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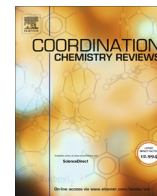
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Review

Isomerization of allylic alcohols in water catalyzed by transition metal complexes

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ABSTRACT

Isomerisation of allylic alcohols in water mediated catalytically by water soluble metal complexes is an elegant synthetic procedure for obtaining carbonyl compounds in a completely atom-economical eco-benign process with several useful applications in natural-product synthesis and in bulk chemical processes. This review is targeted to provide a general view of the goals obtained in isomerisation catalysis in water. Complexes that catalyze the isomerization of allylic alcohols in water, together with ligands and reaction conditions are compared with respect to yield, turnovers, rate and selectivity. A general overview of the mechanisms proposed for the isomerisation of allylic alcohols is also presented. Crystal structures and selected bond lengths are presented for the most representative catalytically active metal complexes.

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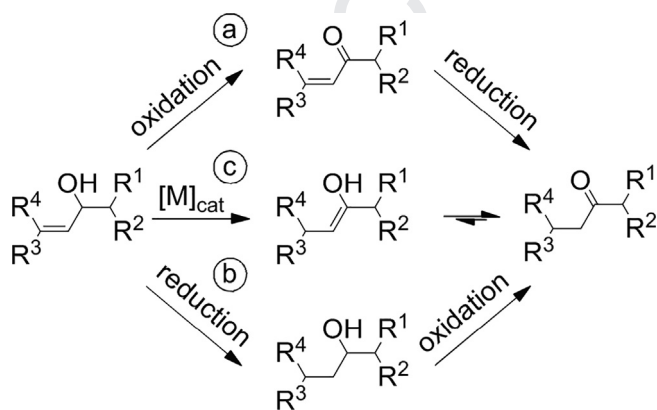
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1. Introduction

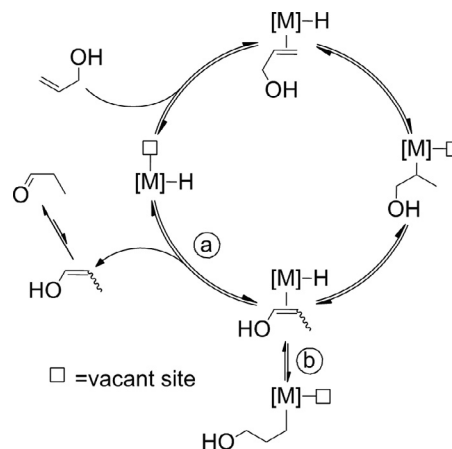
Classical isomerization of allylic alcohols leads to ketones and aldehydes by a two steps process that combines oxidation/reduction or reduction/oxidation (Scheme 1). Sensitive substrates may not survive the conditions of oxidation and/or reduction and therefore new more convenient processes are required [1–3]. From the seminal works of Blum [4] and Trost [5] a large number of efforts were targeted to the development of the methods for catalyzing the isomerization of allylic alcohols under as mild conditions as possible and in eco-friendly solvents such as water. The developed redox-isomerization reactions catalyzed by transition metal complexes were showed as an atom-economical route to obtain ketones and aldehydes with a 100% atom economy [6–10].

Despite the large efforts made to use water most of the metal complexes that efficiently catalyze isomerisation processes have been studied in organic solvents [11–13]. As an inexpensive, available and renewable feedstock, water is attracting more and more interest both from industrial and academic perception as a replacement for traditionally used organic solvents [14–16]. The catalytic reactions in water mediated by hydrosoluble coordination compounds could provide an interesting solution to most of the problems of the catalytic synthetic processes in organic solvents. Ideally, after completing the catalytic reaction: one phase contains the products and the other one includes the catalyst. Therefore, the phase where the catalyst is recovered may be used without any further separation and without any significant catalyst lost. The economy of the process is improved and the metal pollution reduced.

Another important possible advantage of the catalytic processes in water is the reduced contamination by metal containing particles and therefore being used for synthesizing compounds that are required in high purity such as alimentary additives, medicines and drugs. Water-soluble metal complexes have been reported as active catalyst for isomerisation of allylic alcohols, which have been summarized partially in nice reviews that have boarded the subject from different point of view [17–24]. Here we present a comprehensive review on isomerisation of allylic alcohols in water catalyzed by water-soluble metal complexes.



Scheme 1. Possible pathways for the isomerization of allylic alcohols.



Scheme 2. Metal hydride addition-elimination mechanism.

2. Isomerization mechanisms.

The catalytic mechanism for the isomerisation of allylic alcohols in aqueous media was initially investigated by McGrath and Grubbs by using $[\text{Ru}(\text{H}_2\text{O})_6](\text{tos})_2$ ($\text{tos} = p$ -toluene sulfonate) (**1**) as catalyst [25]. The most efficient one-step isomerisation process (Scheme 2, path a) requires the double bond migration into an enol (or enolate) intermediate that then rapidly tautomerizes to afford the saturated carbonyl compound [7,29–34]. Over the years, three main mechanisms have been proposed for the metal catalyzed isomerization of allyl alcohols [5,7,11,12,26,35–37]: a) metal hydride addition-elimination mechanism, also named alkyl mechanism; b) π -allyl metal hydride or η^3 -allyl mechanism; c) mechanism involving oxygen coordination, also named enone mechanism.

