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The importance of copper placement in chiral catalysts supported on heteropolyanions: Lacunary vs external exchanged

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A B S T R A C T

Lacunary $[PCuW_{11}O_{39}]^{5-}$ species modified with chiral bis(oxazoline) leads to very poor results as catalyst in the enantioselective cyclopropanation, in contrast with the Cu-bis(oxazoline) complex exchanged on the Keggin $[PW_{12}O_{40}]^{3-}$ species. The incomplete neutralization and/or exchange of the Keggin species produces a loss in symmetry that leads to spectra in solid phase (IR and NMR) similar to those obtained for the lacunary species. The symmetry is averaged in solution, but additional characterization methods are necessary to determine the true nature of the solid heteropolyanionic species. These results demonstrate that the efficiency of copper-bis(oxazoline) complexes is related to its placement in an external exchange position, whereas the copper included in the heteropolyanion structure is not active for cyclopropanation reactions.

1. Introduction

The immobilization of chiral metal complexes to obtain heterogeneous catalysts for enantioselective processes [1–4] is in principle an attractive strategy to improve the productivity and applicability of the homogeneous catalysts. However, the additional cost immobilization has a negative impact in its implementation, especially in the case of covalent immobilization due to the required supplementary substitution on the ligand. This additional functionalization is not necessary in many non-covalent strategies of immobilization [5] with simple and efficient procedures that use the same homogeneous catalysts, which should help to minimize its cost impact.

In the case of charged chiral complexes, the immobilization can be carried out using electrostatic interactions with the support, which acts as a counterion for the chiral complex. Its nature may have a strong influence on the reaction results for example due to the coordination of the anion to the metal center and the subsequent change in the geometry of the catalytic site [6–8]. For this reason, in most of cases anions with a poor coordinating ability are needed, such as nafion-like solids [9]. However, the price and the textural properties of this kind of solids limit their applications in this field.

Keggin type heteropolyacids [10] are strong acids that can be used as catalysts in many organic reactions [11–14], either in homogeneous phase or supported on different solids, such as silica or alumina. As poorly coordinating anions, they can be used to immobilize cationic complexes through electrostatic interactions. In fact, they have been used as anionic linker between alumina support and different types of chiral complexes, such as Rh-diphosphine [15–19], Ru-Binap [20], Rh-prolinamide [21], and Rh-MonoPhos [22], to be used in enantioselective hydrogenation reactions. However, the immobilization of other types of complexes and the application in enantioselective reactions different from hydrogenation has been scarcely described.

Bis(oxazoline)-metal complexes are among the most versatile enantioselective catalysts [23] and their immobilization has been widely studied [24,25], and specially with non-covalent immobilization methods. In fact, bis(oxazoline)-copper complexes immobilized by non-covalent methods have been used as catalysts in cyclopropanation [9,24–26], aziridination [27], carbene insertions into C—H bonds [28,29], Diels–Alder [7], hetero-Diels-Alder [30], Mukaiyama aldol [31,32], Mukaiyama-Michael [33] and ene reactions [34].

However, only two examples deal with the use of supported heteropolyanions as carriers for chiral bis(oxazoline)-copper complexes, in both cases using the Keggin phosphotungstate anion $PW_{12}O_{40}{}^{3-}$ (PW_{12}). In one case the catalyst was prepared by successive treatment of PW_{12}-TUD-alumina with one Cu(I) salt (chloride or triflate) and then with the chiral bis(oxazoline) ligand [35]. In the other one, the most efficient catalyst was obtained by exchange of the pre-formed azabis(oxazoline)-copper(II) complex on the ammonium form of PW_{12}-silica [36]. Some observations pointed to a possible formation of a lacunary species of the heteropolyanion in the neutralization process, which

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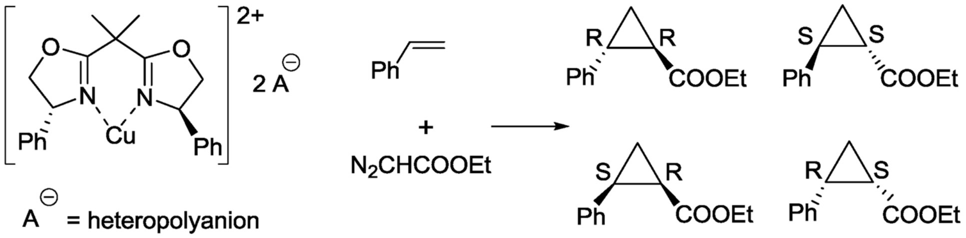


Scheme 1. Cyclopropanation of styrene with ethyl diazoacetate.

generated doubts about the true nature of the active sites responsible for the good behavior of the catalyst. In this paper we present the comparison of the modification of the true lacunary species $[PCuW_{11}O_{39}]^{5-}$ ($PCuW_{11}$) with a chiral bis(oxazoline) ligand with the previously reported immobilization method on supported phosphotungstate (PW_{12}). For this purpose, the cyclopropanation of styrene with ethyl diazoacetate has been used as benchmark reaction (Scheme 1).

