

RESEARCH ARTICLE

Ru complexes containing *N*-methyl-1,3,5-triaza-7-phosphaadamantane (mPTA) as catalysts for the isomerization of 2-cyclohexen-1-ol

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The complex $[\text{RuCp}(\text{H}_2\text{O}-\kappa\text{O})(\text{mPTA})_2](\text{CF}_3\text{SO}_3)_3 \cdot \text{MeOH}$ (**4**·MeOH) was synthesized and characterized by spectroscopic techniques and its crystal structure determined by single-crystal X-ray diffraction (mPTA = *N*-methyl-1,3,5-triaza-7-phosphaadamantane). The catalytic activity of **4** for the redox isomerization of 2-cyclohexen-1-ol into cyclohexanone was studied in water, methanol/water, and biphasic systems, reaching the highest conversion rate in biphasic water/cyclohexane (1:1) at pH 1.7 and under N₂. The aqueous phase containing **4** was recycled up to 7 consecutive runs, reaching a total turnover number (TON) of 471 without significant losses of catalyst. Therefore, this reaction is a unique procedure for the isomerization of cyclic allylic alcohols without metal contamination of the product. The catalytic reaction mechanism was studied by nuclear magnetic resonance (NMR), showing that the reaction probably proceeds through the formation of an intermediate in which the substrate is η²-coordinated to the metal.

KEYWORDS

adamantanophosphines, catalytic isomerization, cyclic allylic alcohols, Ru complexes, water

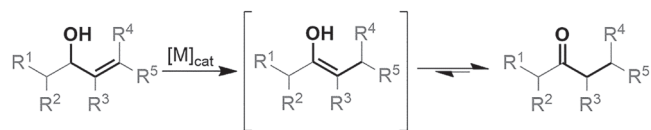
1 | INTRODUCTION

The redox isomerization of allylic alcohols by metal complexes is a one-pot procedure that allows the migration of the C=C double bond, giving an enolate or enol that finally tautomerizes into the corresponding carbonyl (Scheme 1). Highly substituted or cyclic allylic alcohols have potential pharmaceutical importance, as they are present in different classes of natural products, such as terpenes and opioids.^[1,2] The catalytic redox isomerization of linear allylic alcohols was largely studied and found to be

strongly influenced by the catalyst used, the size of the alcohol, and the substituents on the double bond.^[3] Among them, secondary allylic alcohols from 1-propen-3-ol to 1-octen-3-ol are easily isomerized by known catalysts.^[4-12] Nevertheless, isomerization of substituted allylic alcohols, particularly with bulky groups, is scarce or non-existent.^[10] Thus, additional research efforts should be done to determine the influence of substituents on the catalytic isomerization of allylic alcohols, particularly to develop new methods to isomerize natural products containing functionalized allylic alcohol groups.^[13-17]

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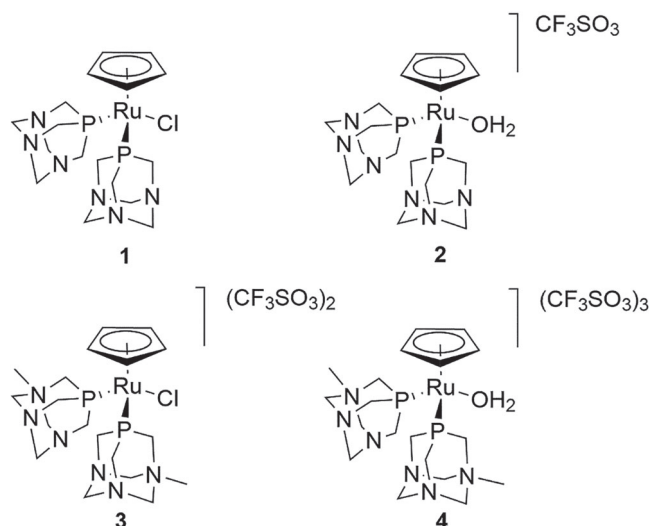
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SCHEME 1 Metal isomerization of allylic alcohols

An adequate catalyst should isomerize the allylic alcohols under mild reaction conditions and in non-harmful solvents such as water.^[18] Complexes containing Ni, Pd, Os, Ir, Ru, Rh, and Mo were found to be catalysts for the isomerization of allylic alcohols,^[19,20] but ruthenium-based compounds are among the most used and studied due to the fact that Ru presents several important features: a wide range of available oxidation states, a great coordination versatility, and is cheaper than other noble metals such as Ir or Rh. Hydrosoluble ruthenium complexes that showed to be excellent catalysts for many reactions in water^[21–27] commonly contain hydrophilic tertiary organophosphines,^[28] N-heterocyclic carbenes,^[29] and tetrahydrosulfosalan or tetrahydrosulfosalene ligands.^[30]

Our research group is interested in the synthesis of water-soluble ruthenium complexes for the isomerization of linear allylic alcohols in water. The water solubility and catalytic activity of these complexes were achieved by using hydrosoluble phosphines such as triphenylphosphines (Na-mTPPMS, Na₃-mTPPTS),^[31,32] the adamantane-like ligand 1,3,5-triaza-7-phosphaadamantane (PTA), and its derivatives. These last ligands are easy and cheap to synthesize and display a high solubility in water and the ability to stabilize metals in low oxidation states.^[33,34] Among the complexes that we have most extensively studied as catalysts for the isomerization of allylic alcohols, the complex [RuClCp(PTA)₂] (**1**)^[35,36] was found to be an adequate catalyst for the isomerization of linear allylic alcohols in water under mild conditions. Nevertheless, further studies showed that the real reaction catalyst is the complex [RuCp(H₂O-κO)(PTA)₂]CF₃SO₃ (**2**), which is formed in few amounts when complex **1** is dissolved in water.^[37] This complex showed excellent activity for the isomerization of linear allylic alcohols, much better than that of complex **1**. It is important to point out that complexes **1** and **2** were significantly active as catalysts for the isomerization of the cyclic allylic alcohol 2-cyclohexen-1-ol in water and biphasic media (turnover number [TON] = 647 in water and TON = 3420 in H₂O/cyclohexane after 7 recycling),^[38] complex **2** being the most active catalysts for this reaction.^[16,39–43] The limited number of runs that this complex could be recycled suggested that its activity is related to its capacity to be dissolved not only in water but also in organic solvents. Therefore, progressive leaching of

SCHEME 2 Structure of [RuClCp(PTA)₂] (**1**), [RuCp(H₂O-κO)(PTA)₂](CF₃SO₃) (**2**), [RuClCp(mPTA)₂](CF₃SO₃)₂ (**3**), and [RuCp(H₂O-κO)(mPTA)₂](CF₃SO₃)₃ (**4**)

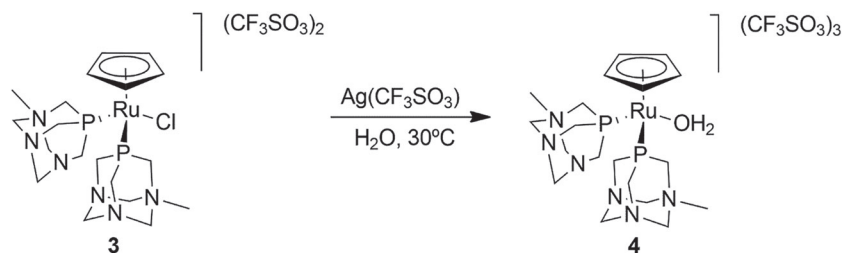
the complex into the organic phase took place in biphasic conditions, leading to its progressive loss.

