Rhodium(III) complexes containing the ligand 2,6-bis[4′-(S)-isopropyloxazolin-2′-yl]pyridine ((S,S)-^{i}Pr-pybox): Efficient catalysts for asymmetric hydrosilylation of acetophenone

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Abstract

The dinuclear complexes $[Rh_2(\mu\text{-}Cl)_2(R)_2\{(S,S)\text{-}^iPr\text{-pybox}\}_2][BF_4]_2$ (R = (E)-C(Me)=CH(Ph), C(Ph)=CH₂) have been synthesized by the reaction of the complexes *trans*-[RhCl₂(R){(S,S)-^{i}Pr-pybox}] (R = (E)-C(Me)=CH(Ph), C(Ph)=CH₂) with AgBF₄. The rhodium(III) complexes *cis*-[RhCl₂(R){(S,S)-^{i}Pr-pybox}] (R = COPh, CH₂C(Me)=CH₂, CH₂CH=CH₂, CH₂CH=CH(Ph), CH=C=CH₂) and *trans*-[RhCl₂{(E)-C(Me)=CH(Ph)}{(S,S)-^{i}Pr-pybox}], recently reported, and the novel dinuclear complex $[Rh_2(\mu\text{-}Cl)_2\{(E)\text{-}C(Me)=CH(Ph)\}_2\{(S,S)\text{-}^iPr\text{-pybox}\}_2][BF_4]_2$, exhibit high enantioselectivity in the hydrosilylation of acetophenone affording (S)-1-phenylethanol with high conversions and up to 89% ee. The species "RhCl{(S,S)-^{i}Pr-pybox}" is proposed as the real active rhodium catalyst and a pathway for its formation is also tentatively provided.

1. Introduction

Asymmetric synthesis catalyzed by transition-metal complexes bearing enantiopure pybox as ancillary ligands has experienced a pronounced growth in the last decade [1]. The pioneering work by Nishiyama et al. on the enantioselective reduction of ketones via hydrosilylation with the complexes [RhCl₃(R-pybox)] in the presence of AgBF₄ can be seen as one of the most outstanding application in this particular area [2]. Although no mechanistic studies were carried out, the authors assumed the rhodium(I) "[Rh(R-pybox)]⁺" species, formed by reduction of the precatalyst by diphenylsilane in the presence of AgBF₄, to be the catalyst [2b,c].

As a part of our ongoing research dealing with groups 8–9 metal complexes bearing enantiopure pybox ligands [3], we report herein the catalytic activity of the complexes [RhCl₂(R){(S,S)-^{i}Pr-pybox}] (R = acyl, allyl, allenyl, alkenyl),

recently synthesized in our laboratory [3a,b] (see Chart 1), in the hydrosilylation of acetophenone. Moreover, the novel dinuclear complex $[Rh_2(\mu\text{-}Cl)_2\{(E)\text{-}C(Me)=CH(Ph)\}_2\{(S,S)\text{-}^iPr\text{-pybox}\}_2)][BF_4]_2$ has been synthesized and its ability as precatalyst studied. The nature and the formation of plausible active catalytic species are also discussed.

2. Experimental

The manipulations were performed under an atmosphere of dry nitrogen using vacuum-line and standard Schlenk techniques. All reagents were obtained from commercial suppliers and used without further purification. Solvents were dried by standard methods and distilled under nitrogen before use. The compounds **1**, **2a–c**, **3**, **4a** and **4b** were prepared according to methods previously reported [3a,b]. The conductivities were measured at room temperature in acetone solutions, with a Jenway PCM3 conductimeter. The C, H and N analysis was carried out with a Perkin-Elmer 240-B microanalyzer. The mass spectrum (FAB) was determined with a VG-AUTOSPEC mass

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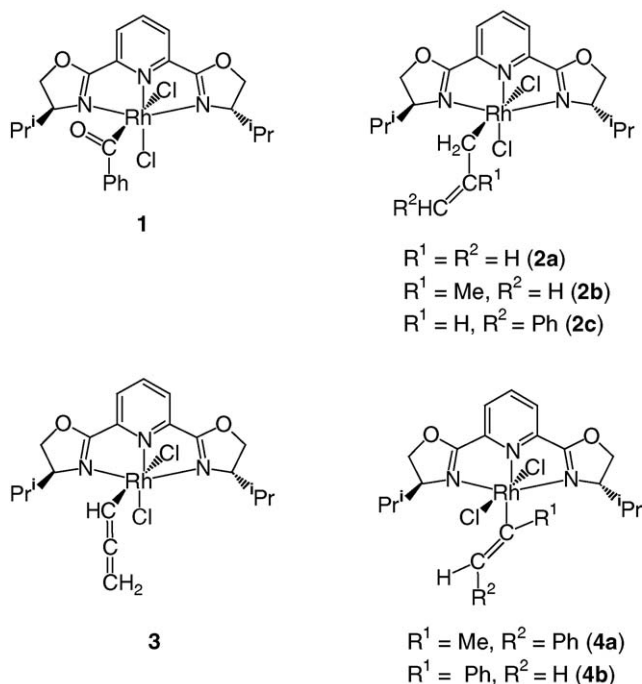 *E-mail address:* pgb@uniovi.es (M.P. Gamasa).

