 1.02-1.10 (m, 18H, -CH(C<u>H</u>$_3$)$_2$ *p*-cymene + -CHC<u>H</u>$_3$); ^{13}C NMR (δ ppm, $CDCl_3$): 137.63, 133.10, 139.43, 158.95 (*ipso* aromatic carbons); 121.01, 126.79, 127.74, 128.08, 128.95, 130.85, 132,86, 132.97, (aromatic carbons) ; 97.48, 111,25 (*i*-<u>C</u>$_6$H$_4$); 87.40, 88.17, 89.54, 90.63, 87.42 (d, *J*= 4.0 Hz, *ipso p*-cymene), 88.14 (d, *J*= 6.0 Hz, *ipso p*-cymene), 89.56 (d, *J*= 4.0 Hz, *ipso p*-cymene), 90.61 (d, *J*= 4.0 Hz, *ipso p*-cymene); 74.31 (-CH<u>C</u>H$_2$); 60.77 (-<u>C</u>HCH$_2$); 59.27-59.66 (-N<u>C</u>H$_2$+N<u>C</u>H$_2$Ph); 29.99 (-<u>C</u>H$(CH_3)_2$ *p*-cymene); 21.79, 21.93 (-CH(<u>C</u>H$_3$)$_2$ *p*-cymene); 20.45 (-CHC<u>H</u>$_3$); 17.45 (-<u>C</u>H$_3$ *p*-cymene); ^{31}P-{^{1}H}-NMR (δ ppm,

$CDCl_3$): 110.30 (s); **(Fig S11)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3056, 2960, 2923; υ(C=C): 1574, 1456, 1435; υ(O-P): 970; m/z: 1415.25 [M-H^+] $C_{71}H_{81}N_3O_2P_2Ru_2Cl_4$ (MA: 1414.23) **(Fig S12)**.

Complex 21

Prepared from bis(phosphinite) ligand **10** (1.5 mmol, 1.43 g) according to the general procedure **2.2.3.** Yield (**21**); 2.15 g, 92 %, m.p: 144-146 ^oC. $[\alpha]_D^{20}$ = -40.9^o (c: 0.5, CH_2Cl_2); Anal.Calcd. for $C_{84}H_{90}N_2O_2P_2Ru_2$; C 64.46; H 5.80; N 1.79; found; C 64.12; H 5.53; N 1.58; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.02-7.95 (m, 44H aromatic protons); 5.08 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$); 4.99 (d, 2H, *J*= 5.9 Hz, *p*-cymene $C_6\underline{H}_4$); 4.81 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$); 4.77 (d, 2H, *J*= 5.7 Hz *p*-cymene C_6H_4); 3.90 (m, 4H, (-C$\underline{H}_2$OP); 3.57-3.71 (m,4H, -NC$\underline{H}_2$+4H, NC$\underline{H}_2$Ph); 3.14 (m, 2H, -C$\underline{H}$N); 3.00 (m, 2H, CHC$\underline{H}_2$Ph (a)); 2.54-2.60 (m, 2H, CHC$\underline{H}_2$Ph (b) + 2H C$\underline{H}$(CH_3)$_2$ *p*-cymene); 1.50 (s, 6H, C$\underline{H}_3$ *p*-cymene); 1.06 (t, 12H, *J*= 6.1 Hz, CH(C$\underline{H}_3$)$_2$ *p*-cymene); ^{13}C NMR (δ ppm, $CDCl_3$): 138,24, 139.74, 139.77, 139.89 (aromatic *ipso* carbons); 126.07, 126.81, 127.88, 128.16, 128.43, 128.55, 128.67, 129.45, 130.73, 130.94, 131.64, 133.48, 133.59, (aromatic carbons) ; 98.40 (s, *ipso p*-cymene), 112,91 (d, *J*= 4.0 Hz, *ipso p*-cymene), 87.83, 88.15, 88.57, 87.86 (d, *J*= 5.0 Hz, *ipso p*-cymene), 88.12 (d, *J*= 6.0 Hz, *ipso p*-cymene), 88.57 (br, *ipso p*-cymene), 89.11 (d, *J*= 4.0 Hz, *ipso p*-cymene); (*p*-cymene $\underline{C}_6H_4$); 65.97 ($\underline{C}H_2$OP); 60.42 (-$\underline{C}$HCH_2Ph): 53.48, 53.79 (-N$\underline{C}H_2$+N$\underline{C}H_2$Ph); 33.94 (-CH$\underline{C}H_2$Ph); 30.04 ($\underline{C}$H(CH_3)$_2$ *p*-cymene); 21.82, 21.90 (CH($\underline{C}H_3$)$_2$ *p*-cymene); 17.27 ($\underline{C}H_3$ *p*-cymene); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 112.40 (s); **(Fig S13)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3056, 3025, 2958; υ(C=C): 1478, 1452, 1377; υ(O-P): 1024; m/z: 1566.35 [M-H^+] $C_{84}H_{90}N_2O_2P_2Ru_2Cl_4$ (MA: 1565.23) **(Fig S14)**.