The complexes [RuClCp(mPTA)₂](CF₃SO₃)₂ (**3**)^[44] and [RuCp(H₂O-κO)(mPTA)₂](CF₃SO₃)₃ (**4**)^[45,46] (Scheme 2), containing the monocationic ligand mPTA (*N*-methyl-1,3,5-triaza-7-phosphaadamantane; the *N*-monomethylated derivative of PTA), were synthesized and tested. These complexes showed lower catalytic activity than **1** and **2** for the isomerization of several secondary linear allylic alcohols in water.^[36,37,45,47] Nevertheless, their virtual insolubility in organic solvents, which is due to their increased charge concerning **1** and **2**, should be enough to exclude the leaching of the complexes into the organic phase. In this paper, the catalytic activity of complexes **3** and **4** for the isomerization of 2-cyclohexen-1-ol is presented. Complex **3** was tested only in water, while the trials with **4** were run also in water/CH₃OH, and biphasic water/cyclohexane mixtures, and also compared with the catalytic activity of complex **2**.

2 | RESULTS AND DISCUSSION

2.1 | Synthesis of [RuCp(H₂O-κO)(mPTA)₂](CF₃SO₃)₃ (**4**)

Complex **4** was synthesized as a yellow-orange microcrystalline powder by reaction of **3** with the stoichiometric amount of AgCF₃SO₃ in water (Scheme 3), following a slightly different procedure to that previously published.^[46] The obtained product was characterized by multinuclear nuclear magnetic resonance (NMR) and infrared (IR). The crystal structure of the complex was

SCHEME 3 Synthesis of **4**

determined by single-crystal X-ray diffraction, confirming the spectroscopic characterization. The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of **4** in D_2O displays a singlet at $\delta = -10.69$ ppm that can be ascribable only to the two equivalent phosphorus atoms of mPTA ligands, arising at a similar chemical shift to that for **3** ($\delta^{31}\text{P} = -10.74$ ppm). The ^1H NMR spectrum of **4** in D_2O shows the distinctive resonances of the mPTA ($\text{NCH}_3 = 2.82$ ppm; $\text{NCH}_2\text{P} = 3.96\text{--}4.18$ ppm; $\text{NCH}_2\text{N} = 4.42\text{--}5.05$ ppm) and Cp (4.84 ppm). The ^{13}C NMR spectrum of **4** in D_2O displays the characteristic resonances of the mPTA ($\text{NCH}_3 = 49.25$ ppm; $\text{NCH}_2\text{P} = 50.56$ ppm; $\text{NCH}_2\text{N} = 51.74$ ppm; $\text{CH}_3\text{NCH}_2\text{P} = 59.54$ ppm; $\text{NCH}_2\text{N} = 68.87$ ppm; $\text{CH}_3\text{NCH}_2\text{N} = 80.21$), the Cp (77.26 ppm), and CF_3SO_3^- anion (117.52 ppm). All the signals were unambiguously assigned by $^1\text{H}\text{--}^1\text{H}$ and $^1\text{H}\text{--}^{13}\text{C}$ correlations (Figures S5 and S6). Finally, the presence of the CF_3SO_3^- anion was supported by IR ($\nu_{(\text{SO})} = 1239$ cm^{-1} ; Figure S7) and $^{19}\text{F}\{^1\text{H}\}$ NMR ($\delta^{19}\text{F} = -78.90$ ppm) (Figure S4).

2.2 | Crystal structure of **4**

Yellow crystals of **4**·MeOH suitable for single-crystal X-ray diffraction were obtained by evaporation of a concentrated solution of the complex in MeOH/ H_2O . The asymmetric unit contains 0.5 of $[\text{RuCp}(\text{H}_2\text{O}\text{-}\kappa\text{O})(\text{mPTA})_2]^{3+}$, 1.5 of TFO^- , and 0.5 molecule of MeOH solvat. The crystal structure of **4** is displayed in Figure 1 and selected interatomic distances and angles are given in the caption (for more details, see the supporting information).

The Ru atom exhibits a distorted pseudo-octahedral coordination geometry, being bonded to one Cp, two P of the mPTA ligands, and one O of the H_2O . The P–Ru–P angle ($\text{P1}\text{--}\text{Ru}\text{--}\text{P1}^1 = 97.62(3)^\circ$) is in the range of CpRu complexes bearing PTA and derivatives, such as **1**, **2**, and **3** (**1**: $\text{P1}\text{--}\text{Ru}\text{--}\text{P2} = 96.18(7)^\circ$ ^[35]; **2**: $\text{P1}\text{--}\text{Ru}\text{--}\text{P2} = 95.455(14)^\circ$ ^[37]; **3**: $\text{P1}\text{--}\text{Ru}\text{--}\text{P2} = 99.94(4)^\circ$ ^[46]). In contrast, the Ru–P bond lengths of **4** ($\text{Ru1}\text{--}\text{P1} = 2.2722(7)$ Å; $\text{Ru1}\text{--}\text{P1}^1 = 2.2722(7)$ Å) are slightly shorter than those for complexes **1**, **2**, and **3** (**1**: $\text{Ru1}\text{--}\text{P1} = 2.2845(14)$ Å, $\text{Ru1}\text{--}\text{P2} = 2.2872(16)$ Å^[35]; **2**: $\text{Ru1}\text{--}\text{P1} = 2.2653(4)$ Å; $\text{Ru1}\text{--}\text{P2} = 2.2610(4)$ Å^[37]; **3**: $\text{Ru1}\text{--}\text{P1} = 2.2509(12)$ Å;

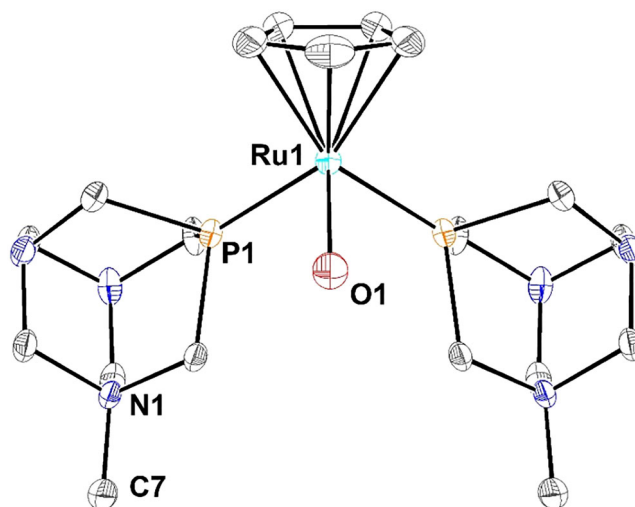


FIGURE 1 Crystal structure of **4**. Selected interatomic distances and angles: $\text{Ru1}\text{--}\text{P1} = 2.2722(7)$ Å; $\text{Ru1}\text{--}\text{P1}^1 = 2.2722(7)$ Å, $\text{Ru1}\text{--}\text{O1} = 2.175(3)$ Å; $\text{Ru}\text{--}\text{Cp}_{\text{cent}}$ = 1.537 Å; $\text{P1}\text{--}\text{C1} = 1.846(3)$ Å; $\text{N1}\text{--}\text{C1} = 1.510(3)$ Å; $\text{N1}\text{--}\text{C7} = 1.492(4)$ Å; $\text{N1}\text{--}\text{C4} = 1.533(3)$ Å; $\text{N1}\text{--}\text{C5} = 1.543(4)$ Å; $\text{P1}\text{--}\text{Ru}\text{--}\text{P1}^1 = 97.62(3)^\circ$; $\text{P1}\text{--}\text{C1}\text{--}\text{N1} = 112.67(18)^\circ$; $\text{C1}\text{--}\text{N1}\text{--}\text{C7} = 109.4(2)^\circ$; $\text{C4}\text{--}\text{N1}\text{--}\text{C7} = 109.4(2)^\circ$; $\text{C5}\text{--}\text{N1}\text{--}\text{C7} = 109.6(2)^\circ$. Hydrogen atoms, anions, and solvate molecules have been omitted for clarity.