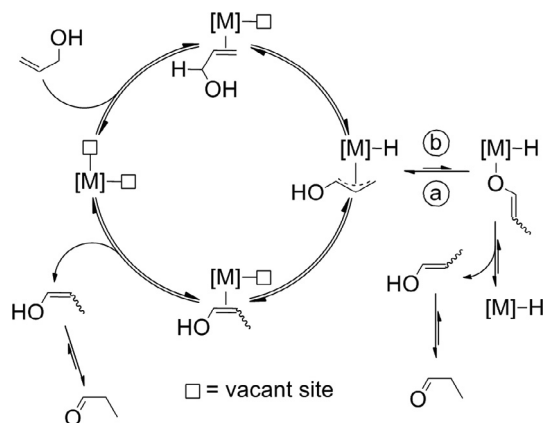
2.1. Metal hydride addition-elimination mechanism

The metal hydride addition-elimination mechanism (a) (Scheme 2) requires a metal-hydride $\text{M}-\text{H}$ species, which can be the starting complex or could be formed in situ from the starting metal complex. The allyl alcohol insertion into the $\text{M}-\text{H}$ bond leads to a metal alkyl intermediate where the alcohol is π -coordinated to the metal. The system evolves to an active secondary σ -hydroxo-alkyl-metal complex that further suffers a β -hydrogen elimination, which leads to the corresponding η^2 -enol-hydride-complex (path a). The intermediate releases the enol giving back the starting hydride catalytic species and the resulting enol tautomerizes into the carbonyl derivative.

On the base of the experimental data, a non-productive alternative step (path b) was also proposed; which involves the formation of a primary σ -alkyl-metal complex by a β -hydrogen elimination [26].

2.2. π -Allyl metal hydride

The π -allyl metal hydride or also named η^3 -allyl mechanism starts with the η^2 -complexation of the allylic alcohol on the metal, which does not coordinate to a hydride ligand contrasting with previously described alkyl-mechanism (Scheme 3). The migration



Scheme 3. π -Allyl-metal hydride mechanism.

of the hydrogen linked to the carbinol centre onto the metal gives rise to a π -hydroxo-allyl-metal-hydride (path a). Further incorporation of the hydride ligand into hydroxo-allyl ligand leads to a η^2 -enol complex that generates the starting catalytic species and the carbonyl compound through the tautomerization of the previously formed enol. Here again, an alternative associative mechanism could be considered (path b). The [1,3]-hydrogen shift of the hydrogen in α position is possible with a first migration onto the metal, followed by a second migration to the carbon vicinal to the resulting carbonyl, which evolves into an intermediate complex that finally generates the active catalyst and give the transposed product. The metal oxidation state changes by two in some steps of the mechanism; as at some point the oxidation state has to be raised by two, usually is needed a low-valent metal complex as catalyst.

In both possible pathways described above, steric as well as electronic factors are expected to play significant roles in the formation of key intermediates such as the σ -bonded complexes or the π -allyl derivatives. Therefore, such factors could strongly influence the scope and limitation of the isomerization reaction.

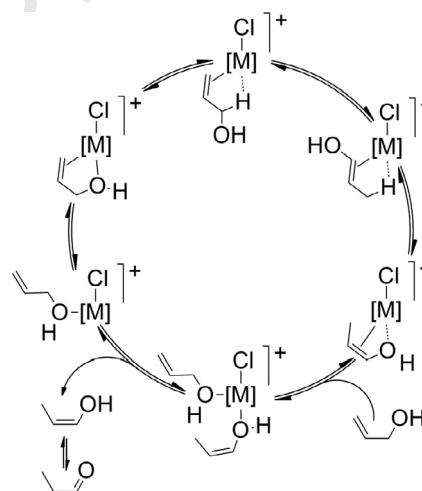
2.3. Mechanism invoking oxygen coordination

In both alkyl and η^3 -allyl mechanisms the alcoholic oxygen does not play any role, thus they cannot explain why some catalysts iso-

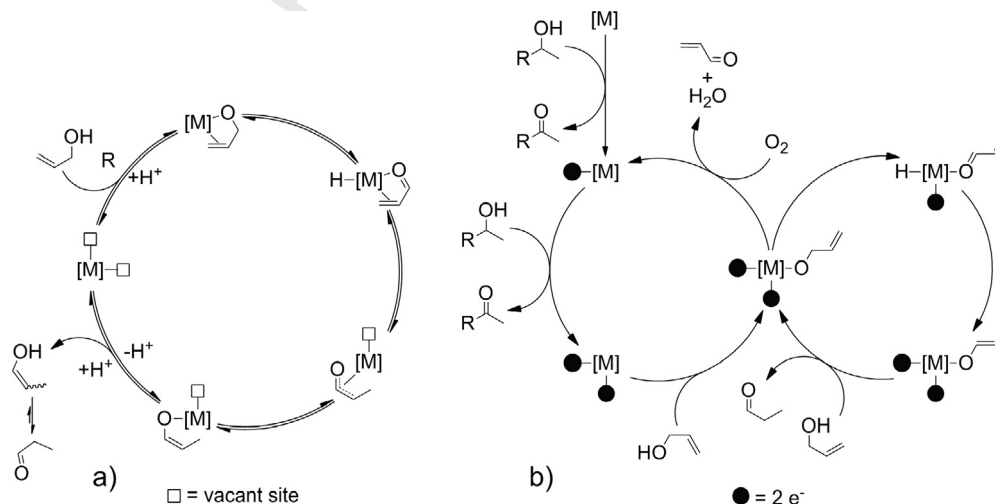
merize allylic alcohols faster than unfunctionalized alkenes [5,30,35] or even display selectivity for allylic alcohols [38,39]. To account for these facts, a third type of mechanism was proposed by Trost and Kulawiec [5].