Chart 1.

spectrometer, operating in the positive mode; 3-nitrobenzyl alcohol (NBA) was used as the matrix. NMR spectra were recorded on a Bruker DPX-300 instrument at 300 MHz (^{1}H) or 75.4 MHz (^{13}C) using SiMe$_4$ as standard. Coupling constants J are given in Hertz. Abbreviations used: s, singlet; d, doublet; t, triplet; m, multiplet.

2.1. Synthesis of the complexes [Rh$_2$(μ-Cl)$_2$(R)$_2${(S,S)-^{i}Pr-pybox}$_2$][BF$_4$]$_2$ (R = (E)-C(Me)=CH(Ph) (5a), C(Ph)=CH$_2$ (5b))

To a solution of alkenyl complexes **4a** or **4b** (0.259 mmol) in 15 ml of THF, silver tetrafluoroborate (0.061 mg, 0.311 mmol) was added. The mixture was stirred in the absence of light for 30 min at room temperature. The solvent was then removed under vacuum, the solid residue was extracted with dichloromethane and the solution filtered over kieselguhr. The resulting solution was then concentrated to ca. 3 and 30 ml of diethyl ether were added yielding a solid which was washed with diethyl ether (2 ml × 30 ml) and vacuum-dried.

Complex **5a**: Yield: 98% (0.163 g), orange solid. ^{1}H NMR (acetone-d_6): δ = 8.75 (t, 2H, J(HH) = 8.1 Hz, H$_4$ of C$_5$H$_3$N), 8.45 (m, 4H, H$_{3,5}$ of C$_5$H$_3$N), 7.26–7.01 (m, 12H, Ph and C*H*Ph), 5.17 (m, 8H, OCH$_2$), 4.77 (m, 4H, C*H*^{i}Pr), 2.53 and 2.36 (m, 2H each one, C*H*Me$_2$), 2.03 (s, 6H, Rh–C–Me), 1.01 (m, 24H, CH*Me$_2$*). ^{13}C{^{1}H} NMR (acetone-d_6): δ = 168.7 and 168.6 (s, C=N), 147.8 and 147.6 (s, C$_{2,6}$ of C$_5$H$_3$N), 143.5 (s, C$_4$ of C$_5$H$_3$N), 142.1 (d, J(CRh) = 27.1 Hz, Rh–C), 137.2 (s) and 126.3–129.9 (Ph, C$_{3,5}$ of C$_5$H$_3$N and C*H*Ph), 74.5 and 74.1 (s, OCH$_2$), 69.0 and 68.4 (s, C*H*^{i}Pr), 29.8 (s, CHMe$_2$), 23.0 (s, Rh–C–*Me*), 19.1, 18.81, 15.1 and 14.3 (s, CH*Me$_2$*). IR (KBr, cm^{-1}): ν (BF$_4$$^-$) 1064. Conductivity (acetone 18 °C,

Ω^{-1} cm^2 mol^{-1}): 216. FAB-MS: m/z 556 [RhClR(^{i}Pr-pybox)-1]$^+$, [Rh$_2$Cl$_2$R$_2$(^{i}Pr-pybox)$_2$-1]$^{2+}$ R = {C(Me)=CH(Ph)}.