2. Experimental

2.1. Preparation of Box-Cu/PW_{12} and Box-Cu/PW_{12}-S_R

These catalysts were prepared by cation exchange of a preformed Box-Cu on a neutralized tungstophosphoric acid following the method previously described [36]. The Box-Cu complex was prepared by mixing the chiral ligand (0.02 mmol) and $Cu(OTf)_2$ (0.02 mmol) in anhydrous dichloromethane under an argon atmosphere, microfiltered and the solvent was evaporated. $H_3PW_{12}O_{40}\cdot nH_2O$ (PW_{12}, Fluka) was calcined and then neutralized by adding triethylamine (0.2 mL) to a suspension of calcined PW_{12} (1 g) in dichloromethane (5 mL). The complex was exchanged on the neutralized PW_{12} in nitroethane to get **Box-Cu/PW_{12}**.

PW_{12} was supported on Ralt-Chemie silica (S_R, surface area 253 m^2/g, pore volume 1.1 cm^3/g, mean pore diameter 11.3 nm, particle size 0.15 − 0.21 mm) by using the pore filling impregnation method [37]. The supported PW_{12}-S_R was neutralized with triethylamine and the preformed Box-Cu complex was exchanged in nitroethane to get **Box-Cu/PW_{12}-S_R**.

2.2. Preparation of $PCuW_{11}$ and $PCuW_{11}$-S_R

The lacunary $[PCuW_{11}O_{39}]^{5-}$ ($PCuW_{11}$) was prepared according to a procedure described in the literature [38,39]. PW_{12} (1 g, 0.35 mmol) was dissolved into distilled water (10 mL) and a saturated solution of $NaHCO_3$ was slowly added until pH = 5. The solution was stirred at 65 °C for 10 min. Then $Cu(OAc)_2$ (63 mg, 0.35 mmol) dissolved in the minimum water volume was added, the mixture was stirred at 65 °C for 24 h and the water was evaporated under vacuum. The resulting solid was crystallized in water and dried at rt. $PCuW_{11}$ was supported on Ralt-Chemie silica in the same way as PW_{12} (section 2.1) to get $PCuW_{11}$-S_R. The catalysts Box/$PCuW_{11}$ and Box/$PCuW_{11}$-S_R were prepared *in situ* in the reaction medium by adding the required amount of chiral ligand previously to the addition of the reagents. Samples for analysis were prepared by addition of Box (0.02 mmol) to a suspension of $PCuW_{11}$ or $PCuW_{11}$-S_R in nitroethane. The resulting mixture was stirred overnight, filtered and dried under vacuum.

2.3. Characterization

Elemental analysis was performed in a Perkin-Elmer 2400 elemental analyzer. Copper and tungsten analysis was carried out by ICP in a Perkin-Elmer Plasma 40 emission spectrometer. FT-IR spectra of KBr wafers treated at 200 °C under vacuum (10^{-4} torr) were recorded in a Nicolet Avatar 360 FTIR spectrophotometer.

2.4. Cyclopropanation reaction

Ethyl diazoacetate (5 mmol) was slowly added (2 h) with a syringe pump over a stirred solution or suspension formed by styrene (5 mmol), *n*-decane (100 mg, internal standard) and catalyst (see Tables for amounts) in dichloromethane (4 mL) at rt. The reaction was stirred for 24 h and the results were determined by GC as described elsewhere [36]. The solid was recovered by centrifugation, washed with hexane (3 × 3 mL), and reused without drying under the same conditions.

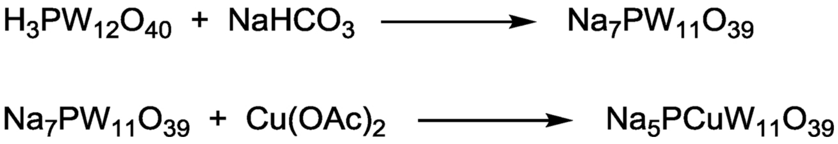
2.5. Reduction tests

The copper salt, Cu(II) acetate, Cu(II) chloride and Cu(II) triflate (0.5 mmol), was suspended in acetonitrile (1.5 mL) and stirred at room temperature. Then, phenyl hydrazine (1 mmol) was added and the mixture was stirred for 1 h. In the case of heteropolyacids, $PCuW_{11}$ and Box-Cu/PW_{12}-S_R (0.05 mmol) were suspended in acetonitrile (0.5 mL) and phenyl hydrazine (0.5 mmol) was added in the same way. The solution was microfiltered and analysed by GC–MS.

