# Chiral (η6-p-Cymene) ruthenium (II) Complexes Containing Monodentate Acylthiourea Ligands for Efficient Asymmetric Transfer Hydrogenation of Ketones

**ARTICLE** *in* ORGANOMETALLICS · JANUARY 2014

Impact Factor: 4.13 · DOI: 10.1021/om4010548

ORGANOMETALLICS

Article

pubs.acs.org/Organometallics

# Chiral ($\eta^6$-*p*-Cymene)ruthenium(II) Complexes Containing Monodentate Acylthiourea Ligands for Efficient Asymmetric Transfer Hydrogenation of Ketones

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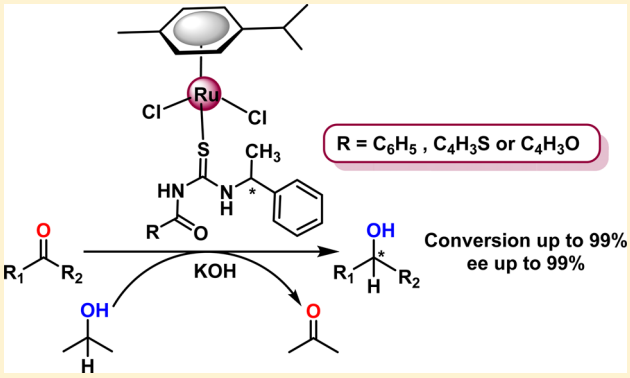
Supporting Information

**ABSTRACT:** The new chiral ligands (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)benzamide (**L1**/**L2**), (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)thiophene-2-carboxamide (**L3**/**L4**), and (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)furan-2-carboxamide (**L5**/**L6**) were synthesized, characterized, and used to prepare novel chiral Ru(II) complexes. The chiral Ru(II) complexes **1**−**6** were obtained from reactions between the chiral ligands **L1**−**L6** and $[RuCl_2(p\text{-cymene})_2]_2$. The complexes were characterized by analytical and spectroscopic (NMR, FT-IR, electronic) techniques. The solid-state structures of the ligands **L1** and **L3** and complexes **1**, **4**, and **6** were determined by single-crystal X-ray diffraction methods. In all of the complexes, the ligand is bound to the Ru(II) center only via the sulfur donor atom. This monodentate coordination of the acylthiourea ligands was observed for the first time with ruthenium. The Ru(II) complexes **1**−**6** all act as efficient catalysts for the asymmetric transfer hydrogenation of aromatic ketones in the presence of 2-propanol and KOH to produce chiral alcohols. All of the catalysts showed excellent conversions of up to 99% and enantiomeric excesses of up to 99%.




## INTRODUCTION

The coordination chemistry of *N*-(alkyl/aryl)-*N*′-acylthiourea ligands with transition-metal ions was first explored by the groups of Hoyer and Konig.[1,2] Due to the presence of O, N, S, and N′ donor atoms, the substituted acylthiourea ligands exhibit a variety of coordination modes: (a) O and S bonded to M (monobasic bidentate),[3] (b) only S bonded to M (neutral monodentate),[4] (c) O and N bonded to M (neutral bidentate),[5] (d) S and N bonded to M (neutral bidentate),[6] and (e) O and S bonded to M and N bonded to M′ (monobasic bridging ligand).[7] These coordination modes are depicted in Figure 1. Among these, the monobasic bidentate (O,S) mode of coordination is very common and many reports are available.[3] Coordination of these ligands to the metal ion only through the S atom is much rarer and has been reported in few metal complexes containing Pd(II),[3c] Au(I),[8] Ag(I),[9] Hg(II),[10] Cu(I),[4b,c,11] and Pt(II).[12] It has been suggested that the monodentate coordination of these ligands only through the S donor atom is due to intramolecular hydrogen bonding between the thiourea N−H and the amidic O donor atom to form a six-membered ring.[5] However, our results in a previous report[4c] revealed that the intramolecular hydrogen bond is not the only factor responsible for the monodentate coordination of these ligands. We and others have been investigating the structures of Ru(II) and Ru(III) complexes containing acylthiourea ligands.[13] In this article we report for the first time the monodentate coordination of these ligands in ruthenium complexes.

Transition-metal complexes of acylthiourea ligands were reported to exhibit various biological, analytical, and catalytic applications. For example, Co(III) benzoylthiourea derivatives were shown to exhibit antibacterial[14] and antifungal[15] activities, Ni(II) complexes containing 3-dialkyl/aryl-1-benzoylthiourea ligands were shown to be cytotoxic against T47D cell lines,[16] and water-soluble (2,2′-bipyridyl)- and (1,10-phenanthroline)-platinum(II) benzoylthiourea complexes were shown to have significant antimalarial activity.[17] Acylthiourea ligands were used for the extraction of some transition-metal and post-transition-metal ions.[18] Moreover, these ligands are capable of

**Received:** October 30, 2013

   dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX

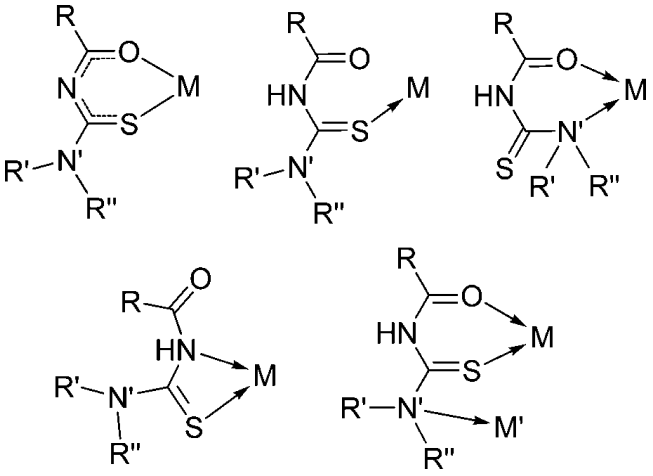


**Figure 1.** Five different coordination modes of the acylthiourea ligands.

altering electronic and steric effects in their complexes; this might help in designing effective catalysts. Ru(II),[13a] Ru(III),[13b] Cu(I),[4c] and Co(III)[19] complexes of benzoyl thiourea ligands were used as efficient catalysts for the oxidation of alcohols to the corresponding carbonyl compounds. Surprisingly, acylthiourea ligands have been hardly employed in asymmetric synthesis.

Chiral alcohols are very important building blocks and synthetic intermediates in organic synthesis and the pharmaceutical industry.[20] Asymmetric transfer hydrogenation is one of the easiest ways to produce chiral alcohols, in which hydrogen is transferred from one organic molecule to another. This is of great importance in organic synthesis and is very helpful to avoid the use of molecular hydrogen. During the past decade, several catalytic systems have been developed for transfer hydrogenation of ketones using chiral Ru(II), Rh(I), Ir(I), and lanthanoid complexes as catalysts and 2-propanol/base or HCOOH/$Et_3N$ or HCOONa/$H_2O$ as the hydride source.[21,22] Among the different hydride sources, 2-propanol/base combinations are more attractive because of their stability, easy accessibility, nontoxicity, low relative cost, and environmentally benign nature.[23]

Ruthenium complexes are among the most efficient catalysts for transfer hydrogenation of ketones,[24] and this has been thoroughly explored by Noyori and co-workers.[21,25] Systems which have been successfully applied to the asymmetric transfer hydrogenation of carbonyl groups include several ruthenium arene complexes containing ancillary ligands such as chiral amines,[26] chiral diamines,[27] diphosphonites,[28] $\beta$-aminoethanethioltrityl ethers,[29] *N,N′*-bis[(1*S*)-1-benzyl-2-(diphenylphosphinite)ethyl]ethanediamides,[30] calix[4]arene-bearing amino alcohols,[31] (2*R*)-2-[benzyl(2-((diphenylphosphanyl)oxy)ethyl)amino]-butyldiphenylphosphinites,[32] (2*R*)-2-[benzyl(2-((dicyclohexylphosphanyl)oxy)ethyl)amino]-butyldicyclohexylphosphinites,[32] (1,2,3,4-tetrahydroquinolinyl)oxazolines,[33] proline amides,[34] (phosphinoferrocenyl)oxazolines,[35] amino alcohols,[22,36] $\alpha$-amino carboxylates,[37] and amino acid derivatives.[38] Ruthenium complexes have shown excellent performance in asymmetric inductions,[39] and it is cheaper relative to other metals such as rhodium.[40] Hence, we investigated the utility of chiral Ru(II) complexes for the asymmetric transfer hydrogenation of ketones.