Complex **5b**: Yield: 98% (0.160 g), yellow solid. ^{1}H NMR (acetone-d_6): δ = 8.48 (t, 2H, J(HH) = 8.0 Hz, H$_4$ of C$_5$H$_3$N), 8.27 (d, 2H, J(HH) = 8.0 Hz, H$_{3,5}$ of C$_5$H$_3$N), 7.95 (d, 2H, J(HH) = 8.0 Hz, H$_{3,5}$ of C$_5$H$_3$N), 6.98 (m, 10H, Ph), 5.07 (m, 8H), 4.65 (m, 4H) (OCH$_2$ and C=CH$_2$), 4.27 and 3.98 (m, 2H each one, C*H*^{i}Pr), 2.89 and 2.70 (m, 2H each one, C*H*Me$_2$), 1.10–0.77 (m, 24H, CH*Me$_2$*). ^{13}C{^{1}H} NMR (acetone-d_6): δ = 169.5 and 168.6 (s, C=N), 149.0 (s, C$_{2,6}$ of C$_5$H$_3$N), 147.4 (d, J(CRh) = 16.9 Hz, Rh–C), 143.6 (s, C$_{ipso}$ of Ph), 142.5 (s, C$_4$ of C$_5$H$_3$N), 129.0–126.6 (Ph and C$_{3,5}$ of C$_5$H$_3$N), 122.4 (s, C=CH$_2$), 74.4 and 74.2 (s, OCH$_2$), 70.2 and 68.8 (s, CH^{i}Pr), 29.6 and 29.3 (s, CHMe$_2$), 20.8, 19.4, 16.2 and 14.6 (s, CH*Me$_2$*). IR (KBr, cm^{-1}): ν (BF$_4$$^-$) 1062. Conductivity (acetone 18 °C, Ω^{-1} cm^2 mol^{-1}): 208. Anal. calcd. for C$_{50}$H$_{60}$B$_2$Cl$_2$F$_8$N$_6$O$_4$Rh$_2$·CH$_2$Cl$_2$; C: 45.57, H: 4.65, N: 6.25. Found C: 45.86, H: 4.80, N: 5.86.

2.2. General procedure for the hydrosilylation of acetophenone

A 10-ml flask was charged under a dry nitrogen atmosphere with the complex catalyst (0.04 mmol, 1 mol%), (S,S)-^{i}Pr-pybox (0.16 mmol, 4 mol%), AgBF$_4$ (0.08 mmol), when it is used, and acetophenone (4.00 mmol). The reaction mixture was stirred at room temperature for 1 h. After cooling to −10 °C, Ph$_2$SiH$_2$ (6.4 mmol) was added dropwise. Then, the reaction mixture was allowed to warm up to 0 °C and stirred for 24 h. The disappearance of acetophenone was monitored by TLC. Before the aqueous work-up, an aliquot was taken and examined by ^{1}H NMR spectroscopy. The work-up of the reaction mixture was carried out as described by Nishiyama [2]. The enantiomeric excesses ee were determined after hydrolysis by GC analyses with a Supelco β-DEX 120 chiral capillary column.

2.3. Experiments of conductivities at variable concentration

C = concentration values (M), Δ_e = specific conductivity. For complex **5a**: $C = 4 \times 10^{-4}$, $\Delta_e = 35.3$; $C = 1.6 \times 10^{-3}$, $\Delta_e = 132.1$; $C = 3.6 \times 10^{-3}$, $\Delta_e = 273.0$; $C = 6.4 \times 10^{-3}$, $\Delta_e = 439$. For complex Rh$_2$(μ-Cl)$_2$(Me)$_2${(S,S)-^{i}Pr-pybox}$_2$][OTf]$_2$: $C = 4 \times 10^{-4}$, $\Delta_e = 29.6$; $C = 1.6 \times 10^{-3}$, $\Delta_e = 110.6$; $C = 3.6 \times 10^{-3}$, $\Delta_e = 219.9$; $C = 6.4 \times 10^{-3}$, $\Delta_e = 351$. For complex [Rh(Me)I(CO){((S,S)-^{i}Pr-pybox)}][PF$_6$]: $C = 4 \times 10^{-4}$, $\Delta_e = 31.0$; $C = 9 \times 10^{-4}$, $\Delta_e = 69.0$; $C = 1.6 \times 10^{-3}$, $\Delta_e = 119.3$; $C = 3.6 \times 10^{-3}$, $\Delta_e = 265$.