Complex 22

Prepared from bis(phosphinite) ligand **16** (1.5 mmol, 1.39 g) according to the general procedure **2.2.3.** Yield (**22**); 2.05 g, 89 %, m.p: 139-141 ^oC. $[\alpha]_D^{20}$ = -30.8^o (c:1, CH_2Cl_2); Anal.Calcd. for $C_{82}H_{86}N_2O_2P_2Ru_2Cl_4$; C 64.06; H 5.64; N 1.82; found; C 63.90; H 5.48; N 1.75; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.16-7.79 (m, 44H, aromatic protons); 5.13 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$);

5.08 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$); 5.04 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$); 4.97 (d, 2H, *J*= 5.8 Hz *p*-cymene $C_6\underline{H}_4$); 4.32 (m, 2H, -$C\underline{H}_2$OP (a)); 4.15 (m, 2H, -$C\underline{H}_2$OP (b)); 3.98 (m, 2H, -NC<u>H</u>); 3.69 (d, 4H, *J*=13.8 Hz -N$C\underline{H}_2$ (a)+N$C\underline{H}_2$Ph (a)); 3.29 (d, 4H, *J*= 13.8 Hz -N$C\underline{H}_2$ (b)+N$C\underline{H}_2$Ph (b)); 2.59 (m, 2H, -C<u>H</u>$(CH_3)_2$ *p*-cymene); 1.66 (s, 6H, -$C\underline{H}_3$ *p*-cymene); 1.02 (m, 12H, -CH($C\underline{H}_3$)$_2$ *p*-cymene); ^{13}C NMR (δ ppm, $CDCl_3$): 136.02, 136.40, 136.05, 136.52, 137.29, 139.65, (*i*-$\underline{C}_6H_4$); 126.87, 127.48, 127.73, 127.79, 127.83, 128.15, 128.24, 128.78, 129.15, 130.81, 132.58, 132.69, 132.73, (aromatic carbons) ; 97.40, 111,80 (*ipso p*-cymene); 90.44 (d, *J*= 4.0 Hz, *p*-cymene $\underline{C}_6H_4$); 90.12 (d, *J*= 3.1 Hz, *p*-cymene $\underline{C}_6H_4$); 87.70 (d, *J*= 6.0 Hz, *p*-cymene $\underline{C}_6H_4$); 87.31 (d, *J*= 6.0 Hz, *p*-cymene $\underline{C}_6H_4$); 66.83 (-$\underline{C}H_2$OP); 62.45 (d, *J*= 8.1 Hz -<u>C</u>HPh): 53.99 (-N$\underline{C}H_2$+N$\underline{C}H_2$Ph); 30.06 (-<u>C</u>H$(CH_3)_2$ *p*-cymene); 21.73, 21.86 (-CH($\underline{C}H_3$)$_2$ *p*-cymene); 17.34 (-$\underline{C}H_3$ *p*-cymene); ^{31}P-{^{1}H}- NMR (δ ppm, $CDCl_3$): 112.54 (s); **(Fig S15)**; IR (KBr pellet in, cm^{-1}):υ(CH): 3055, 2958, 2923; υ(C=C): 1436, 1417, 1373; υ(O-P): 1023. m/z: 1539.30 [M-H$^+$] $C_{82}H_{86}N_2O_2P_2Ru_2Cl_4$ (MA: 1537.48) **(Fig S16)**.

Complex 23

Prepared from bis(phosphinite) ligand **15** (1.5 mmol, 1.24 g) according to the general procedure **2.2.3.** Yield (**23**); 1.9 g, 88%, m.p: 140-142 ^oC. $[\alpha]_D^{20}$ = -20.7^o (c:1, CH_2Cl_2); Anal.Calcd. for $C_{74}H_{86}N_2O_2P_2Ru_2Cl_4$; C 61.67; H 6.01; N 1.94; Found; C 61.22; H 5.88; N 1.65; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.21-7.92 (m, 34H, aromatic protons); 5.15 (br, 8H, *p*-cymene $C_6\underline{H}_4$); 3.84 (br, 4H, -$C\underline{H}_2$OP), 3.48-3.65 (m, 8H, -N$C\underline{H}_2$ + -N$C\underline{H}_2$Ph); 2.62-2.64 (m, 4H, -<u>C</u>HCH_2CH_3 + -<u>C</u>H$(CH_3)_2$ *p*-cymene); 1.79 (s, 6H, -$C\underline{H}_3$ *p*-cymene); 1.63 (m, 2H, -CHC$\underline{H}_2$$CH_3$ (a)); 1.29 (m, 2H, -CHC$\underline{H}_2$$CH_3$ (b)); 1.07 (m, 12H, -CH($C\underline{H}_3$)$_2$ *p*-cymene); 0.84 (br, 6H, -$CHCH_2C\underline{H}_3$); ^{13}C NMR (δ ppm, $CDCl_3$): 137.76, 140.24, 140.38 (aromatic *ipso* carbons); 126.69, 127.74, 127.84, 128.09, 128.74, 130.81 130.99, 132.14, 133.26 (aromatic carbons); 97.29, 111,67 (*i*-$\underline{C}_6H_4$); 87.41 (d, *J*= 6.0 Hz, *ipso p*-cymene), 87.52 (d, *J*= 6.0 Hz, *ipso p*-cymene), 90.31 (d, *J*= 4.0 Hz, *ipso p*-

cymene), 90.55 (d, *J*= 4.0 Hz, *ipso p*-cymene); 66.73 (-$\underline{C}H_2OP$); 59.51 (-$\underline{C}HCH_2CH_3$): 53.66-53.82 (-N$\underline{C}H_2$+ -N$\underline{C}H_2$Ph); 30.10 ($\underline{C}H(CH_3)_2$ *p*-cymene); 21.77, 21.92 (-CH($\underline{C}H_3)_2$ *p*-cymene); 21.13 (-CH$\underline{C}H_2CH_3$); 17.52 (-$\underline{C}H_3$ *p*-cymene); 11.78 (-$CHCH_2\underline{C}H_3$); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 111.80 (s); **(Fig S17)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3055, 2959, 2927; υ(C=C): 1459, 1435, 1375; υ(O-P): 1026; m/z: 1442.30 [M-H$^+$] $C_{74}H_{86}N_2O_2P_2Ru_2Cl_4$ (MA: 1441.39) **(Fig S18)**.