In this paper, we describe the synthesis and characterization of the new chiral acylthiourea ligands (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)benzamide (**L1**/**L2**), (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)thiophene-2-carboxamide (**L3**/**L4**), and (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)furan-2-carboxamide (**L5**/**L6**) (Scheme 1) and their Ru(II) *p*-cymene complexes **1**−**6** (Scheme 2). These Ru(II) complexes were investigated as catalysts for the asymmetric transfer hydrogenation of ketones to their corresponding chiral alcohols.

## EXPERIMENTAL SECTION

**General Methods.** The solvents were dried according to literature methods and stored over activated molecular sieves. $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$ was prepared by a standard literature procedure.[41] UV−vis spectra were recorded using a PG Instruments double-beam UV−vis spectrophotometer, Model-T90+ with a quartz cell of 1 cm path length. FT-IR spectra in the range 4000−600 $cm^{-1}$ were recorded on a Nicolet iS5 FT-IR spectrophotometer with KBr pellets. CHNS analyses were performed using an Elementar Vario EL III elemental analyzer. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker 500 or 400 MHz and 125 or 100 MHz spectrometer, respectively. Melting points were determined in open capillary tubes on a Sigma melting point apparatus and are uncorrected. GC measurements for catalytic experiments were performed using a Shimadzu GC 2010 gas chromatograph with a Restek-5 capillary column. Enantiomeric excesses (ee) were determined using a Shimadzu HPLC instrument with a Daicel Chiralcel OB-H column. Specific rotation values were measured on a Rudolph Autopol IV polarimeter.

**Synthesis of L1 and L2.** A solution of benzoyl chloride (0.6 mL, 5 mmol) in acetone (30 mL) was added to a suspension of potassium thiocyanate (0.4859 g, 5 mmol) in acetone (30 mL). The reaction mixture was heated (70 °C) under reflux for 45 min and then cooled to room temperature. A solution of (*R*)-(+)-1-phenylethylamine or (*S*)-(−)-1-phenylethylamine (0.6 mL, 5 mmol) in acetone (30 mL) was added, and the resulting mixture was stirred for 3 h at 27 °C. Hydrochloric acid (0.1 N, 300 mL) was then added, and the resulting solid was filtered off. The solid product was washed with water and purified by recrystallization from an ethanol/dichloromethane mixture (1/2).

*(R)-N-((1-Phenylethyl)carbamothioyl)benzamide (**L1**).* Yield: 1.08 g, 77%. Mp: 74 °C. $[\alpha]_D^{27}$: +21.2°. Anal. Calcd for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85; S, 11.28. Found: C, 67.61; H, 5.72; N, 9.91; S, 11.32. ESI-MS (*m*/*z*): found 307.0 (L + $Na^+$); calcd value for $C_{16}H_{16}N_2OS$ 284.38. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 1.66 (d, 3H, *J* = 10 Hz, $CH_3$), 5.61 (m, 1H, asymmetric hydrogen), 7.29−7.83 (m, 10H, CH of phenyl rings), 9.01 (s, 1H, C═O and C═S attached N−H), 11.12 (d, 1H, *J* = 5 Hz, C═S attached N−H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 21.5 ($CH_3$), 55.0 (asymmetric carbon), 126.2, 127.3, 127.5, 128.7, 129.0, 131.6, 133.4, 141.5 (CH), 166.9 (C═O), 178.7 (C═S). FT-IR (KBr, $cm^{-1}$): 3412 (m; $\nu$(amide N−H)), 3214 (s; $\nu$(thiourea N−H)), 1670 (s; $\nu$(C═O)), 1248 (s; $\nu$(C═S)).

*(S)-N-((1-Phenylethyl)carbamothioyl)benzamide (**L2**).* Yield: 1.03 g, 73%. Mp: 75 °C. $[\alpha]_D^{27}$: −17.4°. Anal. Calcd for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85; S, 11.28. Found: C, 67.63; H, 5.63; N, 9.87; S, 11.37. ESI-MS (*m*/*z*): found 307.0 (L + $Na^+$); calcd value for $C_{16}H_{16}N_2OS$ 284.38. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.66 (d, 3H, *J* = 8 Hz, $CH_3$), 5.61 (m, 1H, asymmetric hydrogen), 7.25−7.83 (m, 10H, CH of phenyl rings), 9.04 (s, 1H, C═O and C═S attached N−H), 11.14 (d, 1H, *J* = 8 Hz, C═S attached N−H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 21.5 ($CH_3$), 55.0 (asymmetric carbon), 126.2, 127.3, 127.5, 128.6, 128.9, 131.5, 133.4, 141.5 (CH), 166.9 (C═O), 178.7 (C═S). FT-IR (KBr, $cm^{-1}$): 3412 (m; $\nu$(amide N−H)), 3214 (s; $\nu$(thiourea N−H)), 1670 (s; $\nu$(C═O)), 1248 (s; $\nu$(C═S)).

**Synthesis of L3 and L4.** A solution of thiophene-2-carbonyl chloride (0.5 mL, 5 mmol) in acetone (30 mL) was added to a suspension of potassium thiocyanate (0.4859 g, 5 mmol) in acetone


dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX

(30 mL). The reaction mixture was heated (70 °C) under reflux for 45 min and then cooled to room temperature. A solution of (*R*)-(+)-1-phenylethylamine or (*S*)-(−)-1-phenylethylamine (0.6 mL, 5 mmol) in acetone (30 mL) was added, and the resulting mixture was stirred for 3 h at 27 °C. Hydrochloric acid (0.1 N, 300 mL) was then added, and the resulting solid was filtered off. The solid product was washed with water and purified by recrystallization from an ethanol/dichloromethane mixture (1/2).

*(R)-N-((1-Phenylethyl)carbamothioyl)thiophene-2-carboxamide* ***(L3)***. Yield: 1.10 g, 78%. Mp: 120 °C. $[\alpha]_D^{27}$: −16.5°. Anal. Calcd for $C_{14}H_{14}N_2OS_2$: C, 57.90; H, 4.86; N, 9.65; S, 22.08. Found: C, 58.03; H, 4.90; N, 9.78; S, 21.99. LC-MS (*m*/*z*): found 290; calcd value for $C_{14}H_{14}N_2OS_2$ 290.40. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.64 (d, 3H, *J* = 5 Hz, $CH_3$), 5.59 (m, 1H, asymmetric hydrogen), 7.67 (dd, 1H, *J* = 5 Hz, CH of thiophene ring), 7.15 (t, 1H, *J* = 10 Hz, CH of thiophene ring), 7.64 (dd, 1H, *J* = 5 Hz, CH of thiophene ring), 7.25−7.38 (m, 5H, CH of phenyl ring), 8.83 (s, 1H, C═O and C═S attached N−H), 10.92 (d, 1H, *J* = 5 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 21.5 ($CH_3$), 55.1 (asymmetric carbon), 126.2, 127.6, 128.3, 128.7, 130.4, 133.9, 136.0, 141.5 (CH), 161.0 (C═O), 178.4 (C═S). FT-IR (KBr, $cm^{-1}$): 3393 (m; ν(amide N−H)), 3217 (s; ν(thiourea N−H)), 1658 (s; ν(C═O)), 1254 (s; ν(C═S)).