This “internal-redox” mechanism also named *enone mechanism*, involves the coordination of the allylic alcohol as a bidentate ligand through the O atom and the C=C enol group (Scheme 4). The formed alkoxy complex leads to an active enone-hydride complex by β -hydride elimination. Further hydride migration yields the active π -oxo-allyl-metal species that upon protonation yields the enol (Scheme 4a). There are four important considerations highlighted from this mechanism: (a) it is specifically for allylic alcohol isomerization; (b) an analogous process appears to be operating in the isomerization of allylamines to enamines where the nitrogen atom plays a key role [5,40–43]; (c) the initial formation of an alkoxide (or alcoholate) species is required, which is in agreement with the improvement of the catalytic activity, particularly when a base is added as co-catalyst [11,44] and (d) the hydride migration in this mechanism is similar to that proposed for intermolecular homogeneous transfer hydrogenation.

Therefore a H-transfer from an alcoholate leads to a α,β -unsaturated carbonyl and further hydride addition to the β -



Scheme 5. Isomerisation catalytic cycle in neutral media.



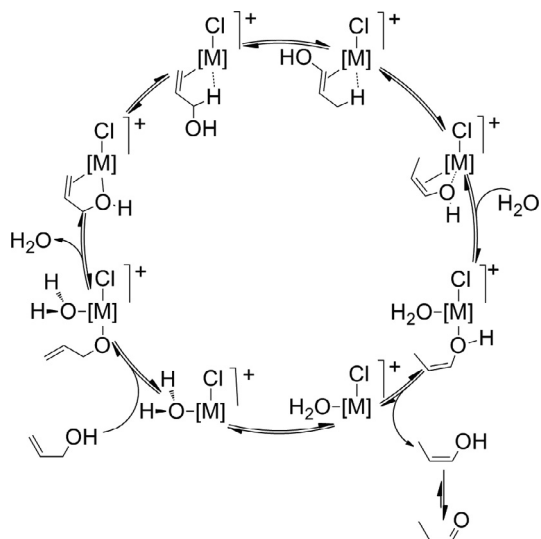
Scheme 4. (a) Proposed allylic alcohol isomerization mechanism invoking oxygen coordination. (b) Alternative mechanism proposed by Markó et al. also invoking oxygen coordination and formation of a metal-hydride.

position (the carbonyl is a much weaker donor than alkoxide), permit quick isomerization and carbonyl releases [11,45,46].

Markó et al. [47] showed that hydrogenation-isomerization products (Scheme 4b) may also be obtained by the aerobic mechanism invoking the "internal redox". Nevertheless, scarce experimental evidence has been provided and all previous attempts to isolate and characterize catalytic intermediates unambiguously, have been unsuccessful [37].

2.4. New approach to enone mechanism

In 2011 Valera-Álvarez, et al. proposed an enone mechanism that involves a cationic alcohol complex as the catalytically active



Scheme 6. Isomerisation catalytic cycle in neutral media involving one water molecule.

species instead of a neutral alkoxy complex [48]. As a feature of the new mechanism, the OH of the allylic alcohol does not undergo deprotonation during the whole cycle and therefore the replacement of the hydrogen atom by other groups should not affect the C=C bond-migration process. This was confirmed by studying the isomerization of allyl ethers to 1-propenyl ethers [25,26]. A somewhat different mechanism was proposed for neutral and basic reaction media.