3. Results and discussion

In our previous paper on this subject [36], both supported and unsupported PW_{12} were neutralized by stirring in a solution of triethylamine (1.2 eq) in dichloromethane prior to exchange with copper complexes, due to the sensitivity of oxazoline-containing ligands to acid- catalysed hydrolysis. Both IR and NMR spectra of the neutralized heteropolyacid pointed to the formation, at least partially, of a lacunary $[PW_{11}O_{39}]^{7-}$ species, that would be subsequently exchanged with the $[\text{Box-Cu}]^{2+}$ complex. In this way, the copper complex may occupy the vacant position left by W. Thus, in an attempt to elucidate if this kind of species was responsible for the catalytic activity and selectivity, a true lacunary $PCuW_{11}$ species was synthesized, to be modified with a chiral bis(oxazoline) ligand.

The copper-modified lacunary Keggin structure was prepared following a reported method [38,39], by treating phosphotungstic acid (PW_{12}) with $NaHCO_3$ to create a vacancy (PW_{11}) and then insertion of a copper ion into the vacancy with $Cu(OAc)_2$ to lead the expected $PCuW_{11}$ species (Scheme 2). While the FT-IR spectrum of PW_{12} shows the typical bands at 1081, 982, 888, and 793 cm^{-1} (Fig. 1a) [40], in



$$H_3PW_{12}O_{40} + NaHCO_3 \longrightarrow Na_7PW_{11}O_{39}$$

$$Na_7PW_{11}O_{39} + Cu(OAc)_2 \longrightarrow Na_5PCuW_{11}O_{39}$$

Scheme 2. Synthesis of the lacunary $PCuW_{11}$ species.

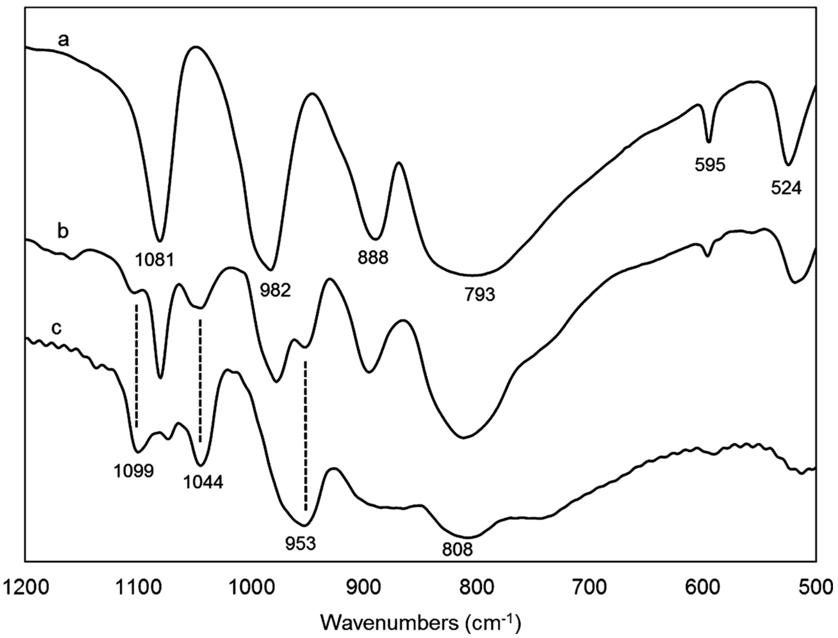


Fig. 1. FT-IR spectra: a) Keggin PW_{12}, b) neutralized (1.2 eq NEt_3) PW_{12}, c) lacunary $PCuW_{11}$.

Table 1
Analysis of the catalysts based on PW_{12} and $PCuW_{11}$.

Entry	Catalyst	Content (mmol/g)		Cu/PW ratio[a]
		W	Cu	
1	$PCuW_{11}$	3.42	0.31	1.1
2	$PCuW_{11}$ after use	2.41	0.21	0.96
3	$PCuW_{11}$-S_R	0.85	0.07	1.0
4	Box/$PCuW_{11}$-S_R	0.83	0.07	1.0
5	PW_{12}(n)[b]	3.51	–	–
6	Box-Cu/PW_{12}	2.95	0.52	2.0
7	PW_{12}(n)-S_R[b]	1.13	–	–
8	Box-$Cu_{(high)}$/PW_{12}-S_R	1.37	0.20	1.6
9	Box-$Cu_{(low)}$/PW_{12}-S_R	0.85	0.06	0.9

[a] Calculated taking into account the presence of 11 or 12 W per PW unit.
[b] (n) indicates that the heteropolyacid had been neutralized with triethylamine.

general the bands in the spectrum of $PCuW_{11}$ were shifted to lower frequencies with a splitting of the ν_{as} P-O_a band at 1099 and 1044 cm^{-1} (Fig. 1c). This splitting (55 cm^{-1}) is even higher than the value reported in the literature (40 cm^{-1}), which was already unexpectedly higher than in other PMW_{11} species [41]. As can be seen, these bands are similar to the additional bands observed in the spectrum of PW_{12} neutralized with 1.2 eq of triethylamine (Fig. 1b), and considered as an important indication of the possible formation of a lacunar species in the neutralization process. The spectra of the silica-supported species are similar to those of the unsupported ones, in the window left by the strong Si-O-Si stretching bands. Moreover, the analysis of $PCuW_{11}$ (Table 1, entry 1) is in good agreement with the theoretical composition of the lacunary species, and the same Cu/W ratio is kept after supporting on silica ($PCuW_{11}$-S_R, entry 2).