$\text{Ru1}\text{--}\text{P2} = 2.2599(12)$ Å).^[46] The Ru– OH_2 bond length (2.175(3) Å) is close to that for the non-methylated complex **2** (2.1784(16) Å)^[37] and is similar to those found for other Ru complexes containing the H_2O ligand.^[48] Also, the Ru– $\text{Cp}_{\text{centroid}}$ distance of **4** (1.845 Å) is in the range found for similar Cp–Ru–phosphine complexes (1.835–1.92 Å),^[34,49,50] and **1**, **2**, and **3** (**1**: 1.844 Å^[35]; **2**: 1.837 Å^[37]; **3**: 1.840 Å^[46]). The remaining distances and angles for **4** are in a similar ranges to that in parent Cp–Ru–phosphine complexes and do not deserve special attention. Additionally, complex **4** is involved in a network of weak hydrogen bonds^[51] connecting the water ligand and the methanol molecule ($\text{H1}\text{--}\text{O1M} = 2.667$ Å), which also interacts with the CF_3SO_3^- anion ($\text{H1M}\text{--}\text{O3TF} = 2.823$ Å). The triflate anion is also linked via non-covalent interactions with the Cp–H9 and H10 ($\text{O1TF}\text{--}\text{H9} = 2.577$, $\text{O1TF}\text{--}\text{H10} = 2.321$ Å) and the mPTA–H1A and H5A ($\text{H1A}\text{--}\text{O5TF} = 2.440$ Å, $\text{H5A}\text{--}\text{O5TF} = 2.377$ Å) (Figure 2).

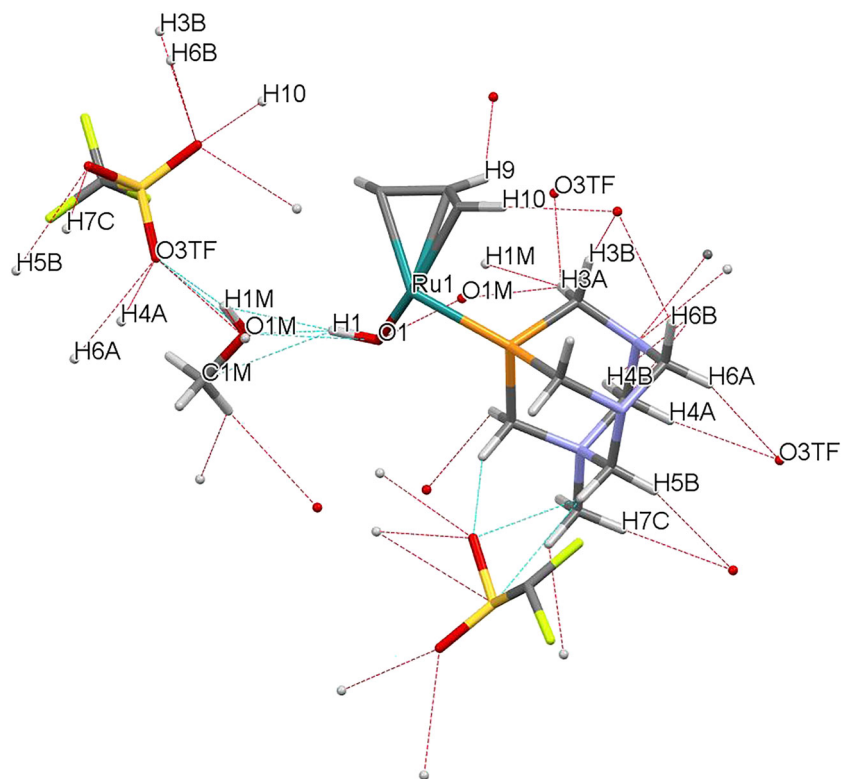


FIGURE 2 Intramolecular interactions network around the asymmetric unit of **4**-MeOH

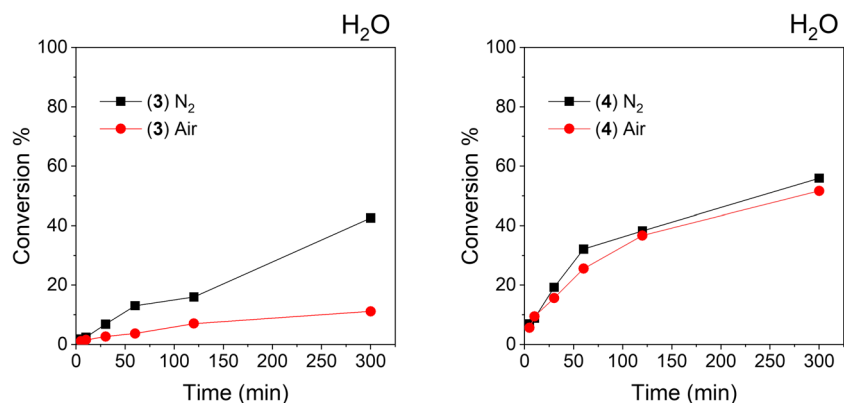


FIGURE 3 Catalytic isomerization of 2-cyclohexen-1-ol by **3** and **4** in water versus time. Reaction conditions: 80°C, 1 mol% [Ru], 1 ml H₂O, N₂ and air. Measured by gas chromatography

2.3 | Isomerization of 2-cyclohexen-1-ol by **3** and **4**

The cyclic allylic alcohol 2-cyclohexen-1-ol was catalytically isomerized in the biphasic medium H₂O/cyclohexane (1:1) by complex **2**, which was recycled up to 7 runs.^[38] Nevertheless, the conversion considerably drops along the consecutive reaction cycles. Complex **2** is partially soluble in organic solvents and some leaching from the aqueous to the organic phase is not ruled out. An option to avoid leaching consists of increasing the hydrophilic-lipophilic balance of the catalyst, which should prevent its passage to the organic phase during the catalytic cycle. This strategy should provide a better catalytic conversion and reduce the metal impurities in

the product as they should remain mainly in the aqueous phase. A strategy to obtain such a complex could be changing the PTA for a more water-soluble derivative, such as mPTA. As discussed above, the structure of complex **4**, containing mPTA instead of PTA, is like **2** but, as expected, displays a higher solubility in the water whereas it is practically insoluble in most organic solvents. Therefore, complex **4** should be completely retained in the aqueous phase during the recycling runs.