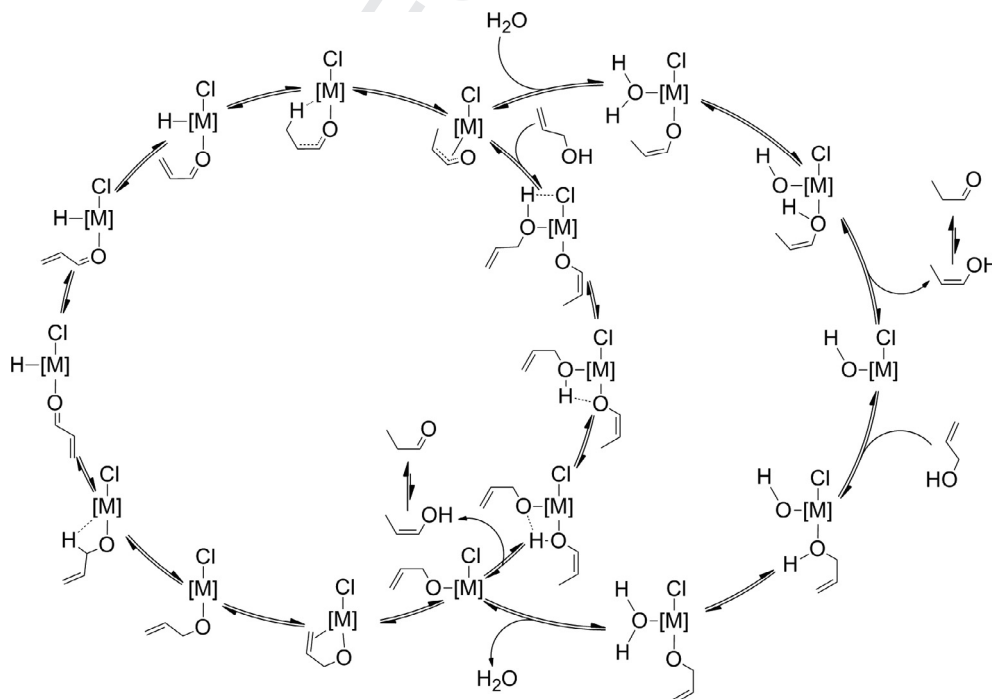
The proposed catalytic cycle under dry neutral conditions (Scheme 5) starts with an allylic alcohol κ -O-complex. The cleavage of the M–O bond and formation of an agostic interaction leads to a species in which both a hydrogen H–COH and the allylic π -bond interact with the metal. Then, the allylic group is transformed into an enol by the breaking and forming of a C–H bond, which further interacts with the metal producing the π -bond shifts from an allylic to an enolic position.

Then, a rotation of the coordinated double bond occurs, giving rise to an enolic oxygen–M bond by cleavage of the agostic interaction. This transformation can also be explained as a hydrogen 1,3-shift that turns the allylic substrate into an enol.

The starting complex is obtained by decoordination of the enol and the coordination of a new allylic substrate. A characteristic of this mechanism, is that both the allylic alcohol and the enol are coordinated by their respective oxygen atoms.

In presence of water the enol decoordination is assisted by a water molecule instead of an allylic alcohol (Scheme 6). Furthermore, the enol is released by the breaking of the Ru–O alcohol bond and the new allylic alcohol molecule which coordinates through its oxygen atom to the metal.

Finally, the starting compound is regenerated by the decoordination of the water molecule and the π -complexation of the allylic double bond. An interesting result obtained from calculations [48], showed that, in neutral aqueous solution, the coordinated water molecule notably lowers the catalytic energy barrier of the process about 7 kcal·mol⁻¹ with respect to what found in dry media.



Scheme 7. Proposed catalytic mechanism for the isomerization of linear allylic alcohols under basic conditions without (left cycle) and with water (right cycle). One molecule of water coordinates the metal and facilitates the catalytic process by exchange of H with the alcohol.

In contrast, in basic medium (Scheme 7) the catalytic reaction is favored in both dry and wet solvent. Another interesting hypothesis is that under basic aqueous conditions, the π -coordinated enolate complex can be coordinated by a water molecule producing the breaking of the π -coordinate enolate ligand and giving rise to a specie with a hydrogen bond between one of the water-OH groups and the oxygen atom of the enolate. The catalytic cycle with water proceeds by coordination of a substrate molecule that transfers a hydrogen atom from the alcohol group to the hydroxyl group and further decoordination of the enol gives rise to the starting species [48].

3. Metal catalysts for allylic alcohols isomerisation in water

Most of the known metals active in isomerisation of allylic alcohols belong to Groups 8 and 9. Among the iron and cobalt triads, ruthenium is the most used metal for isomerization of allylic alcohols, rhodium being the second one and only one example of osmium was found [49,50]. Only some examples of Ni, Pd and Ir complexes have been shown as active catalysts for isomerisation of allylic alcohols in water.

Biphasic catalytic processes in organic and aqueous phases require an accurate experimental control. For example, non-optimized agitation may dramatically affect the yield, reactivity of the catalyst and selectivity of the reaction. In order to avoid most of the problems intrinsic to biphasic reactions and to have standard reaction conditions Bellefon et al. [51,52] have described a new concept to achieve *high throughput screening* (HTS) of polyphasic fluid reactions.

Table 1
Screening of catalysts for the isomerization of 1-hexene-3-ol (TPPTS = tris(m-sulfophenyl)phosphane; BDPPTS = sulfonated (2S,4S)-(–)-2,4-bis(diphenylphosphanyl)pentane; CBDTS = sulfonated (S,S)-1,2-bis(diphenylphosphanyl)methyl)cyclobutane) [51].

| Catalyst | Conversion (%) |
|--|----------------|
| RuCl ₃ /TPPTS | 61 |
| RhCl ₃ /TPPTS | 53 |
| Rh ₂ SO ₄ /TPPTS | 34 |
| [Rh(cod)Cl] ₂ /DPPBTS | 36 |
| [Rh(cod)Cl] ₂ /BDPPTS | 1.5 |
| [Rh(cod)Cl] ₂ /CBDTS | 1.0 |
| [Ni(cod) ₂]/TPPTS | 3.0 |

Under the same controlled biphasic reaction conditions, the isomerization of 1-hexene-3-ol (Table 1) catalyzed by Ru, Rh and Ni complexes showed that: (i) ruthenium and rhodium gave comparable conversions and (ii) the use of nickel, result in a 1,3-transposition of the allylic alcohol hydroxyl group. Additionally, results showed the efficiency of the use of a micromixer coupled to a quite simple setup for discovering new efficient catalytic process, displaying TOF up to 160 h⁻¹ and selectivities up to 94%.