Although the chiral catalyst Box/$PCuW_{11}$-S_R was prepared *in situ* just before the catalytic test by addition of chiral bis(oxazoline) to the $PCuW_{11}$-S_R solid, samples for characterization were prepared in the same way, and the resulting solid was filtered and dried under vacuum. No variations in the amount of copper were observed (Table 1), indicating that copper is not leached from the solid by complexation with Box. For the sake of comparison, Box-Cu/PW_{12} and two Box-Cu/PW_{12}-S_R with different functionalization were prepared by the cation exchange method previously described [36]. The complete exchange should give a $(Box\text{-}Cu)_3[PW_{12}]_2$ species, with 1.5 Cu/PW ratio, but the use of a large excess of $(Box\text{-}Cu)(OTf)_2$ in the exchange process is able to increase that ratio up to 2 (Table 1, entry 6), probably by exchange of $(Box\text{-}Cu\text{-}OTf)^+$ species, as pointed by the presence of sulfur in the semi quantitative XRF analysis. By controlling the amount of complex, a Box-$Cu_{(low)}$/PW_{12}-S_R catalyst with a composition (Cu/PW ratio of 0.9) similar to that of Box/$PCuW_{11}$-S_R can be prepared (Table 1, entry 9).

The catalysts were tested in the benchmark reaction between styrene and ethyl diazoacetate (Scheme 1) and the results are gathered in Table 2. Typically, ethyl diazoacetate is fully converted, and hence the cyclopropanes yield represents the chemoselectivity of the cyclopropanation with respect to side reactions such as dimerization and oligomerization of diazoacetate. The reactions catalysed by the lacunary species $PCuW_{11}$ are the exception, as the conversion of ethyl

Table 2
Results obtained in the cyclopropanation reaction between styrene and ethyl diazoacetate in dichloromethane catalyzed by box-Cu(II) complexes.

Entry	Catalyst	% cat	run	% yield[a]	*trans/cis*[a]	% ee *trans*[a]	% ee *cis*[a]
1	$PCuW_{11}$	0.40	1	2	71/29	–	–
			2	1	70/30		
2	Box/$PCuW_{11}$	0.40	1	5	70/30	40	27
			2	2	60/40	41	38
3	$PCuW_{11}$-S_R	0.38	1	8	61/39	–	–
4	Box/$PCuW_{11}$-S_R	0.30	1	7	60/40	42	40
			2	5	60/40	34	32
5		1	1	10	64/36	50	34
			2	7	67/33	47	36
6	Box-Cu/PW_{12}	0.20	1	38	61/39	55	42
7	Box-$Cu_{(high)}$/ PW_{12}-S_R	0.26	1	14	66/34	58	42
			2	13	62/38	59	39
			3	14	62/38	58	40
8		0.13	1	12	60/40	39	38
9	Box-$Cu_{(low)}$/ PW_{12}-S_R	0.24	1	16	60/40	48	33
			2	16	62/38	36	29
			3	13	60/40	33	28
10		1	1	24	65/35	45	25
			2	25	64/36	41	27

[a] Determined by gas chromatography; 1*S* cyclopropanes are the major products.

diazoacetate was not complete even after 24 h. At the end of the reaction, the catalysts were separated by centrifugation and another portion of diazoacetate was added to the solution to check the leaching of active copper. No further cyclopropanation reaction was detected in solution ($<$ 2% increase in yield), showing that the contribution of the homogeneous reaction is negligible and hence the heterogeneous character of all the catalysts. Some of the recovered catalysts were reused under the same conditions.

The catalytic activity of $PCuW_{11}$ and $PCuW_{11}$-S_R was very low (entries 1 and 3), with very poor yields of cyclopropanes ($<$ 8%) and incomplete conversion of ethyl diazoacetate. The modification with the chiral ligand did not significantly modified this behavior (entries 2 and 4), whereas the enantioselectivity obtained was only moderate (40–42 % ee for *trans* cyclopropanes). The increase in the amount of catalyst (entry 5) produced an increase in the enantioselectivity for *trans* cyclopropanes, and also a slight increase in yield although it remained very low. It is noteworthy, the selectivity is maintained in the reuse, showing the stability of the copper sites formed. Another proof for the stability of the lacunary species comes from the chemical analysis of Box/$PCuW_{11}$ after reaction (Table 1, entry 2). It can be seen that the used catalyst possesses the same Cu/PW ratio (0.96) but a significant decrease in the content of both copper and tungsten (0.21 mmol Cu/g and 2.41 mmol W/g) due to the weight gain associated with the adsorption of ligand and reaction products and by-products.

