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Neutral *p*-cymene ruthenium complexes with *P*-stereogenic monophosphines. New catalytic precursors in enantioselective transfer hydrogenation and cyclopropanation

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ABSTRACT

A family of eight neutral, pseudotetrahedral piano-stool ruthenium complexes **C**, of the type [$RuCl_2$(*p*-cymene)(PArPhR)] (Ar = 1-naphthyl, 9-phenanthryl and 2-biphenylyl; R = Me, *i*-Pr, OMe, $-CH_2SiMe_3$ and $-CH_2SiPh_3$) have been prepared and characterised, including the X-ray crystal structure for **C6** (Ar = 2-biphenylyl; R = *i*-Pr). These complexes catalyse the asymmetric hydrogen transfer reaction of acetophenone in refluxing 2-propanol in the presence of potassium *tert*-butoxyde, reaching full conversions and up to 45% ee after 24 h towards the *S* enantiomer of 1-phenylethanol. Cationic complexes formed upon treatment of **C** with one equivalent of $AgSbF_6$ or $(Et_3O)PF_6$ are active in the cyclopropanation reaction of styrene and α-methylstyrene by ethyl diazoacetate. Low to moderate conversions (up to 58%), diastereoselectivities (up to 40% de), and moderate enantioselectivities (up to 69% ee) have been found. For both reactions, bulky complexes and **C6** in particular lead to the best results.

1. Introduction

Ruthenium is nowadays one of the most intensively used metals in homogeneous catalysis [1–4], due in part to cheaper price compared to other noble metals such as rhodium and palladium and to the wide span of reactions catalysed by Ru(II) complexes, many of them in enantioselective fashion. The most important example is arguably the reduction of ketones by Ru/BINAP and Ru/BINAP/diamine systems, via hydrogenation or transfer hydrogenation [5–7]. Another important transformation is the cyclopropanation reaction [8,9], catalysed by Ru(II) complexes mainly of nitrogen ligands. A common feature of the ligands used in both transformations is that they are either bi- or polydentate [10]. In contrast, monodentate ligands [11–13] are still infrequent in stereoselective ruthenium catalysis. In this work we explore the potential of simple [$RuCl_2$(*p*-cymene)(P*)] complexes in enantioselective hydrogen transfer and cyclopropanation, using a set of monodentate *P*-stereogenic ligands, previously described to be active in both Pd-catalysed hydrovinylation [14] and allylic alkylation [15] and less prone to secondary interactions such as those found in supposedly monodentate phosphoramidites [16,17].

2. Synthesis

The required *P*-stereogenic ligands **1**–**8** (Scheme 1) were prepared following the Jugé-Stephan method [18] as described previously [14,15,19] and obtained as optically pure white solids or colourless oils. Free phosphinites **3** and **5** were also obtained by standard deboronation of the corresponding phosphinite–boranes [20] and their characterisation is given in the experimental part.

Following the usual method [21–23], neutral ruthenium *p*-cymene complexes **C1**–**C8** were easily prepared in moderate to good yields by splitting the ruthenium *p*-cymene chloride dimer [24], dissolved in dichloromethane, with two equivalents of the monophosphorus ligand (Scheme 2).

The reactions were essentially complete after 1 h, as judged by ^{31}P NMR spectroscopy. The isolated compounds **C** were red to brown air-stable solids, soluble in dichloromethane but not in hexane or pentane, whose full characterisation was in agreement with the expected structures. ^{31}P NMR spectra (see experimental part and supplementary material) of complexes bearing phosphines presented singlets whose chemical shift was displaced downfield compared to the free ligands. In contrast, the value of the

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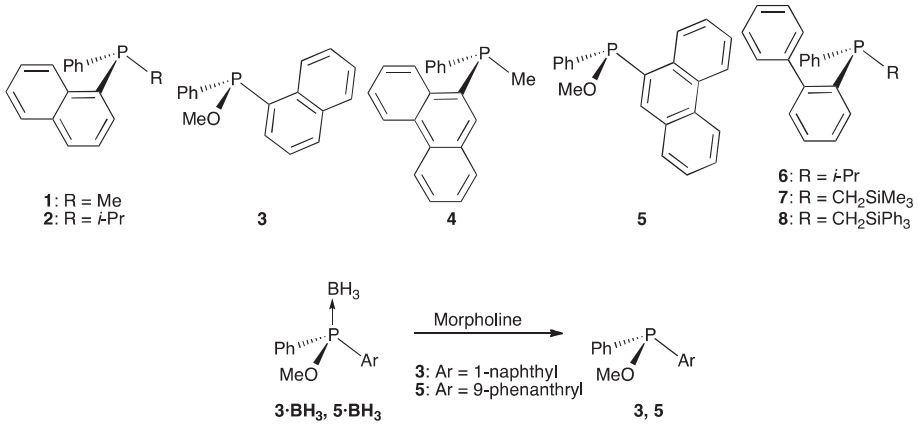
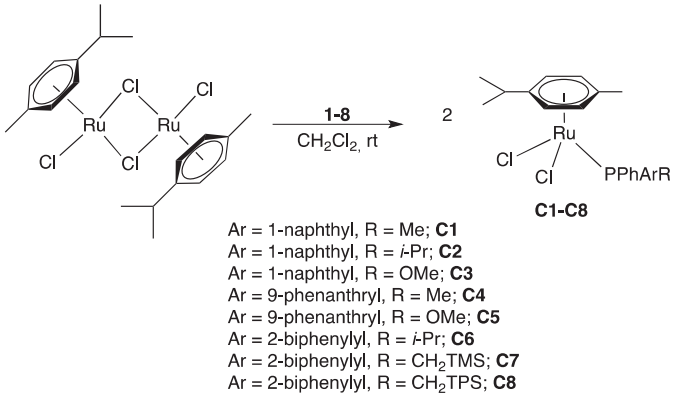