The most important conclusion obtained from the experimental results was to illustrate that two-phase reactions have more advantages than the water monophasic ones: the catalyst separation is easier, the products can be easily isolated from the reaction media, and notably also the final product could depend on the composition of the biphasic system. Therefore, the biphasic reaction systems are more convenient, low costly and eco-benign.

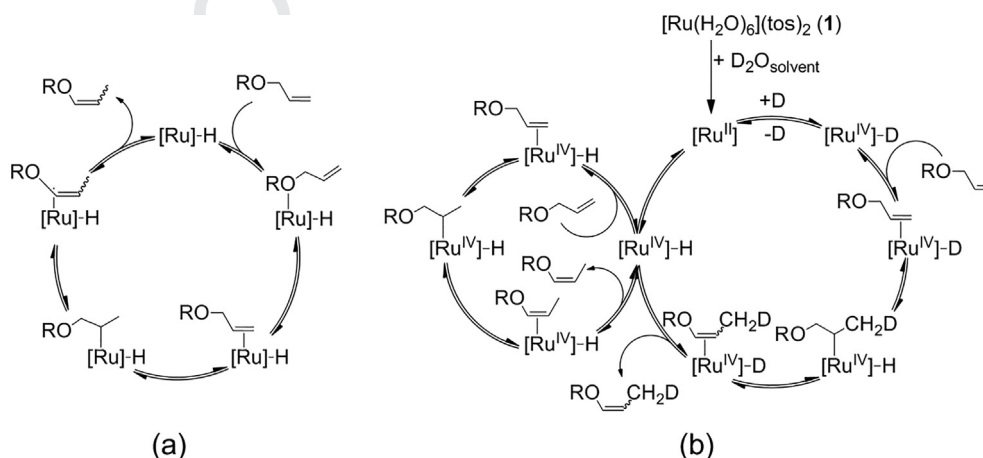
3.1. Catalysts containing ruthenium

Ruthenium exhibits an electronic configuration [Kr]4d⁷5s¹, showing a wide range of oxidation states (from -2 to +8) and coordination geometries in each possible electronic configuration. There is a rich variety of ruthenium complexes characterized by variable oxidation states that are active catalysts for synthesis of organic compounds. Ruthenium complexes are the most numerous metal catalysts for isomerisation of allylic alcohols, particularly Ru(II) and Ru(IV) complexes [49,50].

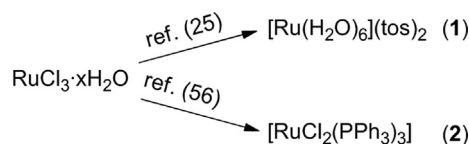
3.1.1. Ru(II) complexes

In the early 1990s, Grubbs et al. [25,26] showed that allylic olefins can be isomerized, although homoallylic alcohols, such as 3-buten-1-ol or 3-penten-1-ol exhibit stability towards isomerization. The complex [Ru(H₂O)₆](tos)₂ (**1**) [25,26,28], was shown to be an efficient catalyst for the isomerisation of allylic ethers in water at room temperature and 45 °C (Scheme 8). An elegant labeling study [26] supported that a possible mechanism of aqueous Ru-catalyzed olefin isomerization involves exclusive [1,3]-hydrogen-shifts through oxygen-directed Markovnikov addition of the [M]-H to the olefin substrate (Scheme 8a). The first step of the process begins when free Ru(II) is oxidized to a [Ru(IV)]-H in a rate-limiting step (Scheme 8b).

The observed regiocontrol of the reaction indicated that the oxygen plays an important role in directing the addition of the metal hydride species. Therefore, the metal-hydride addition-elimination mechanism can display apparent features of a π -allyl-metal hydride mechanism, with the exception of the first



Scheme 8. (a) Metal hydride mechanism proposed for the direct isomerization of allylic alcohols by [Ru(H₂O)₆](tos)₂ (**1**) in water. (b) Catalytic cycle illustration of the initial Ru-deuteride formation from deuterated solvent.



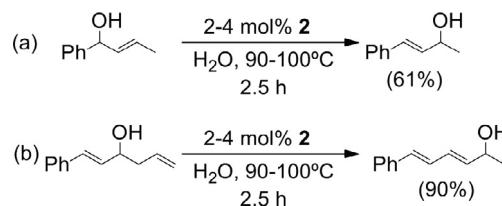
Scheme 9. $\text{RuCl}_3 \cdot \text{H}_2\text{O}$ as starting material for the preparation of some Ru-catalyst for the isomerization of allylic alcohols in water.

[Ru]-H, which was proposed to precede olefin coordination and insertion (*see above*). However, the comparability with the mechanism invoking oxygen coordination [5] raised doubts on the validity of adapting an internal redox mechanism to the aqueous-Ru(II)-systems: non-allylic olefins are isomerized but homo-allylic alcohols exhibit stability towards isomerization [26].