For the sake of comparison with **1** and **2**,^[38] the redox isomerization of 2-cyclohexen-1-ol was evaluated with 1 mol% of **3** and **4**, in water at 80°C under N₂ and air (Figure 3). The obtained catalytic activity of **3** in water is larger under N₂ (43%) than under air (11%), whereas the activity of **4** is similar under both reaction atmospheres

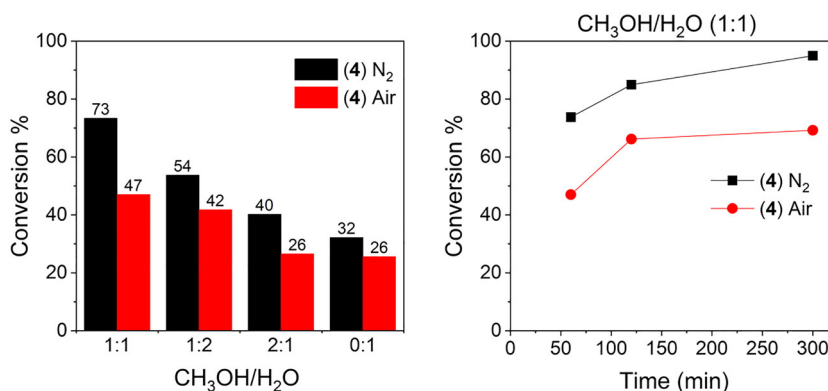
TABLE 1 Catalytic parameters of the isomerization of 2-cyclohexen-1-ol catalyzed by **3** and **4** in monophasic

Catalyst	[Ru] (mol%)	Time (h)	Solvent	Atmosphere	TON	TOF (h ⁻¹)	Conversion (%) ^a
3	1	2	H ₂ O	N ₂	16.04	8.02	16.04
3	1	5	H ₂ O	N ₂	42.57	8.51	42.57
3	1	2	H ₂ O	Air	7.1	3.55	7.1
3	1	5	H ₂ O	Air	11.18	2.24	11.18
4	1	2	H ₂ O	N ₂	38.3	19.15	38.3
4	1	2	CH ₃ OH/H ₂ O	N ₂	84.95	42.48	84.95
4	1	5	H ₂ O	N ₂	55.96	27.98	55.96
4	1	5	CH ₃ OH/H ₂ O	N ₂	94.96	18.99	94.96
4	1	2	H ₂ O	Air	36.73	18.37	36.73
4	1	2	CH ₃ OH/H ₂ O	Air	66.18	33.09	66.18
4	1	5	H ₂ O	Air	51.69	10.34	51.69
4	1	5	CH ₃ OH/H ₂ O	Air	69.2	13.84	69.2
4	0.1	5	H ₂ O	Air	65	13	65
4	0.1	19	H ₂ O	Air	100	5.26	100

Abbreviations: TOF, turnover frequency; TON, turnover number.

^aMeasured by gas chromatography.

FIGURE 4 Catalytic isomerization of 2-cyclohexen-1-ol by **4** in (a) water versus CH₃OH proportion in volume and (b) CH₃OH/H₂O (1:1) versus time. Reaction conditions: 80°C, 1 mol% [Ru], N₂ and air. (a) 1 h, 1 ml of CH₃OH/H₂O (1:1, 1:2, 2:1, 0:1); (b) 1, 2, and 5 h, 1 ml of CH₃OH/H₂O (1:1). Measured by gas chromatography



(N₂: 56%; air: 52%). As expected, complex **4**, which contains an H₂O instead of a Cl coordinated to the metal, catalyzes the isomerization reaction better than **3**, agreeing with the previous results obtained employing complexes **1** and **2**, and for the same reasons.^[38]

Considering that complex **4** is significantly more active than **3**, further experiments were carried out only with this complex. The importance of the solubility of the substrate, 2-cyclohexen-1-ol, in the reaction media was also determined by carrying out the reaction in a mixture of water/CH₃OH. The resulting conversions were significantly better when CH₃OH was added to the reaction, which changed depending on the proportion between both solvents (Table 1). The isomerization conversion was found to be better under N₂ than under air independently of the proportion of water and CH₃OH. The best conversion was obtained in CH₃OH/H₂O (1:1) with

1 mol% of **4** after 1 h of reaction under N₂ (73%), whereas under air, the isomerization was significantly lower (47%) (Figure 4a). The conversion under N₂ was completed at 5 h (Figure 4b), achieving a TON = 95 and turnover frequency (TOF) = 19 h⁻¹ (Table 1), being worse than that achieved with complex **2** in water.^[38]

The recyclability of **4** was evaluated by performing the isomerization reactions at 80°C in a mixture of cyclohexane/water (1:1) and cyclohexane/H₂O/CH₃OH (2:1:1), under air and N₂ (Table 2). The conversion obtained in cyclohexane/water (1:1) (Figure 5a) was 99% at 5 h under air, which is significantly better than those obtained under the same reaction conditions in pure water (air: 52%) and CH₃OH/H₂O (1:1) (air: 69%) (Figures 3b and 4b, respectively). However, when the reaction was performed under N₂, the resulting conversion was significantly worse at 5 h (N₂: 18%) than that

TABLE 2 Catalytic parameters of the isomerization of 2-cyclohexen-1-ol catalyzed by **2** and **4** in a biphasic system

Catalyst	[Ru] (mol%)	Solvent	T (°C)	Time (h)	Atmosphere	TON	TOF (h ⁻¹)	Conversion (%) ^a	Ref
2	1	Cyclohexane/H ₂ O	70	0.5	N ₂	>99	198	99	[38]
2	1	Cyclohexane/H ₂ O	70	0.5	Air	71	142	71	[38]
2	0.1	Cyclohexane/H ₂ O	70	3	N ₂	>999	333	99.9	[38]
2	0.1	Cyclohexane/H ₂ O	70	15	Air	510	34	51	[38]
2	0.02	Cyclohexane/H ₂ O	70	15	N ₂	1550	103.3	31	[38]
2	0.1	Cyclohexane/H ₂ O	70	21	N ₂	3420 ^b	162.9	34.2	[38]
4	1	Cyclohexane/CH ₃ OH/H ₂ O	80	2	Air	41.87	20.94	41.87	This work
4	1	Cyclohexane/CH ₃ OH/H ₂ O	80	2	Air	66.69	13.34	66.69	This work
4	1	Cyclohexane/H ₂ O	80	5	Air	97.11	19.42	97.11	This work
4	1	Cyclohexane/H ₂ O	80	20	Air	312 ^c	15.6	78	This work
4	1	Cyclohexane/H ₂ O (pH = 1.7)	80	5	Air	382 ^d	76.4	76.4	This work
4	1	Cyclohexane/H ₂ O (pH = 1.7)	80	7	N ₂	471 ^e	67.3	67.3	This work

Abbreviations: TOF, turnover frequency; TON, turnover number.

^aMeasured by gas chromatography.

^bTON after 7 cycles under N₂ (cyclohexane/H₂O [1:1], 70°C, 0.1 mol% [Ru], 3 h/cycle).

^cTON after 4 cycles under air (cyclohexane/H₂O [1:1], 80°C, 1 mol% [Ru], 5 h/cycle).

^dTON after 5 cycles under air (cyclohexane/H₂O [pH = 1.7] [1:1], 80°C, 1 mol% [Ru], 1 h/cycle).