Complex 24

Prepared from bis(phosphinite) ligand **12** (1.5 mmol, 1.20 g) according to the general procedure **2.2.3.** Yield (**24**); 1.8 g, 85%, m.p: 132-134 ^oC. $[\alpha]_D^{20}$ = -20.8^o (c:1, CH_2Cl_2); Anal.Calcd. for $C_{72}H_{82}N_2O_2P_2Ru_2Cl_4$; C 61.19; H 5.85; N 1.98; Found; C 60.97; H 5.58; N 1.86; ^{1}H NMR (δ, ppm, $CDCl_3$): 7.09-7.87 (m, 34H, aromatic protons); 5.06-5.29 (m, 8H, *p*-cymene $C_6\underline{H}_4$); 4.57 (br, 2H, -C$\underline{H}CH_3$); 3.50 (d, 4H, *J*= 13.5 Hz, -NC$\underline{H}_2$); 3.14 (d, 4H, *J*= 13.4 Hz, -NC$\underline{H}_2$Ph); 2.58 (br, 2H, -C$\underline{H}(CH_3)_2$ *p*-cymene); 2.44 (d, 2H, *J*= 8.7 Hz, -CHC$\underline{H}_2$ (a)); 2.32 (d, 2H, *J*= 8.8 Hz, -CHC$\underline{H}_2$ (b)); 1.79 (s, 6H, -C$\underline{H}_3$ *p*-cymene); 0.99-1.08 (m, 18H, -CH(C$\underline{H}_3)_2$ *p*-cymene + -CHC$\underline{H}_3$); ^{13}C NMR (δ ppm, $CDCl_3$): 137.86, 139.40, 139.60 (*ipso* aromatic carbons); 126.70, 127.37, 127.78, 128.06, 128.87, 129.29, 130.79, 130.88, 132.96, (aromatic carbons); 97.32, 110.91 (*i*-$\underline{C}_6H_4$); 87.23 (d, *J*= 5.0 Hz, *ipso p*-cymene), 88.15 (d, *J*= 6.0 Hz, *ipso p*-cymene), 89.58 (br, *ipso p*-cymene), 90.55 (br, *ipso p*-cymene); 74.41 (-CH$\underline{C}H_3$); 59.27-59.02 (-N$\underline{C}H_2$+N$\underline{C}H_2$Ph+ -$\underline{C}HCH_2$); 30.00 (-$\underline{C}H(CH_3)_2$ *p*-cymene); 21.96, 21.73 (-CH($\underline{C}H_3)_2$ *p*-cymene); 20.48 (-CHC$\underline{H}_3$); 17.44 (-$\underline{C}H_3$ *p*-cymene); ^{31}P-{^{1}H}-NMR (δ ppm, $CDCl_3$): 110.21 (s); **(Fig S19)**; IR (KBr pellet in, cm^{-1}): υ(CH): 3054, 2960, 2925; υ(C=C): 1436, 1408, 1376; υ(O-P): 969; m/z: 1413.20 [M-H$^+$] $C_{72}H_{82}N_2O_2P_2Ru_2Cl_4$ (MA: 1413.36) **(Fig S20)**.

2.3. General procedure for the asymmetric transfer hydrogenation of ketones.

Typical procedure for the catalytic hydrogen-transfer reaction: a solution of the Ru(II)-complexes **17-24** (0.005mmol), KOH (0.025 mmol) and the corresponding ketone (0.5 mmol) in degassed 2-propanol (5 mL) was refluxed until the reaction was completed. Periodically samples taken from the reaction medium were passed through acetone silicagel column and conversion rates were observed in gas chromatography, which were calculated on unreacted ketone.

3. Results and discussion

3.1. Synthesis and characterization of the C_2-symmetric bis(phosphinites) and their binuclear η^6-*p*-cymene-Ru(II)-phosphinite complexes

Corresponding chiral amino alcohol (D-phenyl alaninol, D-phenyl glycinol, (*R*)-(−)-1-amino-2-propanol or (*R*)-(-)-2-amino-1-butanol) was reacted with commercially available 2,6-bis-(bromomethyl)pyridine) or 1,3-bis(bromomethyl)benzene at 100 ^{o}C for 12 h under argon atmosphere in EtOH according to the literature procedure, respectively[27]. C_2-symmetric chiral amino alcohols **1-8**, were characterized by elemental analysis, FT-IR, and multinuclear NMR spectroscopies. All spectroscopic data for **1-8** are consistent with the proposed structures.

Insert Scheme 1 Here

C_2-symmetric bis(phosphinite) ligands were synthesized by deprotonation of the corresponding chiral amino alcohols **1-8** with two equivalents of Ph_2PCl in the presence of triethylamine in anhydrous toluene under argon atmosphere (Scheme 2). ^{31}P-{^{1}H} NMR spectroscopy was used to follow the progress of these reactions. The signal of the starting material Ph_2PCl at δ= 81.0 ppm disappeared and new singlets appeared at δ = 114.51, 115.02, 114.17, 114.87 ppm (Fig S1-4). The chemical shifts in the ^{31}P–{^{1}H} NMR spectra of the free ligands are in line with the values previously observed for similar compounds[2-4, 16, 28]. The observed singlets indicate that two phosphorus atoms in the each molecule are equivalent [29-31]. Generally, phosphinites

are unstable in the solid state and decompose rapidly when it exposes to air or moisture. However, phosphinite ligands synthesized in this study **9-16** are stable for up to 2 weeks in the ambient air and then decompose gradually to give the corresponding oxide and hydrolysis product diphenylphosphinous acid, $Ph_2P(O)H$[32].