*(S)-N-((1-Phenylethyl)carbamothioyl)thiophene-2-carboxamide* ***(L4)***. Yield: 1.14 g, 81%. Mp: 119 °C. $[\alpha]_D^{27}$: +13.2°. Anal. Calcd for $C_{14}H_{14}N_2OS_2$: C, 57.90; H, 4.86; N, 9.65; S, 22.08. Found: C, 58.67; H, 5.06; N, 9.69; S, 21.92. LC-MS (*m*/*z*): found 290.40; calcd value for $C_{14}H_{14}N_2OS_2$ 290.40. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.64 (d, 3H, *J* = 5 Hz, $CH_3$), 5.59 (m, 1H, asymmetric hydrogen), 7.68 (dd, 1H, *J* = 5 Hz, CH of thiophene ring), 7.15 (t, 1H, *J* = 10 Hz, CH of thiophene ring), 7.64 (dd, 1H, *J* = 5 Hz, CH of thiophene ring), 7.26−7.37 (m, 5H, CH of phenyl ring), 8.83 (s, 1H, C═O and C═S attached N−H), 10.93 (d, 1H, *J* = 5 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 21.6 ($CH_3$), 55.2 (asymmetric carbon), 126.2, 127.6, 128.4, 128.8, 130.4, 134.0, 136.1, 141.5 (CH), 161.0 (C═O), 178.4 (C═S). FT-IR (KBr, $cm^{-1}$): 3393 (m; ν(amide N−H)), 3217 (s; ν(thiourea N−H)), 1658 (s; ν(C═O)), 1255 (s; ν(C═S)).

**Synthesis of L5 and L6.** A solution of furan-2-carbonyl chloride (0.5 mL, 5 mmol) in acetone (30 mL) was added to a suspension of potassium thiocyanate (0.4859 g, 5 mmol) in acetone (30 mL). The reaction mixture was heated (70 °C) under reflux for 45 min and then cooled to room temperature. A solution of (*R*)-(+)-1-phenylethylamine or (*S*)-(−)-1-phenylethylamine (0.6 mL, 5 mmol) in acetone (30 mL) was added, and the resulting mixture was stirred for 3 h at 27 °C. Hydrochloric acid (0.1 N, 300 mL) was then added, whereupon an yellow oil was formed. The aqueous layer was decanted, and the oil was extracted into diethyl ether (40 mL). The aqueous layer was extracted twice with ether (40 mL) and the ether fractions were combined, dried over anhydrous $Na_2SO_4$, and evaporated to dryness under reduced pressure to yield a yellow oil.

*(R)-N-((1-Phenylethyl)carbamothioyl)furan-2-carboxamide* ***(L5)***. Yield: 0.98 g, 75%. $[\alpha]_D^{27}$: +19.2°. Anal. Calcd for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; N, 10.21; S, 11.69. Found: C, 61.36; H, 4.97; N, 11.02; S, 11.82. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.64 (d, 3H, *J* = 5 Hz, $CH_3$), 5.60 (m, 1H, asymmetric hydrogen), 6.59 (q, 1H, *J* = 5 Hz, CH of furan ring), 7.31 (dd, 1H, *J* = 5 Hz, CH of furan ring), 7.57 (q, 1H, *J* = 5 Hz, CH of furan ring), 7.26−7.39 (m, 5H, CH of phenyl ring), 9.09 (s, 1H, C═O and C═S attached N−H), 10.86 (d, 1H, *J* = 5 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 21.5 ($CH_3$), 55.1 (asymmetric carbon), 113.2, 118.5, 126.2, 127.6, 128.7, 141.6, 145.0, 146.2 (CH), 156.7 (C═O), 178.4 (C═S). FT-IR (KBr, $cm^{-1}$): 3407 (m; ν(amide N−H)), 3242 (s; ν(thiourea N−H)), 1668 (s; ν(C═O)), 1267 (s; ν(C═S)).

*(S)-N-((1-Phenylethyl)carbamothioyl)furan-2-carboxamide* ***(L6)***. Yield: 1.02 g, 78%. $[\alpha]_D^{27}$: −34.8°. Anal. Calcd for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; N, 10.21; S, 11.69. Found: C, 61.36; H, 4.97; N, 11.02; S, 11.82. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.64 (d, 3H, *J* = 5 Hz, $CH_3$), 5.59 (m, 1H, asymmetric hydrogen), 6.59 (q, 1H, *J* = 5 Hz, CH of furan ring), 7.31 (dd, 1H, *J* = 5 Hz, CH of furan ring), 7.57 (q, 1H, *J* = 5 Hz, CH of furan ring), 7.26−7.37 (m, 5H, CH of phenyl ring), 9.09 (s, 1H, C═O and C═S attached N−H), 10.86 (d, 1H, *J* = 5 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 21.6 ($CH_3$), 55.1 (asymmetric carbon), 113.2, 118.5, 126.2, 127.6, 128.7, 141.6, 145.0, 146.2 (CH), 156.7 (C═O), 178.4 (C═S). FT-IR (KBr, $cm^{-1}$): 3407 (m; ν(amide N−H)), 3242 (s; ν(thiourea N−H)), 1668 (s; ν(C═O)), 1267 (s; ν(C═S)).

**Synthesis of the Complexes 1−6.** $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$ (0.283 g, 0.44 mmol) and (*R*)-/(*S*)-N-((1-phenylethyl)-carbamothioyl)benzamide (0.250 g, 0.88 mmol), or (*R*)-/(*S*)-N-((1-phenylethyl)carbamothioyl)thiophene-2-carboxamide (0.256 g, 0.88 mmol), or (*R*)-/(*S*)-*N*-((1-phenylethyl)carbamothioyl)furan-2-carboxamide (0.242 g, 0.88 mmol) were dissolved in 25 mL of toluene and stirred for 4−6 h at 27 °C. The solution was concentrated to 2 mL under reduced pressure, and addition of petroleum ether (60−80 °C) (15 mL) gave a clear orange solid. The product was collected by filtration, washed with petroleum ether, and dried in vacuo.

*$[RuCl_2(\eta^6\text{-}p\text{-cymene})$**L1**$]$* ***(1)***. Yield: 0.224 g, 86%. Mp: 128 °C. $[\alpha]_D^{27}$: −31°. Anal. Calcd for $C_{26}H_{30}Cl_2N_2ORuS$: C, 53.46; H, 5.65; N, 4.65; S, 5.29. Found: C, 53.49; H, 5.71; N, 4.68; S, 5.31. ESI-MS (*m*/*z*): found 519.0 (M − $2Cl^-$); calcd value for $C_{26}H_{30}Cl_2N_2ORuS$ 590.60. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.28 (dd, 6H, *J* = 8 Hz, $2CH_3$ of *p*-cymene), 1.69 (d, 3H, *J* = 8 Hz, $CH_3$ of the ligand), 2.24 (s, 3H, $CH_3$ of *p*-cymene), 2.93 (m, 1H, CH of *p*-cymene), 5.23−5.41 (m, 4H, aromatic protons of *p*-cymene), 5.49 (m, 1H, asymmetric hydrogen), 7.26−8.23 (m, 10H, aromatic protons of the ligand), 11.13 (s, 1H, C═O and C═S attached N−H), 11.81 (d, 1H, *J* = 8 Hz, C═S attached N−H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 18.2 ($CH_3$ of *p*-cymene), 22.1 ($2CH_3$ of *p*-cymene), 22.3 ($CH_3$ of the ligand), 30.3 (CH of *p*-cymene), 55.2 (asymmetric carbon), 82.5−84.2 (aromatic carbons of *p*-cymene), 99.9 and 103.2 (quaternary carbons of *p*-cymene), 126.1, 126.2, 127.8, 128.4, 128.8, 128.9, 129.6 131.0, 133.4, 141.0 (CH), 169.3 (C═O), 178.8 (C═S). FT-IR (KBr, $cm^{-1}$): 3446 (m; ν(amide N−H)), 3143 (s; ν(thiourea N−H)), 1667 (s; ν(C═O)), 1197 (s; ν(C═S)). UV−vis ($CHCl_3$; λ, nm (ε, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 445 (1773), 332 (5821), 256 (26310).