These results contrast with those obtained with catalysts prepared by cation exchange. Box-Cu/PW_{12} (entry 6) leads to total conversion of ethyl diazoacetate, with a fair chemoselectivity (38 % yield) and better enantioselectivity (55 % ee for *trans* cyclopropanes), even with only 0.2 % catalyst. The immobilization on silica produces a catalyst with lower catalytic activity but the same enantioselectivity (entry 7), that it is fully recoverable with the same performance at least in two further reaction cycles. It is necessary to use an amount of this catalyst as low as 0.13 % (entry 8) to get results as bad as those obtained with the lacunary catalysts. The catalyst with lower loading of Cu per PW_{12} (entry 9) leads to significant lower enantioselectivity, that it is not improved even using 1% catalyst (entry 10), showing that it is due to a structural effect of the catalyst and the full exchange on the heteropolyanion is required to get good results.

Regarding the structure of the catalysts, the $PCuW_{11}$ lacunary species has been described with anilinium cations as counter-ions [42], although the orientation disorder in the crystal makes it difficult to assign the Cu position. However, it is considered that the terminal oxygen bound to copper corresponds to a coordinated water molecule, as described also for other lacunary species, such as $PAlW_{11}$ [43]. When the box ligand is added, it would coordinate as a monodentate ligand by substituting the water molecule. Considering the crystal structure of a free box ligand with substituted phenyl groups [44], the structure of Box/$PCuW_{11}$ could be represented as in Fig. 2A. On the other hand, the crystal structures of several combinations of polyoxometallates and copper(II) complexes have been also reported. In some cases, one terminal oxygen participates in the coordination sphere of copper, whereas in other cases the complex acts as a cation. Even both roles can be played by the same type complex in one single crystal structure [45]. Taking the structure of Box-$CuBr_2$ as model [46], two structures for Box-Cu/PW_{12} can be hypothesized, coordinated to terminal oxygen (Fig. 2B) or as free cation, far from any coordinating atom of PW_{12} (4.5 Å from the closest terminal oxygen, Fig. 2C).

However, the hypothesis of a monodentate Box-Cu complex in the case of Box/$PCuW_{11}$ is not compatible with the moderate enantioselectivity obtained (Table 2, entry 2), that should be much lower, comparable to that obtained with monodentate oxazoline ligands [47]. Moreover, this type of structure would not either explain the lower activity of Box/$PCuW_{11}$, as shown by the incomplete consumption of ethyl diazoacetate. In any case, all the copper(II) complexes must be considered pre-catalysts, whereas the true catalysts are formed by the Cu(II) to Cu(I) reduction promoted by ethyl diazoacetate. A more difficult reduction of $PCuW_{11}$ would explain the lower activity, and an experiment of comparative reductions were carried out using another typical reductant for cyclopropanation reaction, phenylhydrazine [48], to detect in solution the corresponding oxidized products. Several metal oxides and salts have been used for this kind of reaction, such as Ag_2O [49], MnO_2 [50] or $Pb(OAc)_4$ [51]. It is described that on oxidation, phenylhydrazine leads to molecular nitrogen and phenyl radicals that evolve depending on the reaction medium. In this work we decided to test three different copper(II) salts, in order to check the effect of the anion in a polar non-protic solvent such as acetonitrile. The results are summarized in Table 3.

The reaction with $Cu(OAc)_2$ led to biphenyl as main product, with phenol and azobenzene as the main by-products. In the case of $CuCl_2$, the chloride participates in the reaction and chlorobenzene is the main product, with several by-products. Finally, the most typical cyclopropanation catalyst, $Cu(OTf)_2$, led to azobenzene as the only product, with no detectable by-products. These results indicate that the anion influences the course of the phenylhydrazine oxidation. Additionally, in all the cases it was observable a color change and/or the formation of a precipitate. The addition of phenylhydrazine to $PCuW_{11}$, even in a larger excess did not show any observable change in the medium and the analysis of the reaction mixture did show only the starting phenylhydrazine with no detectable products. On the contrary, the addition of phenylhydrazine to Box-Cu/PW_{12}-S_R did produce a color change of the solid, from light greenish blue to grey. The analysis of the reaction mixture showed a good part of the unreacted phenylhydrazine, that had been added in a larger excess, together with comparable amounts of several of the expected products: biphenyl, phenol, biphenylamine and azobenzene. This result confirms the difference in the reductability of $PCuW_{11}$ and Box-Cu/PW_{12}-S_R and explains the very low activity of $PCuW_{11}$ as cyclopropanation catalyst. This effect on the catalytic activity of copper had been already detected with strongly coordinative anions, such as chloride, in solution [52] and the structure of the lacunar species can be considered as an anion of this type for copper. On the other hand, the addition of a nitrogenated ligand has a positive effect for reactions with ethyl diazoacetate, as seen in the case of carbene insertions [53], which is also in good agreement with the effect observed in the Box/$PCuW_{11}$ catalysts.