Insert Scheme 2 Here

The ability of dimer {[Ru(*p*-cymene)(μ-Cl)Cl]$_2$} to form mononuclear complexes of general formula [Ru(η^6- *p*-cymene) Cl_2L] have been well known for a long time [33, 34]. The *p*-cymene moiety which is strongly coordinated to the ruthenium atom can be modified by simply attaching different substituents. The three remaining coordination sites opposite to the *p*-cymene ligand can be complexed with a wide number of mono-, bi-, or tri-dentate ligands such as phosphorus containing ones (phosphine [1, 29, 30], phosphinite [2-4], phosphite[5] etc.), aminoalcohols [35], diamines[36], sulphur containing ligands[37], heterocyclic ligands[38], with N-, O-, S-, or P-donor atom. The reactions of [Ru(*p*-cymene)(μ-Cl)Cl]$_2$ with ligands **9-16** are depicted in Scheme 3. The reactions of [Ru(*p*-cymene)(μ-Cl)Cl]$_2$ with one equivalent of **9-16** in CH_2Cl_2 at room temperature gave air stable red compounds **17-24**, in high yields. They are all high melting solids and very soluble in most organic solvents. Generally, the P-based ligands were expected to cleave the [Ru(*p*-cymene)(μ-Cl)Cl]$_2$ dimer to give the corresponding monohapto P-coordinated ruthenium complexes[39]. The initial colour change of reaction medium from orange to deep red is attributed to the dimer cleavage by the phosphinite ligand. The chemical purity of the ruthenium complexes was confirmed by ^{31}P-{^{1}H} NMR spectroscopy. ^{31}P-{^{1}H} NMR spectrum exhibits a unique single signal values ranging from 110.21 to 112.54 indicative of both phosphorus being equivalent as a result of the high symmetry of the complexes (please see SI) due to the diphenylphosphinite moiety. A small coordination shift was attributed

to formation of the corresponding C_2-symmetric η^6-*p*-cymene-Ru(II)-phosphinite complexes **17-24.** The structures of complexes were also confirmed by FT-IR spectroscopy, microanalysis, and LC/MS-MSspectra, and found to be in good agreement with the proposed structures (see experimental section in details).

Insert Scheme 3 Here

3.2. Binuclear η^6-*p*-cymene-Ru(II)-phosphinite-catalyzed asymmetric transfer hydrogenation of aryl, alkyl/aryl and alkyl/methyl ketones

Excellent catalytic performance of phosphinite ligands bearing η^6-arene-Ru(II) complexes in transfer hydrogenation of various ketones with 2-propanol, prompted us to search for new phosphinite ligands bearing ruthenium(II) complexes for asymmetric transformation. To evaluate the effectiveness of our new chiral C_2-symmetric binuclear η^6-*p*-cymene-Ru(II)-phosphinite **17-24** as pre-catalysts in asymmetric transfer hydrogenation of aryl, alkyl/aryl and alkyl/methyl ketones, we first investigated the optimal conditions starting with acetophenone as the model substrate and the results are listed in Table 1.

Insert Scheme 4 Here

Initially, complexes **17-24** were tested as catalysts for transfer hydrogenation of acetophenone to (*R*) or (*S*)-1-phenylethanol using 2-propanol in the presence of KOH as base. The results in Table 1 (Entry 17) clearly show that the base is necessary for these reactions. Herewith, we did not observe any conversion in the absence of any base. A blank experiment was also showed that transfer hydrogenation does not occur in the absence of catalyst.

Results of the optimization studies showed that the best conversions were obtained using KOH, as the base, in 2-propanol as solvent and hydrogen source at 82 ^{o}C with 1 mol% of the catalyst. Increasing the substrate-to-catalyst (S/C; 250:1, 500:1, 1000:1) ratio does not cause any

decrease in the conversion of the product (except enantioselectivity and reaction time) in most cases as seen in Table 1, entries 22-25. For example, transfer hydrogenation of acetophenone could be achieved with 90% yield even when the S/C ratio reached 1000:1 though with an increase in the reaction time (7h, TOF $13h^{-1}$) and decrease in enantioselectivity (51 %) (Table 1, entry 25). Due to the reversibility in reaction medium, the prolonged the reaction time led to a decrease in enantioselectivity. Thus, we concluded that prolonged exposure of the product to the catalyst tends to gradually deteriorate the enantiometric purity[40]. These results are presented in Table 1. At room temperature, no significant formation of (*R*)-1-phenylethanol was observed (Table 1, entries 1-8). An increase in the reaction time up to 96 h resulted in 35-48 % conversion with 41-48% ee's. As mentioned above, because of the reversibility of TH reactions at room temperature, the prolonged the reaction time led to a slight decrease in enantioselectivity. Optimization studies obviously indicated that complexes **17, 18, 21** and **22** are quite effective catalysts for transfer hydrogenation of acetophenone.

Insert Table 1 Here

In the next round of experiments, we extended our investigations to include hydrogenation of substituted acetophenone derivatives and the results are summarized in Table 2. For this aim, the reaction of several aromatic ketones with different electronic and steric variations on the substrate backbone was investigated. On comparing the electronic effects of the fluoro, chloro, bromo and nitro substituents on *ortho*- and *para*- position of acetophenone as electron withdrawing group, it was found that the reaction of *p*-fluoro acetophenone took shorter time of (10 min, TOF; 594 h^{-1}) 1/2 h to reach completion as compared to acetophenone for catalyst **17** (Table 2, entries 5-8). The introduction of electron withdrawing substituents, attached to the aryl ring of the ketone, decreased the electron density of the C=O group making it susceptible to attack so that the activity was improved, giving rise to easier hydrogenation [41,

42]. It can be also seen from in Table 2, the effect of changing the location of the substituents from the *para*- to *ortho*- position of the acetophenone resulted in a slightly increase in enantioselectivity, while *meta*- and *para*- substitution to acetophenones have detrimental effect [40]. Hence, the lowest enantioselectivities were observed in transfer hydrogenation of *p*-substituted acetophenones, whereas the highest one was found in the case of *o*-methoxyacetophenone (80% *ee*) as seen in Table 2.