Scheme 1. *P*-stereogenic ligands.

chemical shift was almost unchanged in the case of complexes **C3** and **C5**, bearing phosphinite ligands. ^{1}H and ^{13}C NMR spectra presented the anticipated features (see experimental part and supplementary material). As expected due to the non-symmetric environment produced by the stereogenic phosphorus, the *p*-cymene aromatic ring presented four distinct aromatic proton resonances in the ^{1}H spectra and six distinct carbon resonances in the ^{13}C spectra for most of the complexes. Another feature is the non-equivalence of the diastereotopic methyl groups of the isopropyl fragment in the *p*-cymene, both in ^{1}H and ^{13}C NMR spectra.

A single crystal X-ray structure determination was carried out for complex **C6**. As expected, the complex has a distorted octahedral structure with the typical piano-stool pseudotetrahedral geometry around the Ru atom with the η^6 coordination of the phenyl ring of *p*-cymene. The unit cell contains two crystallographically distinct molecules of the complex (**I** and **II**), whose ORTEP view is displayed in Fig. 1. In both structures the imaginary line defined by the chloro ligands and the line passing through the substituted C carbons of the η^6-coordinated phenyl ring are approximately parallel, which is a common feature of this type of complexes. The main difference between structures **I** and **II** is simply that the η^6-coordinated *p*-cymene ring is rotated by 180°. For this reason, only some distances and angles of structure **I** will be commented.

The structure confirms the expected absolute configuration of the coordinated stereogenic phosphorus atom (*R*). The average of the six Ru–$C_{p\text{-cymene}}$ distances is 2.209 Å. These distances can be divided into two groups featuring relatively short and long bonds. The first one, corresponding to the carbon atoms closer to the phosphine, has an average distance of 2.173 Å whereas for the second the value increases to 2.227 Å. Two slightly different Ru–Cl distances are also observed. The distances are in general similar to other related complexes [22,24–34] although the Ru–P distance is longer for **C6**. The average value of the P–Ru–Cl angles is 91.74° and for the Cl–Ru–Cl moiety the angle is 85.22°. The first value is larger and the second smaller compared to other [Ru(*p*-cymene)(P)Cl_2] complexes (P = phosphine) [24–34] and even compared to an analogous complex with a bulky phosphoramidite [22]. This data points out the rather bulky character of the phosphine ligand in **C6**.



Scheme 2. Synthesis of neutral Ru(*p*-cymene) complexes.

3. Hydrogen transfer

There is some precedent [13,35,36] that neutral [$RuCl_2(\eta^6$-arene)P] (P = monodentate phosphorus ligand) complexes are active in hydrogen transfer from alcohols to ketones. To the best of our knowledge, however, up to date only achiral phosphines have been used. Therefore the optically pure complexes **C** presented here could be interesting precatalysts in enantioselective hydrogen transfer from 2-propanol to acetophenone, which is the model substrate for this reaction (Scheme 3).

Hydrogen transfer reactions were performed in refluxing 2-propanol (82 °C), which was both the solvent and the hydrogen donor in the presence of *t*-BuOK [37]. The catalyst/*t*-BuOK/acetophenone ratio was 1/10/100. The solutions of the complexes were activated (without addition of acetophenone) for 30 min at 82 °C before the addition of acetophenone. The plot of the conversion to 1-phenylethanol vs. time for several complexes **C** is given in Fig. 2 and the plot of the ee of 1-phenylethanol vs. time is given in Fig. 3. Numerical data can be found in the supplementary material.

Fig. 2 shows that all complexes are active in reducing acetophenone, reaching almost full conversion after 24 h. In spite of that, important differences in activity are clearly observed. The activity order is **C6** ≫ **C2** > **C1** ≈ **C4** ≫ **C3** ≈ **C5**. Indeed, with **C6** full conversion is achieved after only 8 h. Surprisingly, Fig. 3 shows that the enantioselectivity follows *exactly* the same order. Although the ee value is higher and rather unreliable at low reaction times, it stabilises to a slightly lower value. Only precursor **C6** gives a moderate ee of around 45%, whereas **C2** provides 1-phenylethanol with just below 20% ee. In both cases the absolute configuration of the product is *S*. The rest of the catalysts give very poor enantioselectivities. The results described here suggest that both activity and enantioselectivity are affected by the same factors for the systems described.

Since the best results were obtained with precursor **C6**, a run at lower temperature was performed with the aim of increasing the