^eTON after 7 cycles under N₂ (cyclohexane/H₂O [pH = 1.7] [1:1], 80°C, 1 mol% [Ru], 1 h/cycle).

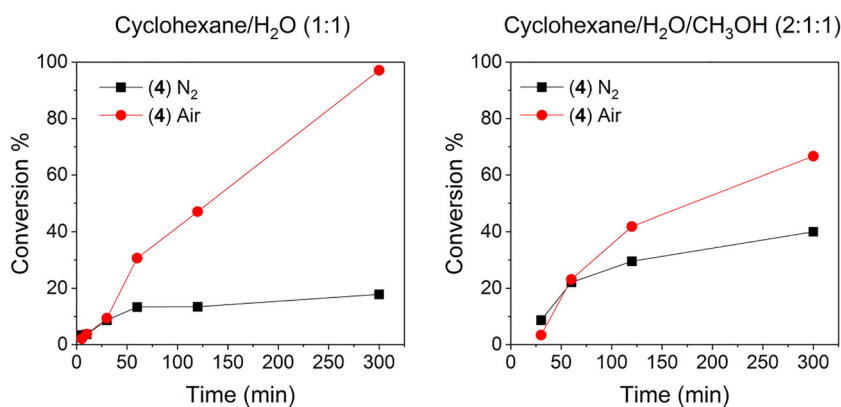


FIGURE 5 Catalytic isomerization of 2-cyclohexen-1-ol catalyzed by **4** in biphasic systems in (a) cyclohexane/H₂O (1:1) and (b) cyclohexane/H₂O/CH₃OH (2:1:1) versus time. Reaction conditions: 80°C, 1 mol% [Ru], N₂ and air. (a) 1 ml H₂O; (b) 1 ml H₂O, 1 ml CH₃OH. Measured by gas chromatography

obtained in pure water (N₂: 56%) and in CH₃OH/H₂O (1:1) (N₂: 95%) (Figures 3b and 4b, respectively). In contrast, (Table 2) the isomerization in cyclohexane/H₂O/CH₃OH (2:1:1) at 5 h (Figure 5b) was comparable (air: 67%) with that in H₂O (air: 52%) and CH₃OH/H₂O (1:1) (air: 69%) (Figures 3b and 4b, respectively), whereas the conversion under N₂ was clearly lower (N₂: 40%) than in pure water (N₂: 56%) and CH₃OH/H₂O (1:1) (N₂: 95%) (Figures 3b and 4b, respectively). Nevertheless, under the same reaction conditions but in cyclohexane/H₂O/CH₃OH (2:1:1) (Figure 5b), the conversion was not improved (67%) under air whereas under N₂, it was significantly better (N₂: 40%) (Figure 5a).

The isomerization of linear allylic alcohols by **4** is very sensitive to the pH, increasing the conversion

when pH decreases. An important finding of the previously reported studies was that phosphate buffer interacts with the triply charged cation **4**.^[45] To avoid these interferences, the influence of pH on the isomerization of 2-cyclohexen-1-ol by **4** was also assessed by using TfOH, which is innocent for what concerns the coordinative behaviour. The reactions were performed in cyclohexane/H₂O (1:1) under air in the pH range of 1.7–4.8, which was fixed using a 0.01 M solution of TfOH in water. The best results were obtained at pH = 1.7, where complex **4** can isomerize more than 99 eq. of 2-cyclohexen-1-ol in 1 h (Figure 6). This conversion is significantly better than that obtained in pure water considering both TON and TOF (Tables 1 and 2).

Recyclability of complex **4** was evaluated under the reaction conditions that provided better conversion: (i) under air for 5 h in water/cyclohexane (1:1) at 80°C and (ii) under air for 1 h in water (pH = 1.7)/cyclohexane (1:1) at 80°C (Table 2). Whereas in pure water/cyclohexane, the catalyst could be reused for 4 consecutive runs, achieving a TON = 312 and TOF = 15.6 h⁻¹ (Figure S8), in acidic water (pH = 1.7)/cyclohexane, the aqueous phase was recycled up to 5 consecutive runs, reaching a TON = 382 and a TOF = 76.4 h⁻¹ (Figure 7a). In addition, in pure water/cyclohexane, the conversion drops drastically after the third cycle (air: 26%) (Figure S8) whereas in water (pH = 1.7)/cyclohexane, the conversion decreases moderately during the fourth (air: 56%) and fifth cycles (air: 52%) (Figure 7a). On the other hand, the overall TON for the activity of **4** after 4 cycles in water (pH = 1.7)/cyclohexane (1:1) (TON = 330) was slightly higher than in water/cyclohexane (1:1) (TON = 312). Also, it is important to note that the reaction in water (pH = 1.7)/cyclohexane (1:1) was much faster

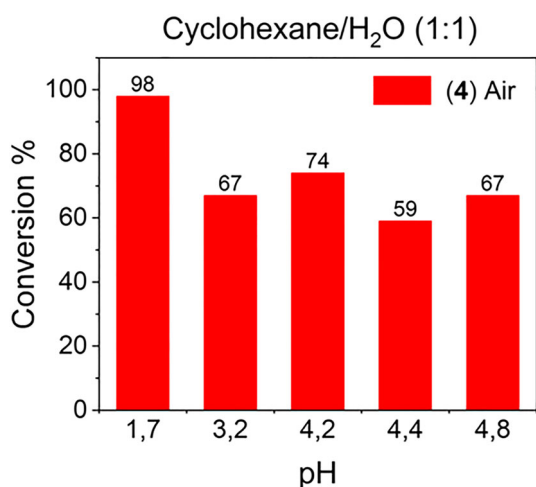
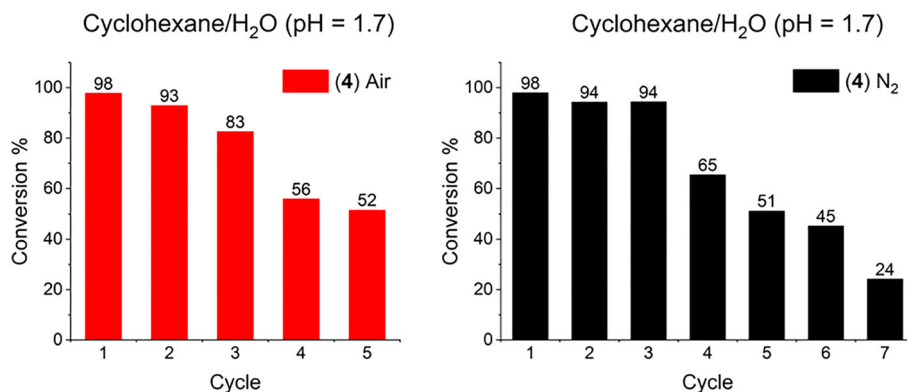


FIGURE 6 Catalytic isomerization of 2-cyclohexen-1-ol catalyzed by **4** in biphasic system cyclohexane/H₂O (1:1) versus pH (1.7, 3.2, 4.2, 4.4, and 4.8). Reaction conditions: 80°C, 1 h, 1 mol% [Ru], 1 ml H₂O, air. Measured by gas chromatography