Insert Table 2 Here

Inspired by these results, the scope of the catalytic study was further extended to investigate a wide range of alkyl/aryl and alkyl/methyl ketones (Table 3). From the results in Table 3, one can easily conclude that the catalytic asymmetric transfer hydrogenation of aliphatic ketones is more difficult than that of aromatic ketones. Thus, it was found that the reaction times are strongly dependent on the linear chain length and steric hindrance of the ketones (Table 3, entries 1-16). The results clearly show that the bulkiness of alkyl group significantly affects the enantioselectivity, which decreases with increasing bulkiness of the alkyl group as anticipitated. Using alkyl/aryl or alkyl methyl ketones as substrates, we found that the efficiency of the chiral ligands have a moderate influence on the final yields, but from moderate to high selectivity was observed (up to 82% *ee*, Table 3, entry 18).

Insert Table 3 Here

Table 4 shows the various phosphinite based Ru(II) complexes which have been tested in the ATH reactions of various ketones to produce the corresponding secondary alcohols at reflux temperature. Our C_2-symmetric Ru(II)-phosphinite complexes **18** and **22** showed quantative conversion (98-99%) and good enantioselectivity (74,76%) for ATH reactions of various ketones (Table 4, entries 1, 2). [5, 43-46]

Insert Table 4 Here

4. Conclusions

In summary, we synthesized eight new binuclear ruthenium(II) complexes bearing a chiral C_2-symmetric bis(phosphinite) unit and a *p*-cymene moiety. The binuclear ruthenium(II) complexes were employed as precursors of catalysts in the hydrogen transfer reaction of ruthenium-catalyzed asymmetric transfer hydrogenation of aromatic, methyl alkyl and alkyl/aryl ketones using 2-propanol as both the hydrogen source and solvent in the presence of KOH. The results indicated that complexes **17, 18, 21** and **22** showed higher conversions (between 96-99%, up to 594 h^{-1} TOF) and enantioselectivities (up to 82% *ee*) among eight binuclear Ru(II) complexes. These ruthenium complexes are selective and active hydrogenation catalysts and hold promise for application in transfer hydrogenation of other substrates.

Acknowledgment

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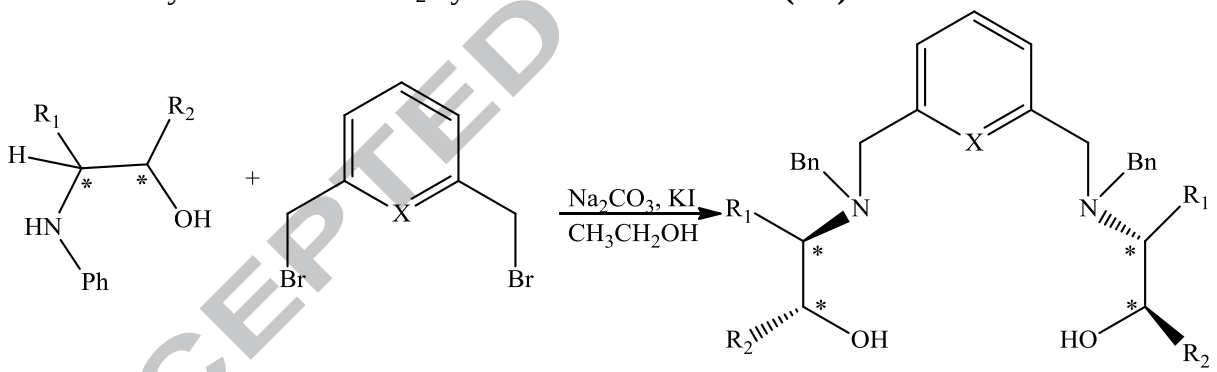
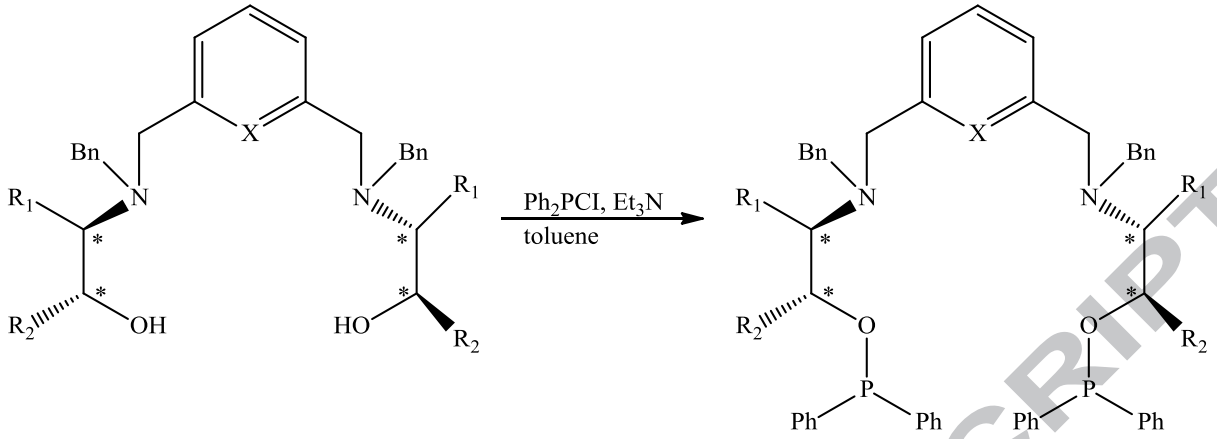
Scheme 1. Synthesis of chiral C_2-symmetric amino alcohols **(1-8).**