3. Results and discussion

3.1. Synthesis of the complexes [Rh$_2$(μ-Cl)$_2$(R)$_2${(S,S)-^{i}Pr-pybox}$_2$][BF$_4$]$_2$ (R = (E)-C(Me)=CH(Ph) (5a), C(Ph)=CH$_2$ (5b))

The reaction of the complexes *trans*-[RhCl$_2${(E)-C(Me)= CH(Ph)}{(S,S)-^{i}Pr-pybox}] (**4a**) and *trans*-[RhCl$_2${C(Ph)=
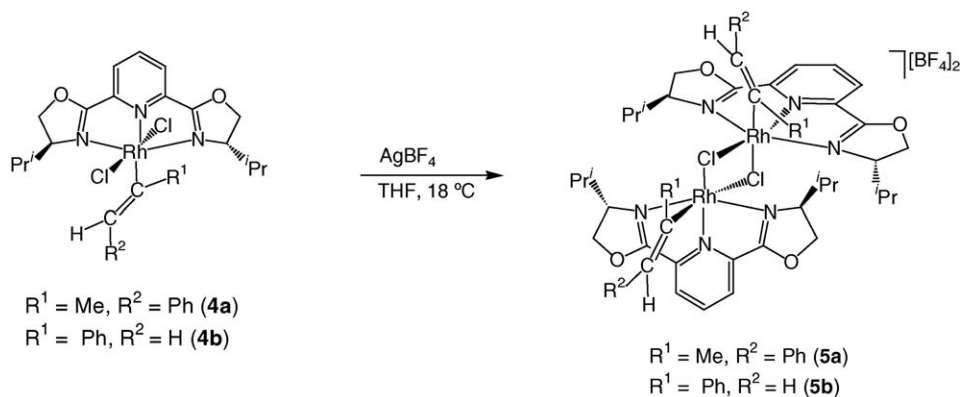
Scheme 1.

CH$_2$}{(S,S)-^{i}Pr-pybox}] (**4b**) [3b] with AgBF$_4$ in THF at room temperature leads to the dinuclear complexes **5a** and **5b** in very high yield (98%) (Scheme 1). Complexes **5a** and **5b** have been characterized by elemental analyses or mass spectrometry (FAB), and NMR spectroscopy (^{1}H and ^{13}C{^{1}H}). The ^{13}C{^{1}H} NMR spectra show the lack of C$_2$-symmetry of the pybox ligand as two resonances appear for each of the inequivalent carbon nuclei of CH^{i}Pr and CH$_2$ groups of the oxazoline rings (see Section 2 for further details). The conductance values in acetone solutions (208–216 Ω^{-1} cm^2 mol^{-1}), which are in the range of 2:1 electrolytes, and the spectrometric data for **5a** are in concordance with the dinuclear μ-Cl bridged structure shown in the Scheme 2 [4].

The NMR spectroscopic data do not allow the elucidation of the stereochemistry of complexes **5a** and **5b**, among the two possible isomers **A** and **B** (Scheme 2). The stereoisomer **A** is tentatively proposed for complexes **5a** and **5b** (Scheme 1) on the basis of less sterically demanding arrangement of the isopropyl groups of both pybox ligands. All attempts to crystallize complexes **5a** or **5b** in a number of solvents have been unsuccessful, and an X-ray analysis could not be performed. Very recently, we have proposed a similar structure for the complex [Rh$_2$(μ-Cl)$_2$(Me)$_2${(S,S)-^{i}Pr-pybox}$_2$][OTf]$_2$, which is formed by the *one-pot* reaction of [Rh(μ-Cl)(η^2-C$_2$H$_4$)$_2$]$_2$, ^{i}Pr-pybox and methyl triflate [3b].

3.2. Hydrosilylation of acetophenone

We have tested the catalytic activity of the complexes [RhCl$_2$(R){(S,S)-^{i}Pr-pybox}] (R = acyl (**1**), allyl (**2a–c**), allenyl (**3**), alkenyl (**4a**) [3a,b] (Chart 1) in the hydrosilylation of acetophenone with diphenylsilane (Table 1, entries 1–6). For comparison purposes, the results reported by Nishiyama et al. using [RhCl$_3$(^{i}Pr-pybox)] catalyst, in the presence and absence of AgBF$_4$, are displayed in Table 1, entries 8 and 9, respectively. The Nishiyama's complex showed no catalytic activity, even at 30 °C, if no AgBF$_4$ is added [2].