(TOF = 82.5 h⁻¹) than in water/cyclohexane (1:1) (TOF = 15.6 h⁻¹). Despite the good results found in water (pH = 1.7)/cyclohexane (1:1), a significant reduction in conversion was also observed after the fifth cycle (Figure 7a). To determine if the reaction atmosphere is the reason for this behavior, the reaction was carried out under N₂. Supporting our suspicions, the isomerization reaction under N₂ was also fulfilled in 1 h and the aqueous phase could be reused up to 7 consecutive runs, achieving a value of TON = 471 and TOF = 67.29 h⁻¹ (Figure 7b). Comparing the first 5 cycles in both conditions reveals that the activity of **4** under N₂ and in acidic water (pH = 1.7)/cyclohexane (1:1) (TON = 402) (Figure 7b) improved slightly with respect to aerobic conditions (TON = 382) (Figure 7a). It is important to point out that the first three runs performed under N₂ provided the full conversion of the 2-cyclohexen-1-ol, whereas under aerobic conditions, the full conversion was only obtained in the first and second runs. Additionally, the observed conversion under N₂ diminished progressively from the fourth run (N₂: 65%) up to the seventh cycle (N₂: 24%) (Figure 7b), whereas under air, the observed conversion begins to decrease after the fourth cycle (air: 56%) and drops drastically after the fifth cycle (Figure 7a). It is important to point out that available common organic solvents (CH₂Cl₂, Et₂O, etc.) were evaluated to prepare a practical biphasic reaction media, but only the combination of cyclohexane with water provided the better catalytic conversion, but also its manipulation was the most practical from an operational point of view. A better biphasic combination could be obtained but probably using non-common solvents, constituting an interesting new research objective that could be studied in future.

To investigate the possible reasons for the reduction of conversion after each consecutive run, both the aqueous and the organic layers were studied by NMR spectroscopy. The study by ³¹P{¹H} NMR spectroscopy of the reaction aqueous phase (Figure S11) showed a partial transformation of **4** in a new specie

FIGURE 7 Catalytic isomerization of 2-cyclohexen-1-ol catalyzed by **4** in biphasic systems in (a) cyclohexane/H₂O (pH = 1.7) (1:1) under air and (b) cyclohexane/H₂O (pH = 1.7) (1:1) under N₂ versus recycling runs (1 h/cycle). Reaction conditions: 80°C, 1 mol% [Ru]. (a) 1 ml H₂O (pH = 1.7), air; (b) 2 ml H₂O (pH = 1.7), N₂. Measured by gas chromatography

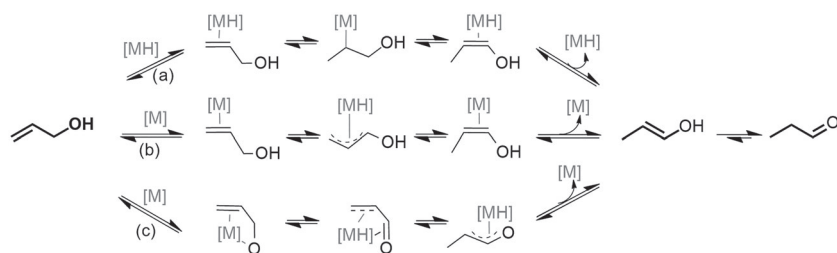


(singlet at -10.83 ppm), whose intensity increased after each run. The chemical shift does not fit with that expected for the oxidation product of mPTA (mPTA = O), which arises in D_2O at -1.47 ppm. Therefore, the observed reaction inactivation after each run is not due to the transformation of complex **4** by losing one ligand mPTA oxidized by air. The reaction of complex **4** with TFOH (pH = 1.7) in 2 ml of water at $80^\circ C$ leads to the observed species, suggesting that it could be a complex in which the triflate anion interacts with the metal. Unfortunately, NMR experiments were not determinant to provide a definite composition and all our attempts to obtain single crystals useful for determining its crystal structure were not fruitful. It is important to point out that not any phosphorus-containing species was observed in the organic phase by $^{31}P\{^1H\}$ NMR but also that less than 3% ($5.6 \cdot 10^{-5}$ mmol) of the starting metal was found in the combined organic phases of the 7 reaction runs, supporting that the leaching occurred during the reaction cycles is negligible.

To the best of our knowledge, the isomerization of 2-cyclohexen-1-ol shown by complexes **2** and **4** in biphasic media is the highest published until now.^[16,39-43] Despite complex **2** being more efficient (**2** can catalyze 7 consecutive runs in 21 h with a TON = 3420 and TOF = $162.9 h^{-1}$),^[38] using complex **4** shows several advantages such as the low contamination with metal product and easy phase separation. The different activities of **2** and **4** can be due to their different solubility in water and organic solvents. In fact, **2** is slightly soluble also in organic solvents, which facilitates the interaction between catalyst and substrate, probably improving the isomerization in the organic phase. In contrast, complex **4** is completely insoluble in organic solvents; thus, it remains in the aqueous phase during the reaction and interaction between catalyst and substrate that can occur only at the interface.

2.4 | Catalytic redox isomerization mechanism

Three mechanisms have been proposed in the literature for the catalytic isomerization of allylic alcohols: the so



SCHEME 4 Literature proposed three different mechanisms for the catalytic isomerization of allylic alcohols.

called “metal hydride addition–elimination mechanism” or “alkyl mechanism”; the “ π -allyl metal hydride” or “ η^3 -allyl mechanism”; and the “enone mechanism” (Scheme 4).^[52]

To determine the mechanism that drives the studied catalytic processes, the reaction between 1 mol% of **4** and 2-cyclohexen-1-ol under N_2 in CD_3OD/D_2O (1:2) was followed by NMR spectroscopy at $80^\circ C$ (see the supporting information for further details). In this reaction, the proportion between methanol and water needed to be 1:2, instead of 1:1, which was used in previously described experiments. After 1 h, the $^{31}P\{^1H\}$ NMR spectrum displays two singlets at -8.41 ppm, corresponding to the complex $[RuCp(OH-\kappa O)(mPTA)_2]^{2+}$ (**5**),^[46] and at -10.60 ppm, which is due to the complex **4**, whereas in the 1H NMR spectrum, the distinctive signals of cyclohexanone start to appear. After 4.5 h, the signals previously found in the $^{31}P\{^1H\}$ NMR spectrum dropped down, whereas two doublets (-9.77 and -25.70 ppm; $^2J_{PP} = 39.21$ Hz) were observed (see Figures S13 and S14 for further details), which presumably correspond to the reaction intermediate **6** where the 2-cyclohexen-1-ol is η^2 -coordinated to the ruthenium atom through the double bond (Figure 8). The progress of the isomerization conversion was corroborated by 1H NMR (60% in 4 h 30 min) (see Figure S12 for further details). We have