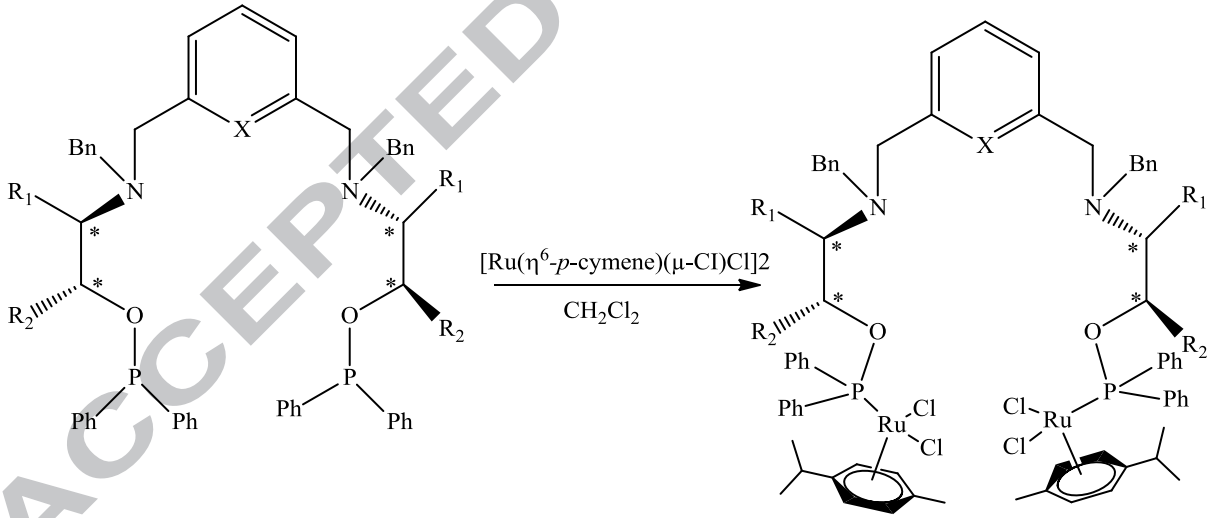
X	R1	R2		X	R1	R2	
N	CH_2Ph	H	**(1)**	N	Ph	H	**(5)**
C	CH_2Ph	H	**(2)**	**N**	CH_2CH_3	H	**(6)**
N	H	CH_3	**(3)**	C	CH_2CH_3	H	**(7)**
C	H	CH_3	**(4)**	C	Ph	H	**(8)**

Scheme 2. Synthesis of chiral C_2-symmetric bis(phosphinite) ligands **(9-16).**



X	R1	R2		X	R1	R2	
N	CH_2Ph	H	**(9)**	N	Ph	H	**(13)**
C	CH_2Ph	H	**(10)**	N	CH_2CH_3	H	**(14)**
N	H	CH_3	**(11)**	C	CH_2CH_3	H	**(15)**
C	H	CH_3	**(12)**	C	Ph	H	**(16)**

Scheme 3. Synthesis of chiral C_2-symmetric bis(phosphinite)-Ru(II) complexes **(17-24).**



X	R1	R2		X	R1	R2	
N	CH_2Ph	H	**(17)**	C	CH_2Ph	H	**(21)**
N	Ph	H	**(18)**	C	Ph	H	**(22)**
N	CH_2CH_3	H	**(19)**	C	CH_2CH_3	H	**(23)**
N	H	CH_3	**(20)**	C	H	CH_3	**(24)**

Scheme 4. Transfer hydrogenation of acetophenone.

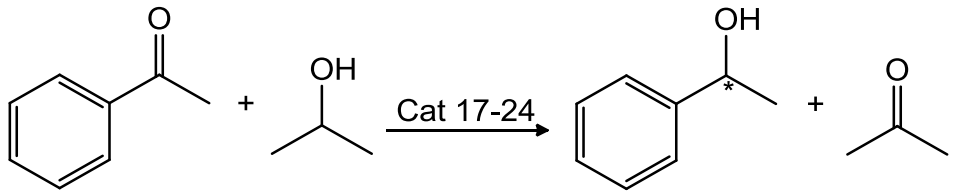
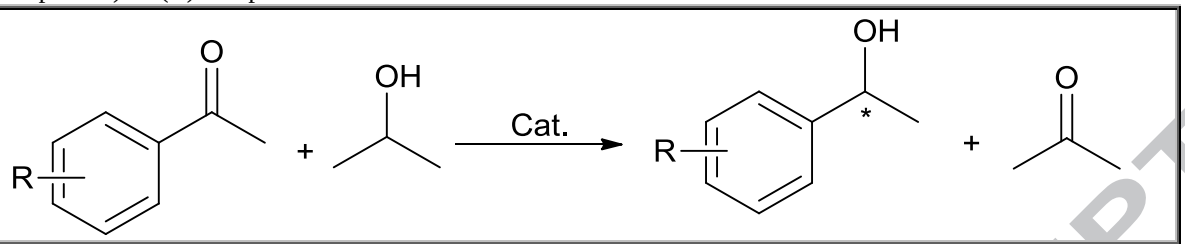


Table 1 Asymmetric transfer hydrogenation of acetophenone with *iso*-PrOH catalyzed by C_2-symmetric bis(phosphinite) Ru(II) complexes (**17-24**).