*$[RuCl_2(\eta^6\text{-}p\text{-cymene})$**L2**$]$* ***(2)***. Yield: 0.213 g, 82%. Mp: 128 °C. $[\alpha]_D^{27}$: +37°. Anal. Calcd for $C_{26}H_{30}Cl_2N_2ORuS$: C, 53.46; H, 5.65; N, 4.65; S, 5.29. Found: C, 53.50; H, 5.71; N, 4.63; S, 5.32. ESI-MS (*m*/*z*): found 519.0 (M − $2Cl^-$); calcd value for $C_{26}H_{30}Cl_2N_2ORuS$ 590.60. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.28 (dd, 6H, *J* = 8 Hz, $2CH_3$ of *p*-cymene), 1.68 (d, 3H, *J* = 8 Hz, $CH_3$ of the ligand), 2.24 (s, 3H, $CH_3$ of *p*-cymene), 2.93 (m, 1H, CH of *p*-cymene), 5.23−5.41 (m, 4H, aromatic protons of *p*-cymene), 5.50 (m, 1H, asymmetric hydrogen), 7.26−8.23 (m, 10H, aromatic protons of the ligand), 11.13 (s, 1H, C═O and C═S attached N−H), 11.81 (d, 1H, *J* = 8 Hz, C═S attached N−H proton). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 18.2 ($CH_3$ of *p*-cymene), 22.1 ($2CH_3$ of *p*-cymene), 22.3 ($CH_3$ of the ligand), 30.4 (CH of *p*-cymene), 55.2 (asymmetric carbon), 82.5−84.3 (aromatic carbons of *p*-cymene), 99.9 and 103.2 (quaternary carbons of *p*-cymene), 126.2, 127.8, 128.4, 128.8, 129.6, 131.1, 133.4, 141.0 (CH), 169.3 (C═O), 178.8 (C═S). FT-IR (KBr, $cm^{-1}$): 3442 (m; ν(amide N−H)), 3144 (s; ν(thiourea N−H)), 1667 (s; ν(C═O), 1197 (s; ν(C═S)). UV−vis ($CHCl_3$; λ, nm (ε, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 445 (1748), 332 (5746), 256 (26177).

*$[RuCl_2(\eta^6\text{-}p\text{-cymene})$**L3**$]$* ***(3)***. Yield: 0.231 g, 88%. Mp: 198 °C. $[\alpha]_D^{27}$: −32.2°. Anal. Calcd for $C_{24}H_{28}Cl_2N_2ORuS_2$: C, 49.09; H, 5.11; N, 4.58; S, 10.49. Found: C, 49.13; H, 5.15; N, 4.63; S, 10.54. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.29 (dd, 6H, *J* = 5 Hz, $2CH_3$ of *p*-cymene), 1.66 (d, 3H, *J* = 5 Hz, $CH_3$ of the ligand), 2.25 (s, 3H, $CH_3$ of *p*-cymene), 2.94 (m, 1H, CH of *p*-cymene), 5.25−5.42 (m, 4H, aromatic protons of *p*-cymene), 5.46 (m, 1H, asymmetric hydrogen), 7.27−8.48 (m, 8H, aromatic protons of the ligand), 10.90 (s, 1H, C═O and C═S attached N−H), 11.50 (d, 1H, *J* = 10 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 18.2 ($CH_3$ of *p*-cymene), 22.1 ($2CH_3$ of *p*-cymene), 22.3 ($CH_3$ of the ligand), 30.4 (CH of *p*-cymene), 55.2 (asymmetric carbon), 82.4−84.3 (aromatic carbons of *p*-cymene), 100.0 and 103.2 (quaternary carbons of *p*-cymene), 126.2, 127.8, 128.8, 128.9, 134.2, 135.3, 136.1, 140.9 (CH), 163.3 (C═O), 178.1 (C═S). FT-IR (KBr, $cm^{-1}$): 3441 (m; ν(amide N−H)), 3212 (s; ν(thiourea N−H)), 1657 (s; ν(C═O)), 1197 (s; ν(C═S)). UV−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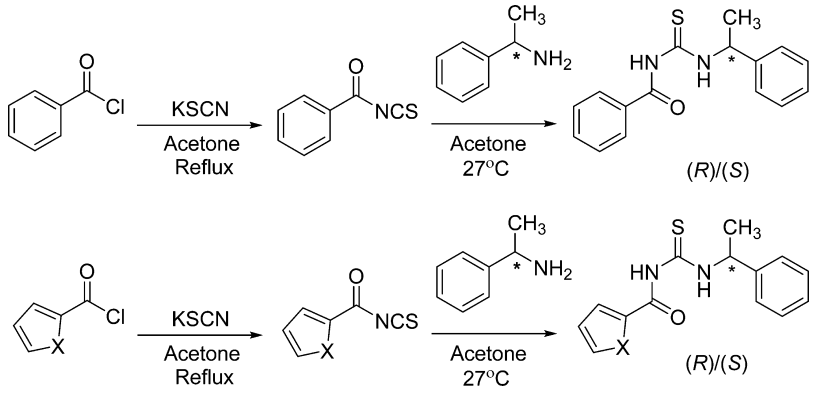
**Scheme 1. Synthesis of the Ligands**




vis ($CHCl_3$; $\lambda$, nm ($\varepsilon$, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 443 (1515), 338 (5280), 294 (12450), 257 (17598).

*[$RuCl_2(\eta^6$-p-cymene)L4] (4).* Yield: 0.221 g, 84%. Mp: 197 °C. $[\alpha]_D^{27}$: +33.6°. Anal. Calcd for $C_{24}H_{28}Cl_2N_2ORuS_2$: C, 49.09; H, 5.11; N, 4.58; S, 10.49. Found: C, 49.13; H, 5.14; N, 4.61; S, 10.53. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.28 (dd, 6H, $J$ = 5 Hz, $2CH_3$ of *p*-cymene), 1.68 (d, 3H, $J$ = 5 Hz, $CH_3$ of the ligand), 2.26 (s, 3H, $CH_3$ of *p*-cymene), 2.94 (m, 1H, CH of *p*-cymene), 5.25−5.42 (m, 4H, aromatic protons of *p*-cymene), 5.45 (m, 1H, asymmetric hydrogen), 7.10−8.48 (m, 8H, aromatic protons of the ligand), 10.90 (s, 1H, C═O and C═S attached N−H), 11.50 (d, 1H, $J$ = 10 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.3 ($CH_3$ of *p*-cymene), 22.2 ($2CH_3$ of *p*-cymene), 22.3 ($CH_3$ of the ligand), 30.4 (CH of *p*-cymene), 55.2 (asymmetric carbon), 82.5−84.3 (aromatic carbons of *p*-cymene), 100.0 and 103.3 (quaternary carbons of *p*-cymene), 126.2, 127.8, 128.9, 128.9, 134.2, 135.3, 136.1, 141.0 (CH), 163.4 (C═O), 178.2 (C═S). FT-IR (KBr, $cm^{-1}$): 3440 (m; $\nu$(amide N−H)), 3212 (s; $\nu$(thiourea N−H)), 1656 (s; $\nu$(C═O)), 1197 (s; $\nu$(C═S)). UV−vis ($CHCl_3$; $\lambda$, nm ($\varepsilon$, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 443 (1673), 340 (6337), 295 (15050), 257 (21113).

*[$RuCl_2(\eta^6$-p-cymene)L5] (5).* Yield: 0.216 g, 85%. Mp: 170 °C. $[\alpha]_D^{27}$: −35°. Anal. Calcd for $C_{24}H_{28}Cl_2N_2O_2RuS$: C, 50.33; H, 5.41; N, 4.70; S, 5.37. Found: C, 50.39; H, 5.43; N, 4.69; S, 5.43. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.28 (dd, 6H, $J$ = 5 Hz, $2CH_3$ of *p*-cymene), 1.66 (d, 3H, $J$ = 5 Hz, $CH_3$ of the ligand), 2.25 (s, 3H, $CH_3$ of *p*-cymene), 2.93 (m, 1H, CH of *p*-cymene), 5.24−5.42 (m, 4H, aromatic protons of *p*-cymene), 5.45 (m, 1H, asymmetric hydrogen), 6.50−7.93 (m, 8H, aromatic protons of the ligand), 10.80 (s, 1H, C═O and C═S attached N−H), 11.42 (d, 1H, $J$ = 10 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.2 ($CH_3$ of *p*-cymene), 22.1 ($2CH_3$ of *p*-cymene), 22.4 ($CH_3$ of the ligand), 30.4 (CH of *p*-cymene), 55.3 (asymmetric carbon), 82.4−84.2 (aromatic carbons of *p*-cymene), 100.0 and 103.3 (quaternary carbons of *p*-cymene), 112.4, 121.4, 126.1, 127.8, 128.9, 140.9, 144.6, 147.7 (CH), 158.8 (C═O), 178.3 (C═S). FT-IR (KBr, $cm^{-1}$): 3441 (m; $\nu$(amide N−H)), 3099 (s; $\nu$(thiourea N−H)), 1680 (s; $\nu$(C═O)), 1214 (s; $\nu$(C═S)). UV−vis ($CHCl_3$; $\lambda$, nm ($\varepsilon$, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 448 (1074), 331 (6312), 283 (22745), 255 (17948).