As shown in Scheme 9, $\text{RuCl}_3 \cdot \text{H}_2\text{O}$ can be used as a starting compound for the synthesis of ruthenium complexes, most of them useful in isomerisation of allylic alcohol. Early experiments refluxing $\text{RuCl}_3 \cdot \text{H}_2\text{O}$ in aqueous allyl alcohols gave a mixture of complexes in which Ru(II) species could be identified [6,7]. Georgoulis et al. [53] observed the first chirality transfer in an acyclic system (Scheme 9). The $\text{RuCl}_3 \cdot \text{NaOH}$ reagent is able to differentiate between the two double-bond diastereotopic faces on allylic alcohols. The mechanism is thought to involve a ruthenium-alkoxide intermediate and, just as with an allylic alcohol, isomerization mechanism invoking oxygen coordination mechanism (Scheme 8a), can explain the positive effect of a base (*vide supra*).

The reduction of $\text{RuCl}_3 \cdot \text{H}_2\text{O}$ in presence of triphenylphosphine gives the complex $[\text{RuCl}_2(\text{PPh}_3)_3]$ (2) [54,55] that is an active catalyst for isomerisation of homoallylic alcohol in water [56,57]. The study of the isomerisation reactions provided useful conclusions (Table 2): (i) reactions show a marked dependence on the Ru(II)-substrate ratio; (ii) by changing the amount of the catalyst, a steady decrease of product selectivity was observed e.g. 1-(*p*-tolyl)but-3-en-1-ol (Table 2); (iii) reactions can be carried out under air and is affected by the reaction temperature more than the rearrangement of homoallylic alcohols (Scheme 10a); (iv) when a substrate is constituted by both an allylic and a homo-allylic functional group, the reaction is caused exclusively by the homo-allylic group to give the conjugated dienol product (Scheme 10b).

Two mechanisms were proposed (Scheme 11) for the homo-allylic alcohol isomerization catalyzed by 2 in water, both including



Scheme 10. Isomerization of phenyl-allylic alcohols catalyzed by $[\text{RuCl}_2(\text{PPh}_3)_3]$ (2) in water and air atmosphere.

a metal-hydride intermediate. It is important to note (Scheme 11b) that the nucleophilic attack of water favors the more stable final product and regenerates the catalyst [49,50,58,59]. The participation of the solvent in the reaction is a reversible process along the entire mechanism, which conditions the final product and yield [4]. Replacement of one of the chlorides in 2 by a hydride leads to a more active catalyst for common isomerization of C=C bonds [56,57].

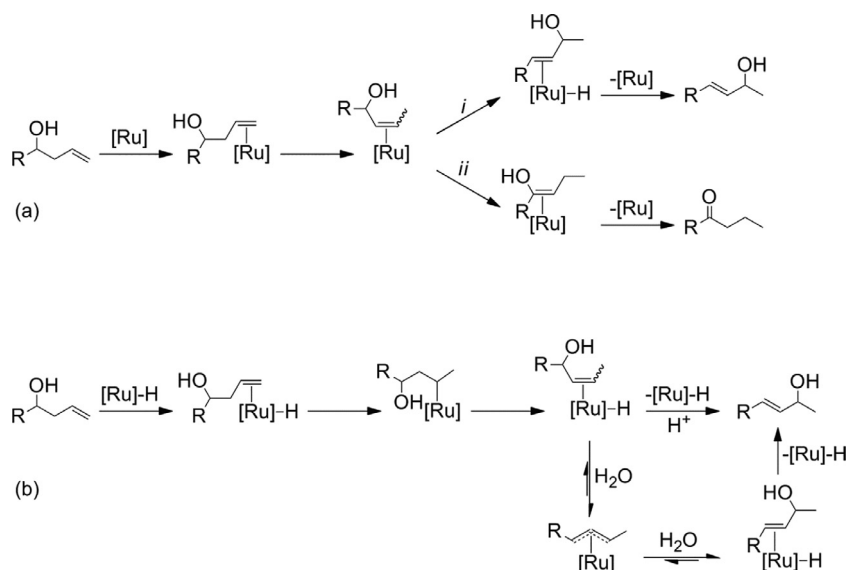
Drent and coworkers [38] reported on the new class of efficient complexes $[\text{Ru}(\text{acac})_3(\text{bipy})(\text{phen})]\text{OTs}$ (acac = acetylacetonate; OTs = *p*-toluene sulfonate) that possess a good activity for intramolecular hydrogen transfer of 3-buten-2-ol to methyl-ethyl-ketone (MEK) in water or water/diglyme (ca. 90% selectivity at 155 °C). In a later study Bouwman et al. [39] showed the feasibility of one-pot synthesis of MEK in water-diglyme at 130 °C. The complex *cis,cis*- $[\text{RuCl}_2(\text{dmsO})_2(\text{phen})]$ (3) (TOF = 260 h^{-1}) catalyzes the direct conversion of 3-buten-2-ol to MEK with over 95% selectivity. The observed activity depends on the substrate tested, and the allyl alcohols bearing the C=C bond in a terminal position are the most reactive (*vide infra*) [60].