Entry	Cat.	Subs./Cat./Base	Time(h)	Conv.(%)[a]	ee (%)[b]	Config.[c]	TOF (h^{-1})[d]
1	**17**[e]	100:1:5	24(96)	13(40)	50(43)	*R*	<3
2	**18**[e]	100:1:5	24(96)	11(44)	52(46)	*R*	<3
3	**19**[e]	100:1:5	24(96)	10(38)	44(40)	*R*	<3
4	**20**[e]	100:1:5	24(96)	10(46)	48(42)	*R*	<3
5	**21**[e]	100:1:5	24(96)	15(42)	52(45)	*R*	<3
6	**22**[e]	100:1:5	24(96)	13(45)	56(47)	*R*	<3
7	**23**[e]	100:1:5	24(96)	11(35)	47(41)	*R*	<3
8	**24**[e]	100:1:5	24(96)	14(48)	50(44)	*R*	<3
9	**17**[f]	100:1:5	1/2	99	62	*R*	198
10	**18**[f]	100:1:5	1	98	76	*R*	98
11	**19**[f]	100:1:5	1/4	98	50	*R*	392
12	**20**[f]	100:1:5	1/2	98	61	*R*	196
13	**21**[f]	100:1:5	1/2	99	63	*R*	198
14	**22**[f]	100:1:5	1	99	74	*R*	99
15	**23**[f]	100:1:5	1/4	98	51	*R*	392
16	**24**[f]	100:1:5	1/2	99	62	*R*	196
17	**17**[g] **- 24**[g]	100:1	96	-	-	-	-
18	**18**[h]	100:1:3	1	98	70	*R*	98
19	**18**[h]	100:1:5	1	98	76	*R*	98
20	**18**[h]	100:1:7	1	94	72	*R*	94
21	**18**[h]	100:1:9	1	92	65	*R*	92
22	**18**[k]	100:1:5	1	98	76	*R*	98
23	**18**[k]	250:1:5	3	98	64	*R*	33
24	**18**[k]	500:1:5	5	95	59	*R*	19
25	**18**[k]	1000:1:5	7	90	51	*R*	13

Reaction conditions: [a]Determined by GC (three independent catalytic experiments), [b]Determined by capillary GC analysis using a chiral Cyclodex B (Agilent) capillary column, [c]Determined by comparison of retention times of enantiomers on the GC traces with literature values; (S) or (R) configuration was obtained in all experiments, [d]TOF= (mol product/mol catalyst) x h^{-1}, [e]At room temperature; acetophenone/Ru/KOH, 100:1:5, [f]Refluxing in iso-PrOH; acetophenone/Ru/KOH, 100:1:5, [g]Refluxing in iso-PrOH; acetophenone/Ru, 100:1, in the absence of base, [h] Refluxing in iso-PrOH; acetophenone/Ru/KOH, 100:1:3, 5, 7, 9, [k] Refluxing in iso-PrOH; acetophenone/Ru/KOH, 250, 500 or 1000:1:5.

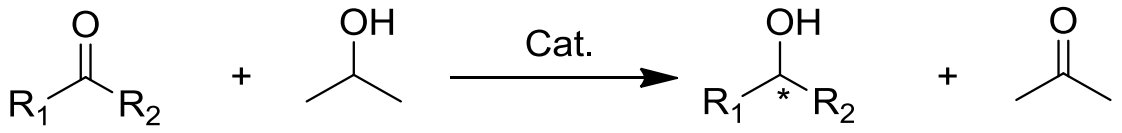
Table 2 Asymmetric transfer hydrogenation results for substituted acetophenones catalyzed by C_2-symmetric bis(phosphinite) Ru(II) complexes [a].



Entry	Cat.	R	Time	Conv.(%)[b]	ee(%)[c]	TOF (h^{-1})[d]	Conf.[e]
1	**17**	2-F	15 min	99	60	396	*R*
2	**18**		30 min	98	74	196	*R*
3	**21**		15 min	99	61	396	*R*
4	**22**		30 min	98	72	196	*R*
5	**17**	4-F	10 min	99	57	594	*R*
6	**18**		15 min	97	70	388	*R*
7	**21**		10 min	98	59	588	*R*
8	**22**		15 min	98	68	392	*R*
9	**17**	4-Cl	15 min	99	56	396	*R*
10	**18**		30 min	97	69	194	*R*
11	**21**		15 min	98	57	392	*R*
12	**22**		30 min	96	66	192	*R*
13	**17**	2-Br	30 min	98	54	196	*R*
14	**18**		60 min	96	66	96	*R*
15	**21**		30 min	98	56	196	*R*
16	**22**		60 min	98	64	98	*R*
17	**17**	4-Br	25 min	99	50	238	*R*
18	**18**		45 min	98	62	131	*R*
19	**21**		25 min	98	53	235	*R*
20	**22**		45 min	97	60	129	*R*
21	**17**	4-NO_2	15 min	99	59	396	*R*
22	**18**		20 min	98	72	294	*R*
23	**21**		15 min	98	62	392	*R*
24	**22**		20 min	98	70	294	*R*
25	**17**	2-MeO	2 h	99	67	50	*R*
26	**18**		3 h	99	82	33	*R*
27	**21**		2 h	98	65	49	*R*
28	**22**		3 h	96	80	33	*R*
29	**17**	4-MeO	4 h	99	60	25	*R*
30	**18**		7 h	99	76	14	*R*
31	**21**		4 h	98	60	25	*R*
32	**22**		7 h	96	75	14	*R*

Reaction conditions: [a] Catalyst (0.005 mmol), substrate (0.5 mmol), 2-propanol (5 mL), KOH (0.025 mmol %), 82 ºC, the concentration of acetophenone derivatives are 0.1 M; [b] Purity of compounds is checked by NMR and GC (three independent catalytic experiments), yields are based on aryl ketone; [c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column (30 m x 0.32 mm I.D. x 0.25 μm film thickness); [d] TOF = (mol product/mol Cat.) x h^{-1}; [e] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values, (*S)* or (*R)* configuration was obtained in all experiments.