The reaction of acetophenone with diphenylsilane catalyzed by acyl (**1**) and allyl (**2b**) complexes for 3 h followed by hydrolysis affords (S)-1-phenylethanol with high enantioselectivity (75 and 85% ee, respectively) and low conversion (24 and 39%) (Table 1, entries 1 and 2). Moreover, using longer reaction times increases notably the conversion without affecting the selectivity. Thus, the reduction of acetophenone catalyzed by **2b** for 24 h resulted in high conversion (97%) and enantioselectivity (85% ee) (entry 3). Therefore, all subsequent reactions have been carried out in a pre-fixed time of 24 h. In a typical experiment a mixture of the rhodium catalyst precursor (1.0 mol%), ^{i}Pr-pybox (4 mol%), acetophenone (4.0 mmol) and AgBF$_4$ (2 mol%) is stirred at room temperature during 1 h and then cooled to −10 °C. Diphenylsilane (6.4 mmol) is added, the
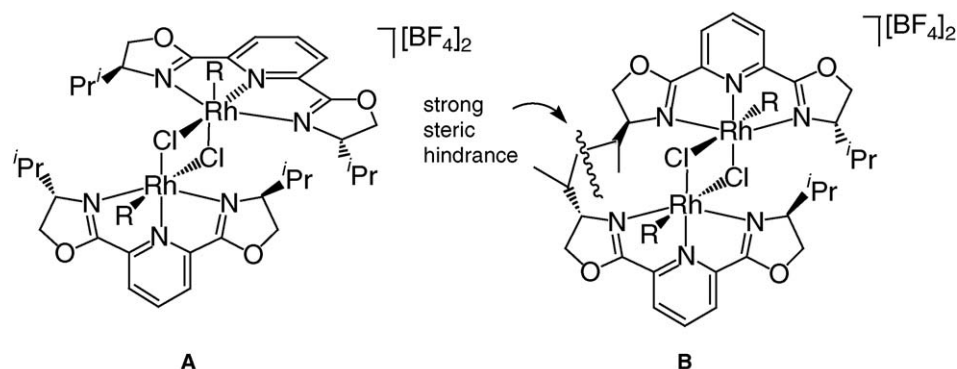
Scheme 2.

Table 1

Reduction of acetophenone with rhodium-*i*Pr-pybox complexes via hydrosilylation

$$\text{Ph} \overset{O}{\underset{}{\parallel}} \quad \xrightarrow[3)\ H_3O^+]{\substack{1)\ cat.,\ (AgBF_4) \\ 2)\ Ph_2SiH_2}} \quad \text{Ph} \overset{OH}{\underset{}{\diagup}}$$
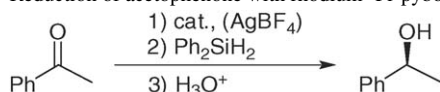
Entry	Catalyst	Additive	*t* (h)[a]	Conversion (%)	ee (%) (*S*)
1	(**1**)	AgBF$_4$	3	24	75
2	(**2b**)	AgBF$_4$	3 (24)	39 (97)	85 (85)
3	(**2a**)	AgBF$_4$	24	98	88
4	(**2c**)	AgBF$_4$	24	92	86
5	(**3**)	AgBF$_4$	24	99	89
6	(**4a**)	AgBF$_4$	24	97	87
7	(**5a**)	–	24	93	83
8	[RhCl$_3${(*S,S*)-*i*Pr-pybox}]	AgBF$_4$	2	91	94
9	[RhCl$_3${(*S,S*)-*i*Pr-pybox}]	–	[b]	–	–

[a] Reactions were carried out at 0 °C under a dry nitrogen atmosphere using the complex catalyst (1 mol%; 0.04 mmol), *i*Pr-pybox (4 mol%; 0.16 mmol), AgBF$_4$ (entries 1–6; 2 mol%; 0.08 mmol), Ph$_2$SiH$_2$ (6.4 mmol) and acetophenone (4.00 mmol). Conversion of acetophenone was monitored by TLC. A sample was taken before aqueous work-up and examined by ^{1}H NMR spectroscopy. The ee's were determined by GC analyses with a Supelco β-DEX 120 chiral capillary column.

[b] The reaction is carried out at 30 °C or below.

resulting mixture stirred a 0 °C during 24 h and then worked up [5] (see Section 2 for details). All the reactions have been carried out in the presence of free *i*Pr-pybox (4 mol% of ligand versus 1 mol% of catalyst precursor) as it is well documented that the enantioselectivity of the hydrosilylation reaction with complexes containing nitrogen ligands is enhanced by the use of ligand excess [2,6].

The efficiency of complexes **2a–c**, **3**, **4a** under the reaction conditions described above is shown in Table 1, entries 3–6. The results are similar in all cases in terms of activity and selectivity (92–99% conversion; 85–89% ee) and reflects that the nature of the η^1-ligand, has very little influence on the reaction. The shorter reaction time required in the case of Nishiyama catalyst (entry 8 versus entries 2–6) points that the replacement of a chlorine ligand with a carbon ligand in the precatalyst has a negative influence on the catalytic reaction rate.