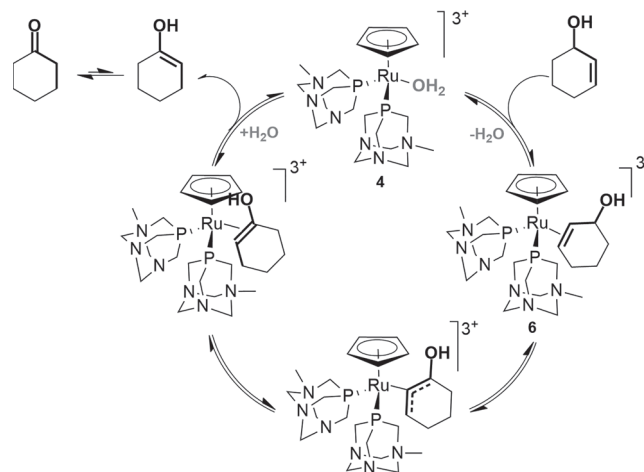


FIGURE 8 Proposed mechanism for the isomerization of 2-cyclohexen-1-ol into 3-methylcyclohexanone catalyzed by **4**

shown in previous studies based on NMR spectroscopy and X-ray diffraction that the isomerization in water of linear and cyclic allyl alcohols by complex **2** goes through an intermediate complex in which the allylic alcohol is η^2 -coordinated to the metal.^[38,47,52,53] It is interesting to point out that the intermediate complex $[\text{RuCp}(\text{PTA})_2(\text{exo-}\eta^2\text{-CH}_2=\text{CH-CHOH-CH}_2\text{-CH}_3)](\text{CF}_3\text{SO}_3)$, isolated by reaction between 1-penten-3-ol and **2** in methanol/water, was the first crystal structure of an aqua-soluble metal complex including a coordinated η^2 -allyl alcohol.^[53] Experimental results suggest that the isomerization of 2-cyclohexen-1-ol into cyclohexanone catalyzed by **4** goes through a similar mechanism to that catalyzed by **2**.^[38]

The analysis of the reaction by $^{31}\text{P}\{^1\text{H}\}$ NMR displayed the formation of $[\text{RuCp}(\text{OH-}\kappa\text{O})(\text{mPTA})_2]^{2+}$ (**5**), which was shown to be a catalytically inactive specie that would block the catalytic process.^[45,46] To support this suspicion, complex **4** was reacted with 1 eq. of NaOH in D_2O under N_2 in a 5 mm NMR tube at room temperature. When complex **4** was fully transformed into **5**, 10 eq. of 2-cyclohexen-1-ol in $\text{CD}_3\text{OD}/\text{D}_2\text{O}$ (1:2) was introduced into the reaction, which was kept at 80°C and studied by $^{31}\text{P}\{^1\text{H}\}$ NMR (see the supporting information for further details). After 1 h, the signal due to **5** was decreased whereas signals at -10.48 and 11.60 ppm arose. The isomerization conversion was only 16% after 4 h 30 min (^1H NMR). Therefore, a neutral or acidic reaction medium is mandatory to avoid deprotonation of **4**.

Finally, the isomerization rate in acid-biphasic media was not influenced by the reaction atmosphere whereas in neutral-biphasic media, the conversion was found to be higher under aerobic conditions than under inert atmosphere. The fact that no oxidation of mPTA was observed during the reaction, whereas a slow decrease of the intensity of the signal (-10.60 ppm, singlet) corresponding to complex **4** took place, suggests that a possible new paramagnetic complex afforded by oxidation of Ru(II) into Ru(III) is produced, which is probably more active for this reaction. This option is currently under study.

3 | CONCLUSIONS

Complex $[\text{RuCp}(\text{H}_2\text{O-}\kappa\text{O})(\text{mPTA})_2](\text{CF}_3\text{SO}_3)_3$ (**4**) was synthesized and fully characterized by single-crystal X-ray diffraction. The catalytic properties of this complex for the isomerization of the cyclic allylic alcohol 2-cyclohexen-1-ol in water and biphasic system were explored and compared with those for the complexes $[\text{RuClCp}(\text{mPTA})_2](\text{CF}_3\text{SO}_3)_2$ (**3**) and $[\text{RuCp}(\text{H}_2\text{O-}\kappa\text{O})(\text{PTA})_2](\text{CF}_3\text{SO}_3)$ (**2**). Complexes **3** and **4** showed poor

catalytic activity for the isomerization of the cyclic allylic alcohols in pure water, but the activity of **4** is notably improved in a mixture of water and CH_3OH (1:1). In addition, a significant enhancement of the conversion was obtained when a biphasic mixture of acidic water at $\text{pH} = 1.7$ and cyclohexane was used as reaction medium, where complex **4** was able to isomerize 99 eq. of 2-cyclohexen-1-ol in 1 h at 80°C , and the water phase could be recycled up to 7 consecutive runs under N_2 , reaching an overall TON of 471. It is important to stress that the resulting metal leaching was less than 3% after 7 runs. On the other hand, interestingly, the spectroscopic studies performed in $\text{CD}_3\text{OD}/\text{D}_2\text{O}$ showed that during the catalytic isomerization of 2-cyclohexen-1-ol by **4**, one η^2 -allyl alcohol intermediate forms, similar to what was observed by using **2**.

The obtained results indicate how important is to maximize the interactions between catalyst and substrates, which could be obtained with cosolvents or additives, but also how sensitive are these reactions to the reaction pH. Finally, an accurate selection of the ligands can improve the recyclability of a water-soluble catalyst when it is used in a biphasic water/organic phase system, achieving cleaner products. This reaction is a handy procedure for the isomerization of cyclic allylic alcohols without metal contamination of the product. In further studies, we want to improve the conversion rates and recyclability of **4** for the isomerization of cyclic allyl alcohols in biphasic systems employing a microchannel reactor, where a high mass and heat transfer rate and rapid mixing of reagents can be achieved.

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AUTHOR CONTRIBUTIONS

Belen Lopez-Sanchez: Data curation; formal analysis; investigation; software; writing-original draft; writing-review and editing. **Ana Belén Bonhome:** Formal analysis; investigation. **Franco Scalambra:** Data curation; formal analysis; investigation; methodology; software; supervision; writing-original draft; writing-review and editing. **Antonio Manuel Romerosa-Nievas:** Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision; validation; writing-original draft; writing-review and editing.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are openly available in a public repository that issues datasets with DOIs.