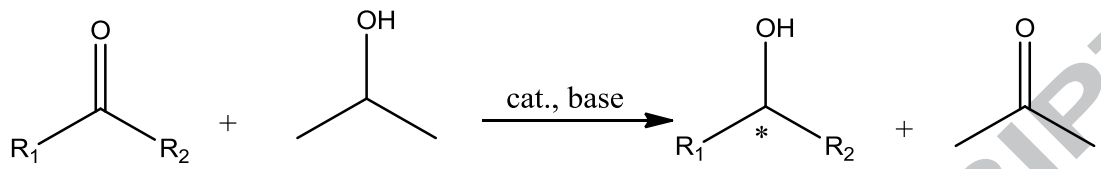
Table 3 Asymmetric transfer hydrogenation results for various ketones catalyzed by C_2–symmetric bis(phosphinite) Ru(II) complexes[a].



Entry	Cat.	R_1	R_2	Time	Conv.(%)[b]	ee (%)[b]	TOF(h^{-1})[d]	Conf.[e]
1	**17**	CH_3	CH_2CH_3	1 h	98	60	98	*R*
2	**18**			2 h	98	74	49	*R*
3	**21**			1 h	99	61	99	*R*
4	**22**			2 h	98	72	49	*R*
5	**17**	CH_3	$CH_2CHC_6H_5$	2 h	99	56	50	*R*
6	**18**			3 h	99	70	33	*R*
7	**21**			2 h	98	57	49	*R*
8	**22**			3 h	98	68	33	*R*
9	**17**	CH_3	$CH(CH_3)_2$	3 h	98	50	33	*R*
10	**18**			5 h	98	64	20	*R*
11	**21**			3 h	98	52	33	*R*
12	**22**			5 h	99	60	20	*R*
13	**17**	CH_3	$CH_2CH(CH_3)_2$	2 h	96	52	48	*R*
14	**18**			4 h	98	63	25	*R*
15	**21**			2 h	97	49	49	*R*
16	**22**			4 h	98	58	25	*R*
17	**17**	CH_3	1-naphthyl	1/2 h	98	67	196	*R*
18	**18**			1 h	98	82	98	*R*
19	**21**			1/2 h	99	69	198	*R*
20	**22**			1 h	99	80	99	*R*
21	**17**	CH_3	n-C_4H_9	2 h	97	57	49	*R*
22	**18**			3 h	98	72	33	*R*
23	**21**			2 h	96	59	48	*R*
24	**22**			3 h	99	70	33	*R*
25	**17**	CH_3	C_6H_5	1 h	98	48	98	*R*
26	**18**			2 h	99	63	49	*R*
27	**21**			1 h	98	50	98	*R*
28	**22**			2 h	98	64	49	*R*
29	**17**	C_6H_5	C_6H_{11}	3 h	98	51	33	*R*
30	**18**			4 h	99	68	25	*R*
31	**21**			3 h	99	53	33	*R*
32	**22**			4 h	99	66	25	*R*

Reaction conditions: [a] Catalyst (0.005 mmol), substrate (0.5 mmol), 2-propanol (5 mL), KOH (0.025 mmol %), 82 °C, the concentration of acetophenone derivatives are 0.1 M; [b] Purity of compounds is checked by NMR and GC (three independent catalytic experiments), yields are based on aryl ketone; [c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column (30 m x 0.32 mm I.D. x 0.25 μm film thickness); [d] TOF = (mol product/mol Cat.) x h^{-1}; [e] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values, (*S)* or (*R)* configuration was obtained in all experiments.

Table 4 Comparing catalytic activity of various phosphinite based Ru(II) complexes have been tested for asymmetric transfer hydrogenation of various ketones.*



Entry	R1/R2	Cat.	Temp. (°C)	Time	Subs./Cat.	Con. (%)	ee (%)	Ref.
1	Ph/CH_3	**18**	82	1 h	100:1	98	76	This study
2	Ph/CH_3	**22**	82	1 h	100:1	99	74	This study
3	CH_3/1-Naphthyl	**18**	82	1 h	100:1	98	82	This study
4	CH_3/1-Naphthyl	**22**	82	1 h	100:1	99	80	This study
5	Ph/Ph	**1a**	82	48 h	200:1	89	-	[43]
6	Ph/Ph	**3**	82	48 h	200:1	77	-	[43]
7	Ph/Ph	**6**	82	48 h	200:1	58	-	[43]
8	CH_3/1-Naphthyl	**1**	82	30 min	100:1	99	62	[44]
9	CH_3/1-Naphthyl	**2**	82	30 min	100:1	98	70	[44]
10	CH_3/1-Naphthyl	**5**	82	30 min	100:1	97	50	[44]
11	CH_3/1-Naphthyl	**4**	82	1 h	100:1	99	77	[25]
12	Ph/CH_3	**1**	80	10 h	100:1	69	-	[5]
13	Ph/CH_3	**3**	80	10 h	100:1	61	-	[5]
14	Ph/CH_3	**4**	80	10 h	100:1	68	-	[5]
15	Ph/CH_3	**6**	80	10 h	100:1	87	-	[5]
16	Ph/CH_3	**1**	82	10 h	100:1	84	-	[45]
17	Ph/Ph	**1**	82	10 h	100:1	91	-	[45]
18	Ph/CH_3	**3**	50	52 h	100:1	98	69	[46]
19	Ph/CH_3	**3**	82	6 h	100:1	96	67	[46]
20	Ph/CH_3	**1f**	82	1 h	100:1	97	16	[2]
21	Ph/CH_3	**1f**	50	24 h	100:1	32	16	[2]

*The catalysts used in Table 4 are given according to the numbers in the references cited.

RESEARCH HIGHLIGHTS

- Chiral C_2-symmetric bis(phosphinite) ligands and their binuclear η^6-*p*-cymene-Ru(II) complexes have been synthesized.
- The asymmetric transfer hydrogenation of alkyl methyl or alkyl/aryl ketones by binuclear η^6-*p*-cymene-Ru(II) complexes have been reported.
- Products were obtained with high conversions (99%) and moderate to good enantioselectivities (up to 82% *ee*).