In order to get more insight into the active catalytic species we tested the activity of the dinuclear complex **5a** in the absence of AgBF$_4$ (entry 7). We found that, the reduction reaction of acetophenone catalyzed by the dinuclear complex **5a** takes place

under the same reaction conditions and with similar efficiency as that catalyzed by its complex precursor **4a** (compare entries 6 and 7).

On the basis of the results reported, the most remarkable features are:

- The substitution of a chlorine by a carbon ligand in the precatalyst decreases the rate of the catalytic reaction (entries 1–6 versus entry 8).
- Roughly, the same results are obtained with the complexes **2a–c**, **3** and **4a** (entries 2–6), showing very little influence of the nature of the organic group and the stereoisomer used. This seems to indicate that the organic group is not present in the active species, otherwise a higher influence on the catalyst efficiency and asymmetric induction should have been probably observed.
- The similar results obtained with the catalysis systems **4a**/AgBF$_4$ and **5a** (entries 6 and 7) seem to indicate that just one chloride in **4a** needs to be extracted by AgBF$_4$ in the first step of the reaction. The dinuclear complex **5a** might form
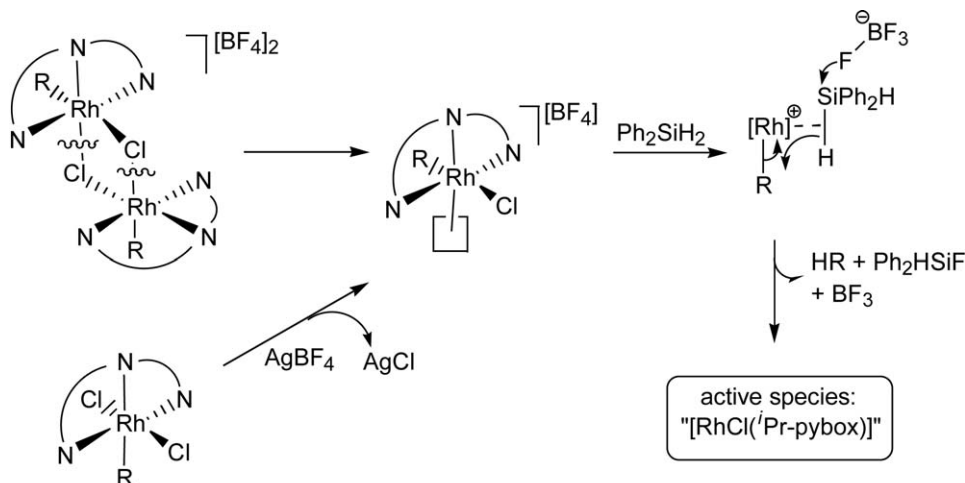
Scheme 3.

the same unsaturated active species directly by μ-Cl bridge breaking, becoming thus unnecessary the addition of silver salt.

Although we have not performed a mechanistic study, we can tentatively propose, on the ground of the above results, the structure "[RhCl(^{i}Pr-pybox)]" as the common active species for all of the catalysts examined. This species might be formed as shown in Scheme 3.

Thus, either the dedimerization of **5a** or the chloride abstraction from **4** would lead to a common unsaturated rhodium(III) species. Then, the reduction of the C–Rh bond by the silane can be rationalized by the sequence: (i) activation of diphenylsilane through η^2-Si–H coordination to the electrophilic rhodium(III) [7], and (ii) nucleophilic attack of the fluoride anion (coming from tetrafluoroborate anion) onto the silicon atom [7a], which would promote the elimination of R–H and Ph_2FSiH.

4. Conclusion

In summary, several organometallic rhodium(III)-^{i}Pr-pybox complexes, recently synthesized in our laboratory (**1**–**4a**) [3a,b], and the novel dinuclear complex **5a** have proved to be active in the hydrosilylation reaction of acetophenone to (*S*)-1-phenylethanol as high conversion (up to 99%) and enantiomeric excess (up to 89%) are reached. It should be noted that not only the system **4a/BF₄**, but also the complex **5a** itself behaves as efficient precursors of the precatalyst "[RhCl{(*E*)-C(Me)=CH(Ph)}{(*S,S*)-^{i}Pr-pybox}]". This is noteworthy in the sense that the use of AgBF₄ as additive can be avoided. On the basis of the results obtained we propose the complex "[RhCl{(*S,S*)-^{i}Pr-pybox}]" as the common active species for all the organometallic rhodium(III) complexes tested. A possible via for the formation of that species from the starting complexes **4** and **5** is also provided.

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