Those catalytic results seem to indicate that the lacunary species does not behave in the same way as the Box-Cu/PW_{12} catalysts prepared by cation exchange. Thus, the identification of lacunary species in the preparation of Box-Cu/PW_{12} based in IR and NMR spectra may be wrong. Some experiments were carried out to check this hypothesis and to confirm the nature of the sites in Box-Cu/PW_{12}. The carbon and nitrogen analysis of the neutralized PW_{12} prepared according to our previous paper with Et_3N/PW_{12} molar ratio of 4.8 (1.2 eq of amine) (Fig. 3b) show that not all the protonic sites are neutralized by triethylamine. Thus, the Keggin PW_{12} was treated with higher amounts of triethylamine (Et_3N/PW_{12} molar ratios of 30 and 300, that is 10 and 100 eq). As can be seen, the excess of base produces a decrease in the intensity of the bands assigned to the lacunary species, that appear first as shoulders (Fig. 3c) and finally disappear when 100 equivalents of amine are used (Fig. 3d). This result seems to indicate that in fact, a lacunary species is not formed during the neutralization process, and the bands assigned in principle to this kind of species correspond to the partially neutralized Keggin species, that loses its symmetry due to the presence of protons and triethylammonium cations in different amounts. In fact, the loss of symmetry is considered the origin of the changes in frequency observed in lacunary species [41]. Thus, the loss of symmetry in the external part of the Keggin species is also able to modify the IR spectrum in the same way as the change in the internal structure of the Keggin polyoxometallate.

However, the NMR spectra in solution, where a fast exchange would presumably take place, should show the features of a Keggin structure, considered as an average of the partially neutralized species. Then, the ^{31}P NMR spectra of Keggin PW_{12} and the different neutralized species

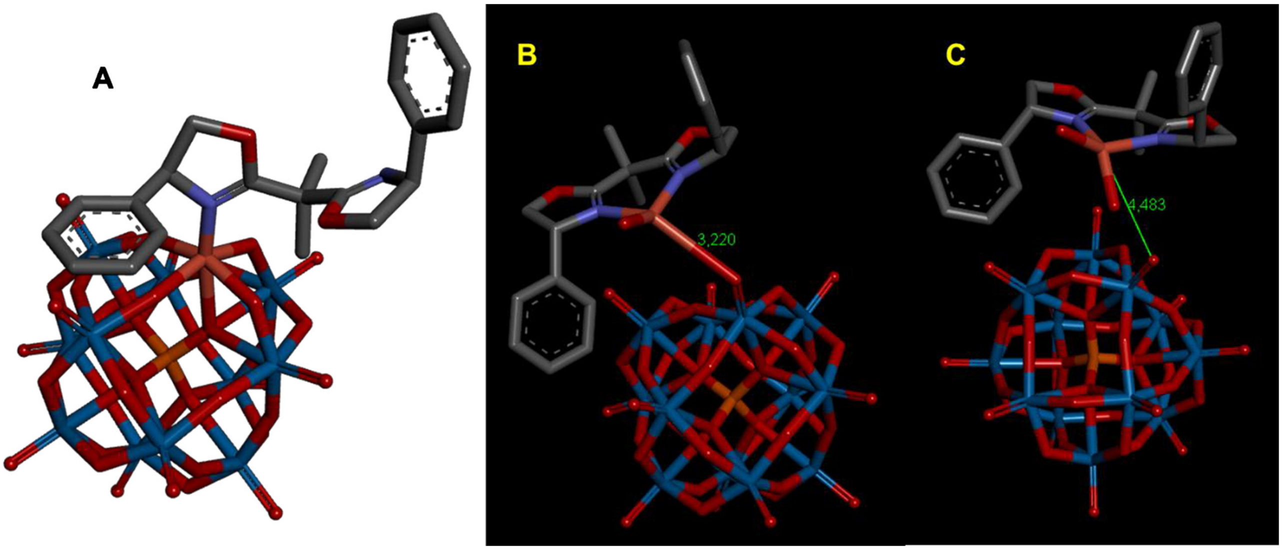


Fig. 2. Models for the Cu(II) pre-catalysts: A) Box/$PCuW_{11}$; B) Box-Cu/PW_{12} with Cu-PW_{12} coordination; C) Box-Cu/PW_{12} with cationic complex.