*[$RuCl_2(\eta^6$-p-cymene)L6] (6).* Yield: 0.209 g, 82%. Mp: 171 °C. $[\alpha]_D^{27}$: +50.03°. Anal. Calcd for $C_{24}H_{28}Cl_2N_2O_2RuS$: C, 50.33; H, 5.41; N, 4.70; S, 5.37. Found: C, 50.37; H, 5.45; N, 4.73; S, 5.41. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.28 (dd, 6H, $J$ = 5 Hz, $2CH_3$ of *p*-cymene), 1.66 (d, 3H, $J$ = 5 Hz, $CH_3$ of the ligand), 2.25 (s, 3H, $CH_3$ of *p*-cymene), 2.93 (m, 1H, CH of *p*-cymene), 5.25−5.42 (m, 4H, aromatic protons of *p*-cymene), 5.46 (m, 1H, asymmetric hydrogen), 6.49−7.93 (m, 8H, aromatic protons of the ligand), 10.80 (s, 1H, C═O and C═S attached N−H), 11.42 (d, 1H, $J$ = 10 Hz, C═S attached N−H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.2 ($CH_3$ of *p*-cymene), 22.1 ($2CH_3$ of *p*-cymene), 22.3 ($CH_3$ of the ligand), 30.3 (CH of *p*-cymene), 55.2 (asymmetric carbon), 82.4−84.2 (aromatic carbons of *p*-cymene), 99.9 and 103.2 (quaternary carbons of *p*-cymene), 112.6, 121.3, 126.1, 127.8, 128.8, 140.9, 144.5, 147.7 (CH), 158.7 (C═O), 178.3 (C═S). FT-IR (KBr, $cm^{-1}$): 3441 (m; $\nu$(amide N−H)), 3099 (s; $\nu$(thiourea N−H)), 1680 (s; $\nu$(C═O)), 1214 (s; $\nu$(C═S)). UV−vis ($CHCl_3$; $\lambda$, nm ($\varepsilon$, $dm^3$ $mol^{-1}$ $cm^{-1}$)): 446 (1165), 334 (6600), 284 (24044), 255 (18931).

**X-ray Structure Determinations.** Details of data collection procedures are given in Table S1 (Supporting Information). Crystals were cooled from ambient temperature to 100 K over a period of 1 h. The frame images were integrated using Denzo (SMN),[42] and the resultant raw intensity .x files were processed using a locally modified version of DENZOX.[43] The resultant intensity measurements were corrected for absorption correction either by Gaussian quadrature,[44] and a second semiempirical correction[45] (without a $\theta$-dependent correction) was applied to remove any residual absorption anisotropy due to the mounting medium and to account for other errors such as machine instabilities. The data were then merged using SORTAV.[46] Structures were solved by direct methods and refined using SHELXL-2013,[47] with full-matrix least squares on $F^2$ and using all the unique data. All non-H atoms were allowed anisotropic thermal motion. The thiourea ligand and isopropyl substituent in complex **2** exhibited a complete 1:1 disorder. Nevertheless, the general conformation of the complex and the monodentate nature of the ligand were clearly defined by the crystal structure analysis. Thermal ellipsoid plots were obtained using the program ORTEP-3 for Windows.[48] All calculations were carried out using the WinGX package[48] of crystallographic programs.

**Procedure for Asymmetric Transfer Hydrogenation of Ketones.** [$RuCl_2(\eta^6$-p-cymene)L] (**1**−**6**; 0.005 mmol) and KOH (1 mmol) were dissolved in 2-propanol (5 mL). This mixture was stirred at 82 °C for 10 min under an $N_2$ atmosphere. After the mixture was cooled to room temperature, 1 mmol of ketone was introduced and then the mixture was stirred at 82 °C. After 24 h, the reaction mixture was cooled to room temperature and then passed through a short silica gel column with *n*-hexane/ethyl acetate (1/1) eluent to remove the Ru complex. Conversions were monitored by GC, and the ee values were determined using HPLC with a Chiralcel OB-H column.

## RESULTS AND DISCUSSION

**Synthesis of Ligands and Complexes.** The chiral ligands **L1**−**L6** were synthesized from benzoyl chloride, or thiophene-2-carbonyl chloride, or furan-2-carbonyl chloride, potassium thiocyanate, and (*R*)-(+)-1-phenylethylamine or (*S*)-(−)-1-phenylethylamine in dry acetone (Scheme 1).[4c] The reaction between [$RuCl_2(\eta^6$-p-cymene)]$_2$ and chiral ligand (L) in toluene led to the formation of a chiral complex of the type [$RuCl_2(\eta^6$-p-cymene)L] (Scheme 2). The ligands and Ru complexes were characterized by elemental analysis and UV−vis, $^1$H NMR, $^{13}$C NMR, mass, and FT-IR spectroscopic methods. The optical rotation of the compounds was obtained by polarimetric studies. The structures of the ligands **L1** and **L3** and the Ru complexes **1**, **4**, and **6** were confirmed by X-ray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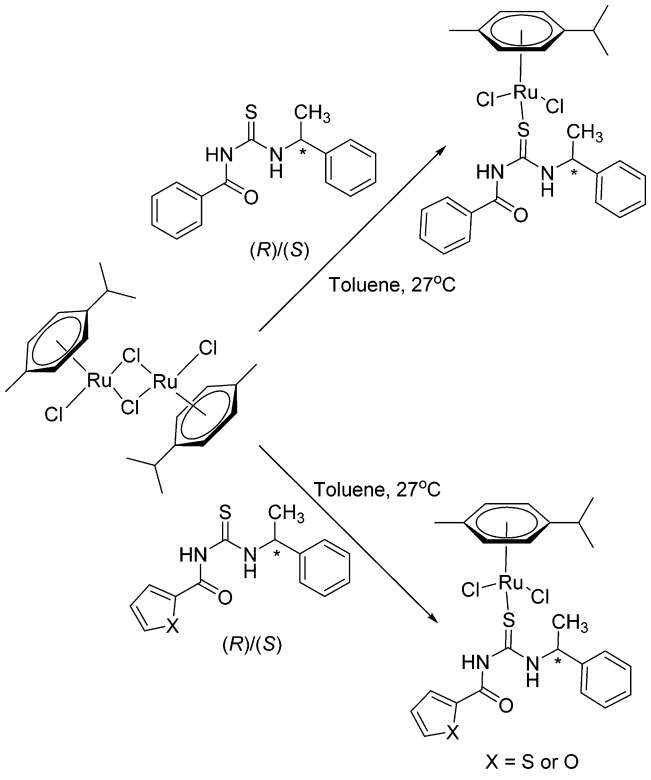
**Scheme 2. Synthesis of the Complexes**




crystallography. All of the ligands and complexes are stable to air and are soluble in toluene, DMSO, DMF, $CH_3OH$, $C_2H_5OH$, $CHCl_3$, $CH_2Cl_2$, and $CH_3CN$.