As pointed out in the introduction section, the use of metal-complexes in combination with water-soluble ligands in water or biphasic conditions provides a convenient strategy for separating the products from the catalyst. Most of the water soluble complexes are constituted by water soluble phosphine ligands such as mono- and trisulfonated triphenylphosphine (TPPMS and TPPTS, respectively), among others. However, comparatively little work has been carried out on hydrophilic trialkylphosphines $\text{P}(\text{CH}_2\text{OH})_3$, $\text{P}(\text{CH}_2\text{CH}_2\text{CH}_2\text{OH})_3$, $\text{P}(\text{CH}_2\text{CH}_2\text{CN})_3$, the cage-like water-soluble phosphines ligands 1,3,5-triaza-7-phosphaadamantane (PTA) or trihydrazinophosphaadamantane (THPA) and sulfonated amines. The increment of the hydrophilic properties of the water-soluble phosphines usually leads to the improvement of the catalytic properties of their metal complexes [11]. Several interesting contributions to the field have been provided by several groups [10,13,61–67,17–24] in the first decade of the 21st century by using water soluble ligands (Scheme 12).

Some of the ruthenium complexes containing water-soluble phosphines have been found to be highly active for catalyzing the isomerisation of allyl alcohols. In 2006 Joó et al. [63] published the first report on the catalytic activity of the water-soluble *N*-heterocyclic carbene-complexes $[\text{RuCl}_2\text{L}(\eta^6\text{-}p\text{-cymene})]$ (L = 1-butyl-3-methyl-imidazolin-2-ylidene; *p*-cymene = *p*-isopropyltoluene) (4) in aqueous-organic biphasic systems. The ruthenium complex is transformed into the active catalyst that is able to carry out the redox isomerization of 1-octen-3-ol to 3-octanone under relatively mild conditions (0.1 M aqueous phosphate buffer pH = 6.9, $\text{P}(\text{H}_2) = 1$ bar, $T = 80$ °C, $t = 40$ min). The total turnover number for the six consecutive runs was 251. It is important to stress that the yield and reaction product distribution strongly depend on the pH and the chloride concentration in the aqueous phase. If a molecule of PTA is coordinated to the metal, the resulting complex $[\text{RuClL}(\text{PTA})(\eta^6\text{-}p\text{-cymene})]$ (L = 1-butyl-3-methyl-imidazolin-2-ylidene; PTA = 1,3,5-triaza-7-phosphaada-

Table 2
Isomerization of some representative examples of homo-allylic alcohols catalyzed by $[\text{RuCl}_2(\text{PPh}_3)_3]$ (2).

| Homoallylic alcohol | Conditions (°C/h) | Catalyst (mol %) | Conversion (%) | Alcohol/Ketone |
|---------------------|-------------------|------------------|----------------|----------------|
| | 60/7 | 4.0 | no reaction | – |
| | 80–90/2 | 4.0 | 63 | 5.4:1 |
| | 90–100/2.5 | 4.0 | 72 | 13:1 |
| | 90–100/2.5 | 2.2 | 18 | >20:1 |
| | 100–105/3 | 4.0 | 87 | >20:1 |
| | 90–100/1 | 2.2 | 82 | 4.1:1 |
| | 90–100/1 | 4.7 | 91 | 1.2:1 |
| | 90–100/2 | 2.2 | 87 | 12:1 |
| | 90–100/2 | 4.5 | 94 | 4.5:1 |
| | 90–100/2 | 7.0 | 90 | 1.7:1 |
| | 90–100/2 | 10.0 | 92 | 1.2:1 |
| | | | | |



Scheme 11. Isomerization of homo-allylic alcohol (a) and functional group reshuffling in homo-allylic alcohol (b) catalyzed by **2**.

392 mantane) (**5**) catalyzes the same reaction with a conversion of
393 95.6% and a TOF of 135 h^{-1} [61].

394 Another relevant contribution was made by Gimeno et al. [62]
395 that showed that complexes $[\text{RuCl}_2(\eta^6\text{-arene})\{\text{P}(\text{CH}_2\text{OH})_3\}]$ (**6–8**)
396 and $[\text{RuCl}_2(\eta^6\text{-arene})\{\text{P}(\text{CH}_2\text{OH})_3\}]\text{Cl}$, (**9–11**) (arene = C_6H_6 , *p*-cym-
397 ene, C_6Me_6) are efficient catalysts for the isomerization of allylic
398 alcohols in biphasic water/*n*-heptane medium (N_2 atmosphere,
399 75°C , Cs_2CO_3). The TON and TOF values were found to be up to
400 782 and 600 h^{-1} , respectively. The same group reported [13] that
401 the arene-ruthenium(II) complex $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\{\text{P}(\text{OEt})_3\}]$
402 (**12**) catalyzes the isomerization of 1-octen-3-ol in water with
403 quantitative conversion to 3-octenone in 130 min (yield 99%,
404 $\text{TOF} = 46 \text{ h}^{-1}$).

405 The same research team published another highly efficient catal-
406 yst for the isomerisation of 1-octen-3-ol and 1-pent-en-3-ol: the
407 complex $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\{\kappa\text{-}(\text{P})\text{-PPh}_{(3-n)}(\text{OCH}_2\text{NMe}_3)_n\}][\text{SbF}_6]$
408 (**13**) (**13a**: $n = 1$; crystal structure and selected bond distances are
409 summarized in Fig. 1; **13b**: $n = 2$) is a pre-catalyst as it needs to
410 be activated in presence of $^t\text{BuOK}$ in H_2O at 75°C [64]. Under these
411 reaction conditions, the 1-octen-3-ol was quantitatively trans-
412 formed into 3-octenone in 10 min. (**13a**: yield 99%, $\text{TOF} = 594 \text{ h}^{-1}$)
413 whereas for 1-pent-en-3-ol, a quantitative conversion was
414 achieved in 5 min. (**13b**: yield 99%, $\text{TOF} = 1188 \text{ h}^{-1}$).