Table 3
Results of the reaction of phenylhydrazine with different copper catalysts.

Catalyst	Major product	Minor products
$Cu(OAc)_2$	Biphenyl	Phenol, Azobenzene
$CuCl_2$	Chlorobenzene	Biphenyl, Chlorobiphenyl, Azobenzene, Diphenylamine
$Cu(OTf)_2$	Azobenzene	
PW_{12}	N.R.[a]	
$PCuW_{11}$	N.R.[a]	
BoxCu/ATPS	-[b]	Phenol, Biphenyl, Biphenylamine, Azobenzene

[a] No reaction. Only phenylhydrazine and aniline (impurity in the starting reagent) are detected.

[b] The phenylhydrazine/Cu ratio was much higher and phenylhydrazine was not completely consumed.

were registered in d_6-dmso (Fig. 4). All the spectra showed a single signal at -15.5 ppm, without any trace of the peak at -10 ppm observed in the solid state spectrum (without fast exchange) of the neutralized PW_{12} species [36]. The different behavior in solution and in solid phase, both in NMR and IR, seems to confirm that the loss of symmetry is the responsible for the bands observed in solid phase, that disappear in solution due to the rapid average of the compensating cations. Therefore, and as a general remark, IR spectra alone cannot be used to justify the presence of lacunary species when symmetry of the Keggin species can be lost by other reasons, such is the presence of different compensating cations.

FT-IR spectrum of Box-Cu/PW_{12} (Fig. 5) show the presence of coordinated Box, mainly because of the stretching band of C=N at 1630 cm^{-1} (1652 cm^{-1} for pure Box). Nevertheless, the lacunary structure of PW_{11} is kept after ligand addition (spectrum superimposable with Fig. 1c, not shown), but the ligand is not detected at all. This result seems to indicate the weak interaction of chiral Box with the copper centers of $PCuW_{11}$, typical of a coordination as a monodentate ligand.

As a general conclusion, the catalysts prepared by the previously reported method [36] are truly exchanged, keeping the structure of the starting Keggin heteropolyanion, and they perform much better than

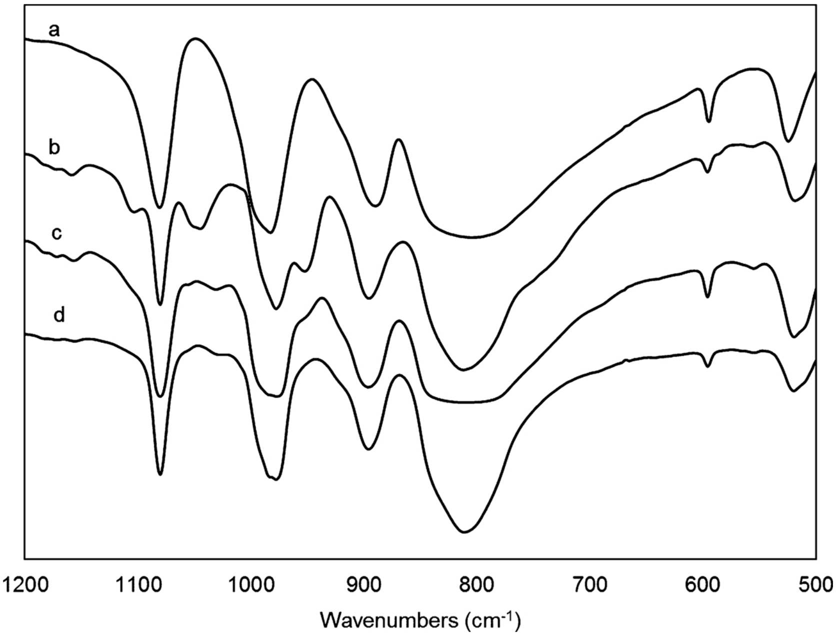


Fig. 3. FT-IR spectra: a) Keggin PW_{12}, and neutralized PW_{12} with different amounts of triethylamine, b) 1.2 eq, c) 10 eq, d) 100 eq.