**Characterization of Ligands and Complexes.** In the $^1H$ NMR spectra of all the chiral acylthiourea derivatives **L1**−**L6**, the carbonyl- and thiocarbonyl-attached N−H and thiocarbonyl-attached N−H protons were observed as singlets and doublets around 8.83−9.09 and 10.85−11.15 ppm, respectively. The signals due to protons of the aromatic rings appeared at 6.59−7.83 ppm in the spectra of all the ligands. For the asymmetric hydrogen, a multiplet was observed at 5.56−5.65 ppm. The $CH_3$ protons of the ligands were observed as a doublet around 1.64−1.67 ppm. The resonances due to protons of the thiophene and furan rings were present in the spectra of **L3** and **L4** and of **L5** and **L6**, respectively. In the $^1H$ NMR spectra of the complexes **1**−**6**, the carbonyl- and thiocarbonyl-attached N−H and thiocarbonyl-attached N−H protons were observed as singlets and doublets around 10.80−11.13 and 11.42−11.81 ppm, respectively. The new signals observed in the regions 1.27−1.30, 2.24−2.98, and 5.23−5.42 ppm indicate the presence of a *p*-cymene moiety in the complexes.[49] All other chemical shift values of the complexes were very similar to those of the free ligands. The $^{13}C$ NMR spectra of the ligands showed signals at 21.5 and 55.1 ppm for the $CH_3$ and asymmetric carbons, respectively. The signals appearing around 113.2−146.2 ppm in the spectra of all ligands were assigned to the aromatic carbons. The resonances due to C═O and C═S were observed around 156.7−166.9 and 178.4−178.7 ppm, respectively. The $^{13}C$ NMR chemical shift values did not change significantly upon coordination of the ligand to Ru. The new signals observed at 18.2, 22.2, 30.4, 84.4, 99.9, and 103.3 ppm confirms the presence of *p*-cymene in all of the complexes.[49]

The FT-IR spectra of the complexes were compared with those of the free ligands. The frequencies of the C═O and amide N−H stretching modes were almost unaltered upon coordination, but the C═S stretching frequency of the complexes decreased by 51−58 $cm^{-1}$, which strongly suggests that the ligands are bound to the ruthenium center via the sulfur atom only.[4c] This was confirmed by the X-ray crystal structures discussed below.

**X-ray Crystallographic Studies.** The molecular structures of ligands **L1** and **L3** and the complexes **1**, **4**, and **6** are shown in Figures 2−6, respectively. All compounds crystallize in the

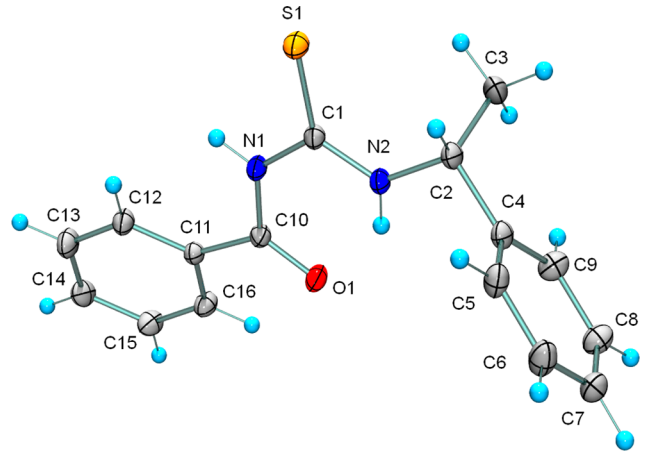



**Figure 2.** ORTEP view of **L1** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level.

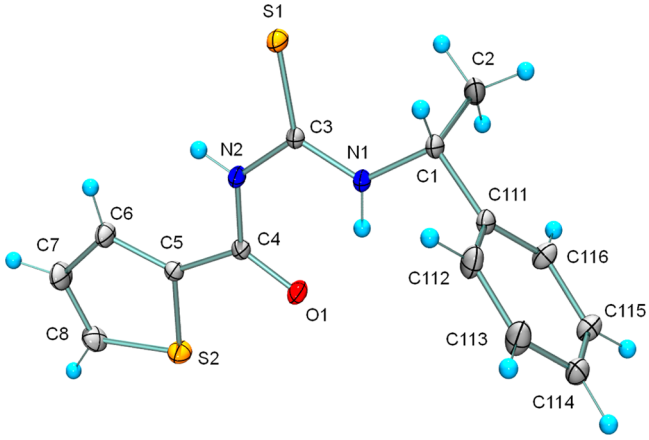



**Figure 3.** ORTEP view of **L3** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level.

chiral orthorhombic space group $P2_12_12_1$. The unit cells and crystal packings for the ligands **L1** and **L3** are very similar, as is also the case for complexes **1**, **4**, and **6** (see Figures S1−S3, Supporting Information). The monodentate nature of the thiourea ligands in all complexes is clearly defined, even for complex **4**, which has significant disorder. To the best of our knowledge, these complexes provide the first examples of monodentate coordination of an acylthiourea ligand with ruthenium. The coordination geometry of the Ru atoms is of the three-legged piano-stool type and is essentially identical in all three complexes.

**Asymmetric Transfer Hydrogenation of Ketones.** The chiral Ru(II) complexes **1**−**6** were all examined as catalysts for


dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX

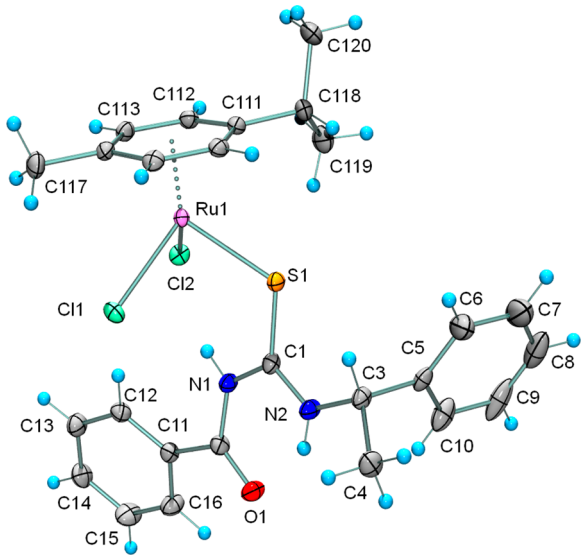



**Figure 4.** ORTEP view of **1** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level.

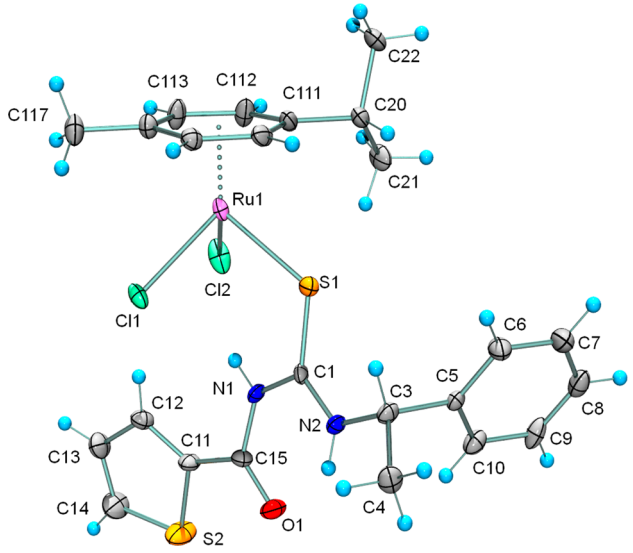



**Figure 5.** ORTEP view of **4** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level. Only one orientation of the disordered molecule is shown.

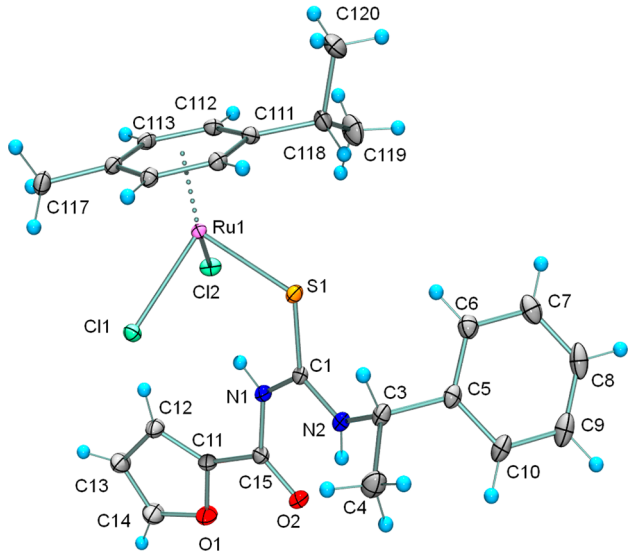


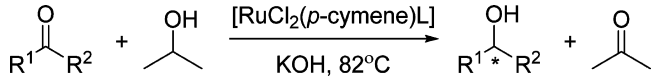

**Figure 6.** ORTEP view of **6** showing the atomic labeling scheme and thermal ellipsoids at the 50% probability level.

the asymmetric transfer hydrogenation of ketones. Reactions were performed in refluxing (82 °C) 2-propanol in the presence of KOH. The optimized substrate:KOH:catalyst ratio was 200:1:1. The reactions proceeded smoothly with up to 99% conversion and 99% enantiomeric excess (ee) after 24 h. The progress of the reactions was monitored by GC, and the results are summarized in Table 1.