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REFERENCES

- [1] A. B. Gómez, P. Holmberg, J. E. Bäckvall, B. Martín-Matute, *RSC Adv.* **2014**, *4*, 39519.
- [2] D. Cahard, S. Gaillard, J. L. Renaud, *Tetrahedron Lett.* **2015**, *56*, 6159.
- [3] J. García-Álvarez, J. Gimeno, F. J. Suárez, *Organometallics* **2011**, *30*, 2893.
- [4] T. Campos-Malpartida, M. Fekete, F. Joó, Á. Kathó, A. Romerosa, M. Saoud, W. Wojtków, *J. Organomet. Chem.* **2008**, *693*, 468.
- [5] E. Bolyog-Nagy, A. Udvardy, Á. Barczáné-Bertók, F. Joó, Á. Kathó, *Inorganica Chim. Acta* **2017**, *455*, 514.
- [6] M. Fekete, F. Joó, *Catal. Commun.* **2006**, *7*, 783.
- [7] A. Mena-Cruz, M. Serrano-Ruiz, P. Lorenzo-Luis, A. Romerosa, Á. Kathó, F. Joó, L. M. Aguilera-Sáez, *J. Mol. Catal. A: Chem.* **2016**, *411*, 27.
- [8] P. Lorenzo-Luis, A. Romerosa, M. Serrano-Ruiz, *ACS Catal.* **2012**, *2*, 1079.
- [9] V. Cadierno, P. Crochet, S. E. García-Garrido, J. Gimeno, *Dalton Trans.* **2004**, 3635.
- [10] R. C. van der Drift, E. Bouwman, E. Drent, *J. Organomet. Chem.* **2002**, *650*, 1.
- [11] C. Bianchini, A. Meli, W. Oberhauser, *New J. Chem.* **2000**, *25*, 11.
- [12] C. E. Czégényi, M. Fekete, E. Tóbiás, A. Udvardy, H. Horváth, G. Papp, F. Joó, *Catalysts* **2020**, *10*, 1.
- [13] P. Crochet, M. A. Fernández-Zúmel, J. Gimeno, M. Scheele, *Organometallics* **2006**, *25*, 4846.
- [14] V. Cadierno, S. E. García-Garrido, J. Gimeno, *Chem. Commun.* **2004**, *4*, 232.
- [15] P. N. Liu, K. D. Ju, C. P. Lau, *Adv. Synth. Catal.* **2011**, *353*, 275.
- [16] L. Bellarosa, J. Diez, J. Gimeno, A. Lledós, F. J. Suárez, G. Ujaque, C. Vicent, *Chem. – A Eur. J.* **2012**, *18*, 7749.
- [17] W. Zhang, C. Meng, Y. Liu, Y. Tang, F. Li, *Adv. Synth. Catal.* **2018**, *360*, 3751.
- [18] N. Ahlsten, A. Bartoszewicz, B. Martín-Matute, *Dalton Trans.* **2012**, *41*, 1660.
- [19] R. Uma, C. Crévisy, R. Grée, *Chem. Rev.* **2002**, *103*, 27.
- [20] X. Zhang, Y. Zhang, L. Liao, Y. Gao, H. E. M. Su, J. Yu, *Chem-CatChem* **2022**, *14*, 1.
- [21] J. Francos, S. E. García-Garrido, J. García-Álvarez, P. Crochet, J. Gimeno, V. Cadierno, *Inorganica Chim. Acta* **2017**, *455*, 398.
- [22] A. Seretis, P. Diamantopoulou, I. Thanou, P. Tzevelekidis, C. Fakas, P. Lilas, G. Papadogianakis, *Front. Chem.* **2020**, *8*, 221.
- [23] T. Naota, H. Takaya, S.-I. Murahashi, *Coord. Chem. Rev.* **1998**, *98*, 2599.
- [24] X. Liu, F. Wang, *Coord. Chem. Rev.* **2012**, *256*, 1115.
- [25] P. G. Jessop, F. Joó, C. C. Tai, *Coord. Chem. Rev.* **2004**, *248*, 2425.
- [26] K. Nomura, *J. Mol. Catal. A: Chem.* **1998**, *130*, 1.
- [27] V. Cadierno, P. Crochet, J. Gimeno, *Synlett* **2008**, *2008*, 1105.
- [28] A. E. Díaz-Álvarez, P. Crochet, M. Zablocka, C. Duhayon, V. Cadierno, J. Gimeno, J. P. Majoral, *Adv. Synth. Catal.* **2006**, *348*, 1671.
- [29] P. Csabai, F. Joó, *Organometallics* **2004**, *23*, 5640.
- [30] K. Voronova, L. Homolya, A. Udvardy, A. C. Bényei, F. Joó, *ChemSusChem* **2014**, *7*, 2230.
- [31] S. Ahrland, J. Chatt, N. R. Davies, A. A. Williams, *J. Chem. Soc.* **1958**, 276.
- [32] F. Joó, J. Kovács, Á. Kathó, A. C. Bényei, T. Decuir, D. J. Darensbourg, A. Miedaner, D. L. Dubois, *John Wiley & Sons* **2007**, *32*, 1.
- [33] A. Mena-Cruz, P. Lorenzo-Luis, A. Romerosa, M. Serrano-Ruiz, *Inorg. Chem.* **2008**, *47*, 2246.
- [34] A. D. Phillips, L. Gonsalvi, A. Romerosa, F. Vizza, M. Peruzzini, *Coord. Chem. Rev.* **2004**, *248*, 955.
- [35] D. N. Akbayeva, L. Gonsalvi, W. Oberhauser, M. Peruzzini, F. Vizza, P. Brüggeller, A. Romerosa, G. Sava, A. Bergamo, *Chem. Comm.* **2003**, 264.
- [36] M. Serrano-Ruiz, P. Lorenzo-Luis, A. Romerosa, A. Mena-Cruz, *Dalton Trans.* **2013**, *42*, 7622.
- [37] F. Scalambra, M. Serrano-Ruiz, A. Romerosa, *Dalton Trans.* **2017**, *46*, 5864.
- [38] F. Scalambra, B. López-Sánchez, A. Romerosa, *Dalton Trans.* **2018**, *47*, 16398.
- [39] D. J. Nelson, J. A. Fernández-Salas, B. J. Truscott, S. P. Nolan, *Org. Biomol. Chem.* **2014**, *12*, 6672.
- [40] M. Batuecas, M. A. Esteruelas, C. García-Yebra, E. Oñate, *Organometallics* **2010**, *29*, 2166.
- [41] A. Bouziane, B. Carboni, C. Bruneau, F. Carreaux, J. L. Renaud, *Tetrahedron Lett.* **2008**, *64*, 11745.
- [42] S. Manzini, A. Poater, D. J. Nelson, L. Cavallo, S. P. Nolan, *Chem. Sci.* **2013**, *5*, 180.
- [43] T. Xia, B. Spiegelberg, Z. Wei, H. Jiao, S. Tin, S. Hinze, J. G. de Vries, *Catal. Sci. Technol.* **2019**, *9*, 6327.
- [44] A. Romerosa, T. Campos-Malpartida, C. Lidrissi, M. Saoud, M. Serrano-Ruiz, M. Peruzzini, J. A. Garrido-Cárdenas, F. García-Maroto, *Inorg. Chem.* **2006**, *45*, 1289.
- [45] B. González, P. Lorenzo-Luis, M. Serrano-Ruiz, É. Papp, M. Fekete, K. Csépe, K. Ósz, Á. Kathó, F. Joó, A. Romerosa, *J. Mol. Catal. A: Chem.* **2010**, *326*, 15.
- [46] B. González, P. Lorenzo-Luis, P. Gili, A. Romerosa, M. Serrano-Ruiz, *J. Organomet. Chem.* **2009**, *694*, 2029.
- [47] F. Scalambra, N. Holzmann, L. Bernasconi, S. Imberti, A. Romerosa, *ACS Catal.* **2018**, *8*, 3812.
- [48] E. V. Kabin, V. A. Emel'yanov, I. A. Baidina, T. I. Nedoseykina, V. A. Vorob'yov, *J. Struct. Chem.* **2010**, *51*, 73.
- [49] M. Serrano-Ruiz, P. Lorenzo-Luis, A. Romerosa, *Inorganica Chim. Acta* **2017**, *455*, 528.
- [50] S. Bolaño, L. Gonsalvi, F. Zanobini, F. Vizza, V. Bertolasi, A. Romerosa, M. Peruzzini, *J. Mol. Catal. A: Chem.* **2004**, *224*, 61.
- [51] A. Romerosa, F. Scalambra, *Non-covalent Interactions in the Synthesis and Design of New Compounds*, **2016** 83.

- [52] F. Scalambra, P. Lorenzo-Luis, I. de los Rios, A. Romerosa, *Coord. Chem. Rev.* **2019**, 393, 118.
- [53] F. Scalambra, B. Lopez-Sanchez, N. Holzmann, L. Bernasconi, A. Romerosa, *Organometallics* **2020**, 39, 4491.

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