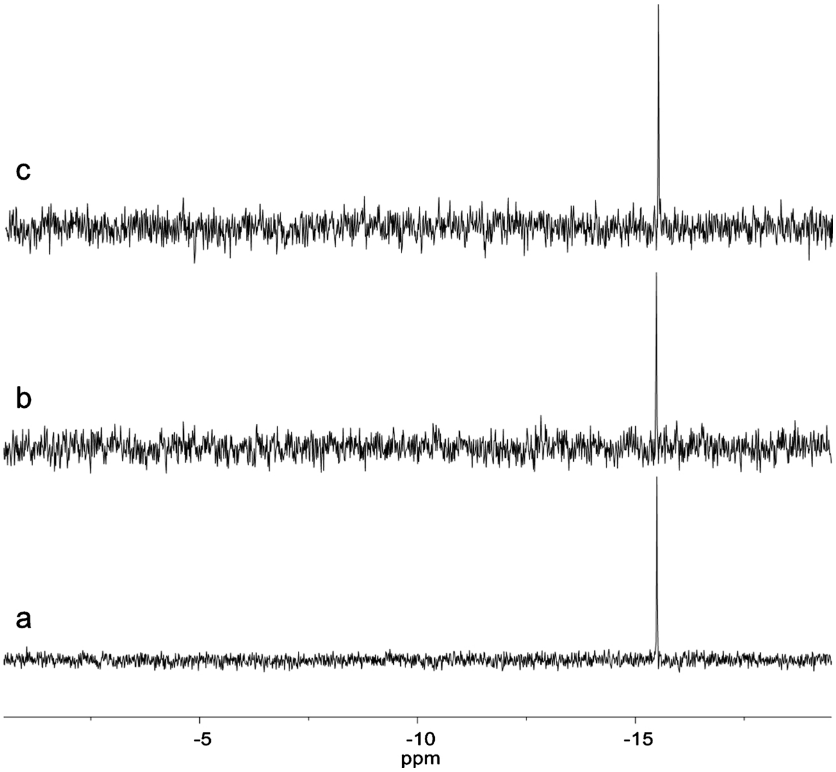


Fig. 4. ^{31}P NMR spectra in d_6-dmso: a) Keggin PW_{12}, and neutralized PW_{12} with different amounts of triethylamine, b) 2 eq, c) 10 eq.

the lacunary $PCuW_{11}$ species modified with the same chiral ligand, mainly with respect to catalytic activity.

4. Conclusions

The comparison between different heteropolyanions as supports for Cu-complex with ligands of the bis(oxazoline) family allows exploring the influence of several factors. The use of a true lacunary heteropolyanion bearing Cu in the structure, such as $PCuW_{11}$, modified with chiral bis(oxazoline) leads to very low yields and slightly lower enantioselectivities in comparison with unsupported and silica supported Box-Cu/PW_{12} prepared by cation exchange with the pre-formed Box-Cu complex. These results show that neutralization and cation exchange does not lead to a lacunar species, whereas changes in the IR and NMR spectra in solid state are due to a loss of symmetry of the whole species due to the presence of different cations around it. Hence, the variations in the IR signals must be taken with care, as they are not sufficient to assess the lacunar structure, which requires additional characterization

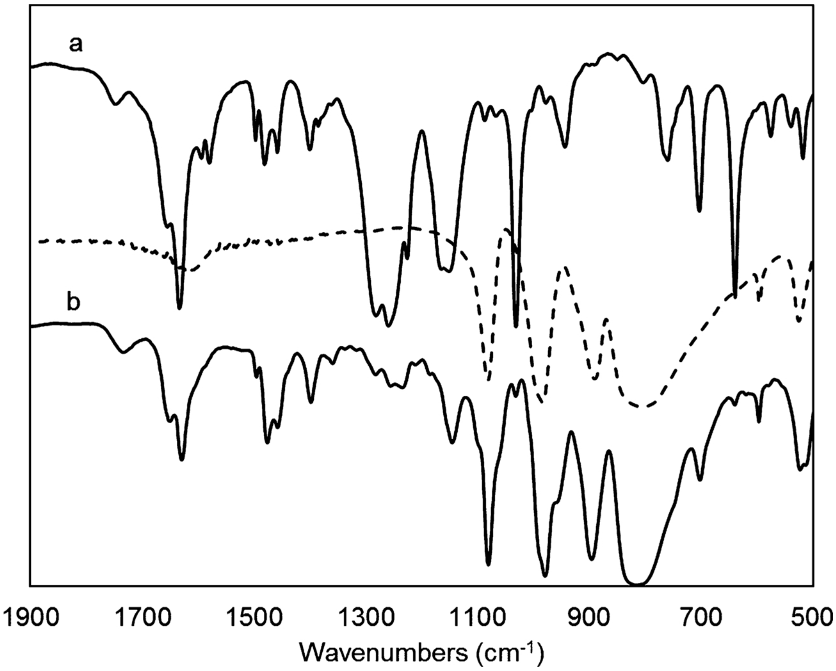


Fig. 5. FT-IR spectra of: a) Box-Cu$(OTf)_2$, b) Box-Cu/PW_{12}. The spectrum of PW_{12} (dashed line) is included for comparison.

techniques.

CRediT authorship contribution statement

M. Rosario Torviso: Investigation, Writing - review & editing, Funding acquisition. **Daniela S. Mansilla:** Investigation. **José M. Fraile:** Validation, Writing - original draft. **José A. Mayoral:** Conceptualization, Writing - review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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