The efficacy of the present catalytic system was compared with that of the already available catalysts based on $[RuCl_2(\eta^6$-*p*-cymene$)]_2$, particularly with respect to the asymmetric reduction of acetophenone (Scheme 3). The $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral *β*-amino alcohol catalytic system gave 1-phenylethanol from acetophenone with a 94% conversion and a 91% ee.[50] For the same substrate, a 99% conversion and 89% ee were observed in our protocol using catalyst **4** (Table 1, entry 4). No significant ee was attained with [Ru(chloro(*p*-cymene)-(*N*,*N*′-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]-ethanediamide))]chloride[30] catalyst, whereas the present catalytic system showed moderate to excellent ee (58−99%). Excellent conversion (99%) and good ee (82%) were reported for the transfer hydrogenation of acetophenone with [*μ*-(2*R*)-2[benzyl{(2-((diphenylphosphanyl)oxy)ethyl)} amino]-butyldiphenylphosphinito]bis[dichloro($\eta^6$-*p*-isopropyltoluene)-ruthenium(II)][32] catalyst after 24 h, which is comparable with the efficiency of **4**. Only 1% ee was reached for 1-phenylethanol with the $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral P,N ferrocenyl ligand[51] as catalyst. $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/(*R*,*R*)-TsDPEN catalyst has converted 81% of acetophenone to 1-phenylethanol (89% ee);[52] the efficiency is slightly lower than that of catalyst **4**. Mixtures of $[RuCl_2(\eta^6$-*p*-cymene$)]_2$ and chiral calix[4]arenes bearing *β*-amino alcohols have been used as catalysts in the asymmetric reduction of acetophenone, which showed comparable conversion (97%) and ee (87%).[31] Better catalytic activity (86% conversion and 83% ee) was achieved with $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral aminoethanethiol trityl ether catalyst at 27 °C.[29] Chen et al. observed superior catalytic activity for $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/(*R*,*R*)-*N*-(4-acetylamino-phenylsulfonyl)-1,2-diphenylethylenediamine catalyst and reported 99% conversion and 97% ee.[53] Excellent conversion (99%) but only moderate ee (64%) was obtained with $[RuCl_2(\eta^6$-*p*-cymene$)]_2$ and chiral phosphinite ligands,[54] whereas our catalysts **2**, **4**, and **6** showed good ee values. $[RuCl_2(\eta^6$-*p*-cymene$)]_2$ with PEG-BsDPEN was found to be better than the present $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral acylthiourea catalyst for the asymmetric transfer hydrogenation of acetophenone, as 99% conversion and 96% ee was observed in the former case.[55] $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral phosphinoferrocenyl oxazoline ligand-catalyzed reduction of acetophenone provided 1-phenylethanol in 91% yield with 41% ee.[35] In comparison to this catalytic system, catalyst **4** showed better performance. $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral *α*-amino acid amides or thioamides showed 83% conversion and 92% ee;[56] the optical purity is slightly better than that for the present system but not the yield. $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/N-PEG-TsDPEN exhibited an excellent performance of 99% conversion and 94% ee.[57] Han et al. reported $[RuCl_2(\eta^6$-*p*-cymene$)]_2$/chiral amino alcohol as a catalyst for the asymmetric


dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX

Table 1. Transfer Hydrogenation of Ketones Catalyzed by Ru(II) Complexes 1−6[a]




| Entry | Catalyst | Substrate | Product | Conversion[b] (%) | ee[c] (%) | Configuration[d] |
|---|---|---|---|---|---|---|
| 1 | (1) | | | 88 | 79 | *S* |
| 2 | (2) | | | 53 | 99 | *S* |
| 3 | (3) | | | 84 | 58 | *S* |
| 4 | (4) | | | 99 | 89 | *S* |
| 5 | (5) | | | 91 | 76 | *S* |
| 6 | (6) | | | 64 | 95 | *S* |
| 7 | (1) | | | 97 | 99 | *R* |
| 8 | (2) | | | 99 | 99 | *S* |
| 9 | (3) | | | 99 | 99 | *R* |
| 10 | (4) | | | 65 | 99 | *R* |
| 11 | (5) | | | 99 | 99 | *R* |
| 12 | (6) | | | 99 | 99 | *S* |
| 13 | (1) | | | 98 | 99 | *S* |
| 14 | (2) | | | 99 | 99 | *R* |
| 15 | (3) | | | 98 | 99 | *R* |
| 16 | (4) | | | 88 | 99 | *R* |
| 17 | (5) | | | 96 | 99 | *R* |
| 18 | (6) | | | 99 | 99 | *R* |
| 19 | (1) | | | 98 | 99 | *S* |
| 20 | (2) | | | 60 | 99 | *R* |
| 21 | (3) | | | 96 | 99 | *R* |
| 22 | (4) | | | 95 | 99 | *S* |
| 23 | (5) | | | 65 | 99 | *R* |
| 24 | (6) | | | 97 | 99 | *R* |
| 25 | (1) | | | 62 | 99 | *R* |
| 26 | (2) | | | 65 | 99 | *R* |
| 27 | (3) | | | 99 | 98 | *S* |
| 28 | (4) | | | 55 | 99 | *S* |
| 29 | (5) | | | 72 | 90 | *S* |
| 30 | (6) | | | 66 | 99 | *S* |

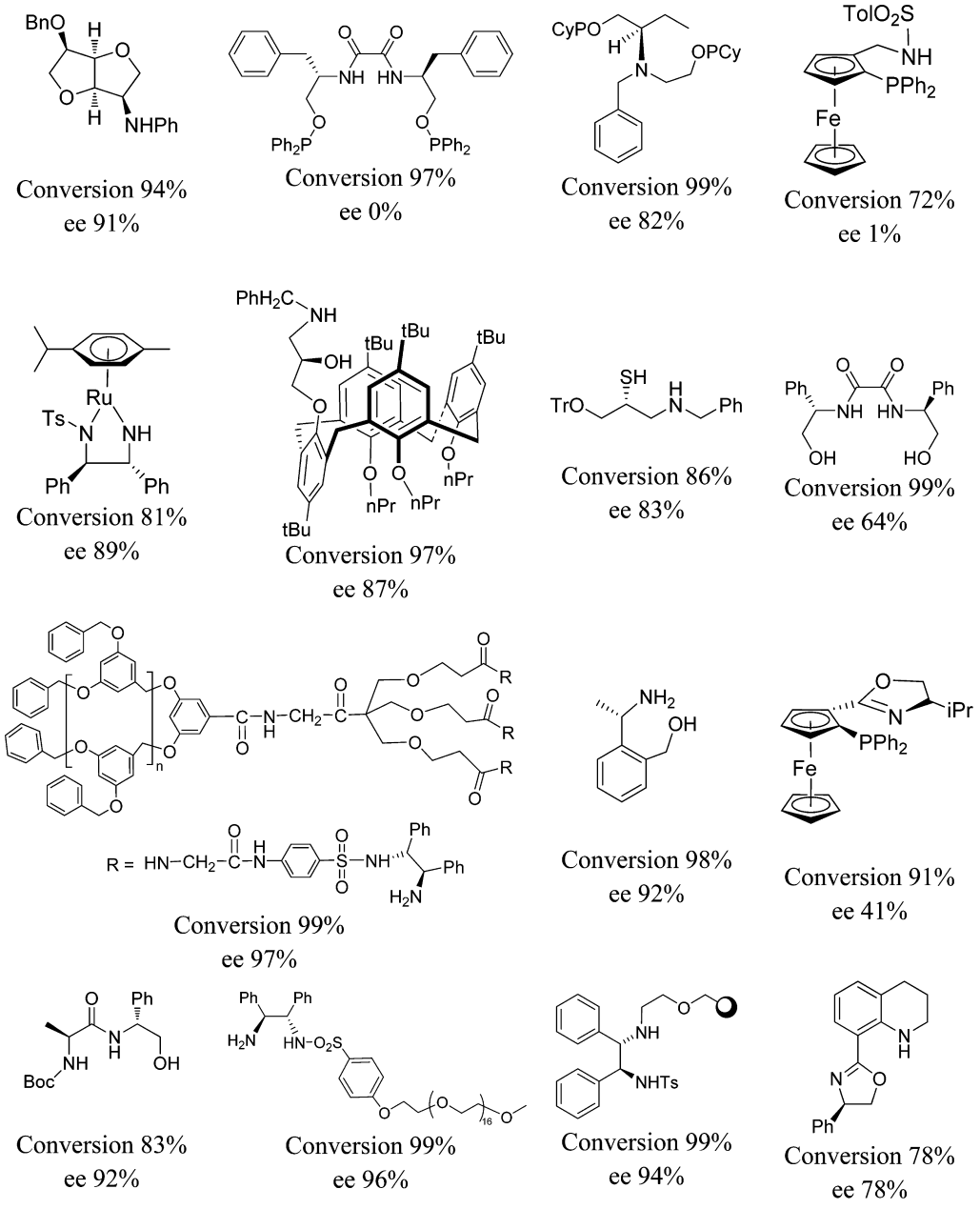
[a]Reactions were carried out at 82 °C using 1 mmol of substrate and 0.005 mmol of Ru(II) complex in 5 mL of 2-propanol and 1 mmol of KOH for 24 h. [b]The conversion was determined by GC. [c]The ee was determined by chiral HPLC. [d]The absolute configuration was determined from the optical rotation values.

reduction of ketones and observed 98% conversion and 92% ee for the transformation of acetophenone to 1-phenylethanol.[36a] $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$/chiral (1,2,3,4-tetrahydroquinolinyl)-oxazoline ligands converted 78% of the acetophenone to 1-phenylethanol with an ee of 78% after 48 h,[33] whereas the present catalytic system showed better activity within 24 h.

Acetophenone with a nitro group in the meta position did not give satisfactory results in the asymmetric transfer hydrogenation catalyzed by $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$/2-azanorbornyl alcohol[58] but gave the best results in our case (Table 1, entries 7−9, 11, and 12). Though many methods exist for the asymmetric transfer hydrogenation of ketones, reports on the enantioselective hydrogenation of heterocyclic ketones are relatively uncommon. The reduction of 3-acetylpyridine performed exceptionally well in our method, which gave the corresponding chiral alcohol quantitatively in 99% ee (Table 1, entries 14 and 18). A chiral benzhydrol derivative is an intermediate in the synthesis of TAK-475, which is a potent squalene synthase inhibitor and was expected to be a good candidate to lower plasma cholesterol.[59] Using the present procedure, we were able to prepare chiral benzhydrols (ee 90−99%) from benzophenones (Table 1, entries 19−30).


dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX

**Scheme 3. Effectiveness of Reported Chiral Ligands with $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$**




**Proposed Mechanism.** The homogeneous hydrogenation of prochiral ketones to the corresponding chiral alcohols, using transition-metal complexes as catalysts, can proceed stepwise via metal hydride species. The suggested mechanism for transfer hydrogenation is illustrated in Figure 7. The Ru–alkoxide active species formed from the reaction between $[RuCl_2(\eta^6\text{-}p\text{-cymene})L]$ (L = chiral acylthiourea ligand) and 2-propanol in the presence of KOH generated an 18-electron Ru–hydride intermediate through intramolecular hydrogen transfer. The Ru–H formation was confirmed by FT-IR and $^1$H NMR spectra. A weak band at 2078 $cm^{-1}$ in the FT-IR spectrum and a new signal at −3.1 ppm in the $^1$H NMR spectrum of a residue obtained from the catalytic asymmetric reduction reaction are consistent with the presence of Ru–hydride species.[60] The Ru–hydride species interacted with the ketone substrate through Ru–H and N–H units to form a six-membered transition state according to Noyori's outer-sphere mechanism. In the course of the reaction, chiral-centered ruthenium complexes were generated and a diastereomeric mixture of the intermediates might be present, but still the ee values of the product alcohols were found to be good. On the other hand, the chirality of the complexes did not influence the configuration of product alcohols in most cases. This might be due to the fact that only diastereomers with equal configuration at the metal and at the nitrogen are active for the present ATH reaction.[26,61] Surprisingly, there was no change observed in the coordination mode of the ligand, even in the presence of a base during the catalytic cycle, as revealed from the FT-IR and $^1$H NMR spectra.

## ■ CONCLUSION

In this paper, we have reported the synthesis and complete characterization of the new chiral acylthiourea ligands L and their novel Ru(II) complexes, which are obtained from the


dx.doi.org/10.1021/om4010548 | Organometallics XXXX, XXX, XXX–XXX

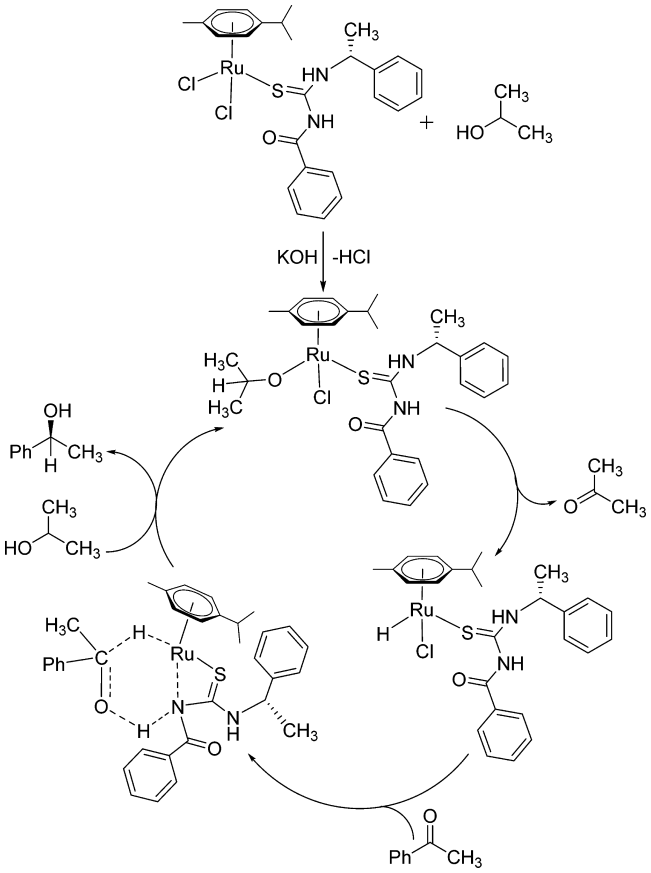



**Figure 7.** Suggested mechanism for transfer hydrogenation of ketones.

reaction between $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$ and L. The structures of representative compounds were confirmed by single-crystal X-ray crystallography. In all cases, monodentate coordination of acylthiourea ligands via a sulfur atom was observed in the Ru(II) complexes. The chiral complexes **1**–**6** were all found to be efficient catalysts for the asymmetric transfer hydrogenation of ketones to their corresponding chiral alcohols. The conversion and ee values were moderate to excellent. The Ru–hydride intermediate has been confirmed by FT-IR and $^1$H NMR spectra. Since the chiral ligands were produced from low-cost materials by using a simple procedure, this method is potentially of considerable industrial interest.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Figures, tables, and CIF files giving X-ray crystallographic data, atomic coordinates, unit cell packing diagrams, $^1$H NMR and $^{13}$C NMR spectra of all the ligands and complexes, and GC and HPLC data. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

M.M.S. thanks the Department of Science and Technology, Ministry of Science and Technology, Government of India, for a fellowship under the INSPIRE scheme. R.K. thanks Sophia University for an STEC fellowship. L.J.F. thanks the EPSRC (UK) for grant GR/M91433 toward the purchase of a KappaCCD diffractometer. We thank Dr. S. Velmathi, NIT, Trichy, for her help in polarimetric analysis.

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dx.doi.org/10.1021/om4010548 | *Organometallics* XXXX, XXX, XXX−XXX