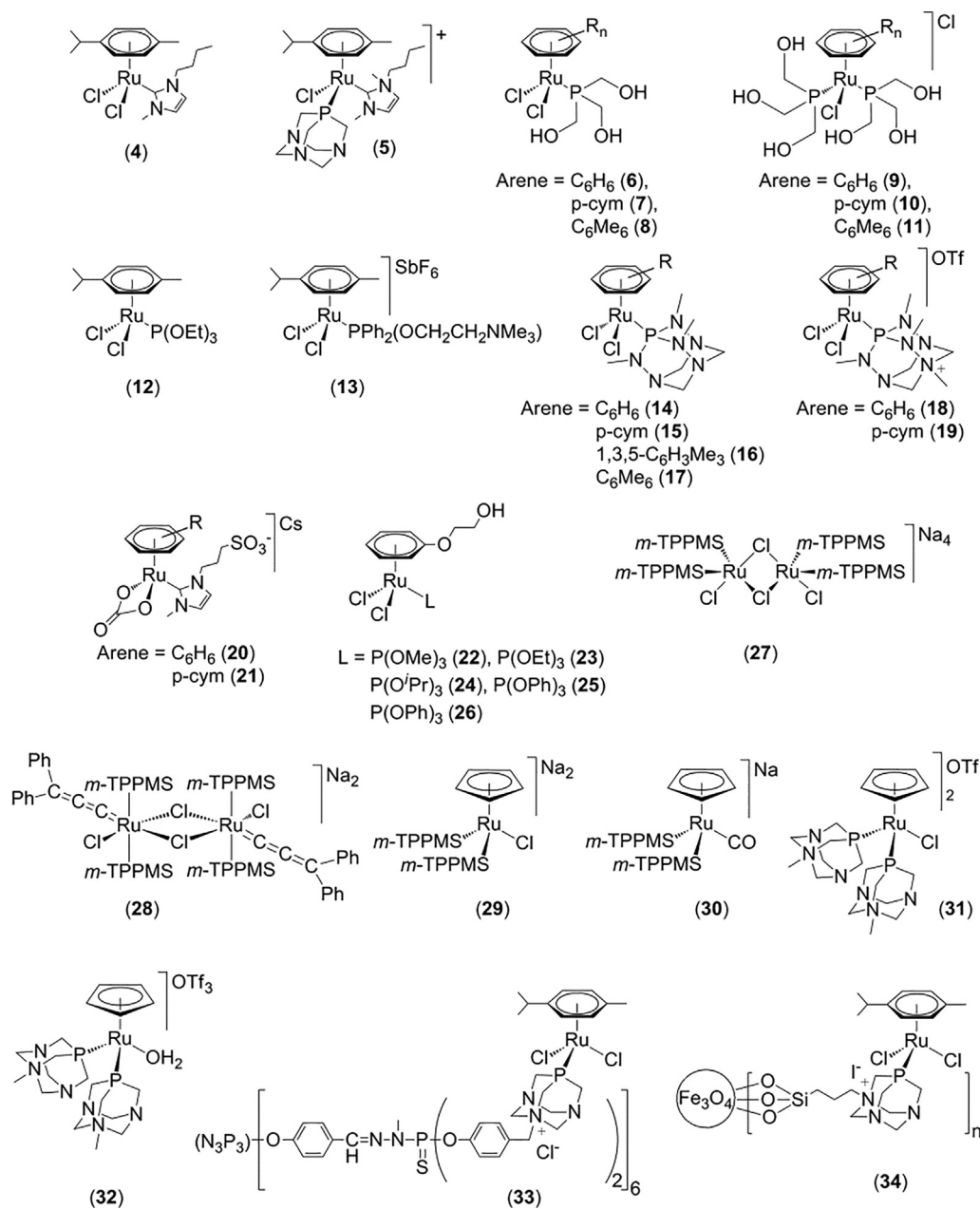
415 Further later, Crochet and co-workers [27] reported that the
416 complexes $[\text{RuCl}_2(\text{THPA})-(\eta^6\text{-arene})]$ (arene = C_6H_6 (**14**), *p*-cymene
417 (**15**), $1,3,5\text{-C}_6\text{H}_3\text{Me}_3$ (**16**), C_6Me_6 (**17**)) (crystal structure and
418 selected bond distances are shown in Fig. 2) and $[\text{RuCl}_2(\text{THPA-}$
419 $\text{Me})-(\eta^6\text{-arene})](\text{OTf})$ (arene = C_6H_6 (**18**), *p*-cymene (**19**)) isomerise
420 quantitatively 1-octen-3-ol to 3-octenone in water and in presence
421 of $^t\text{BuOK}$ in 45–210 min. (yield 99–100%, $\text{TOF} = 132, 99, 50, 29 \text{ h}^{-1}$)
422 and 30–60 min. (yield 99%, $\text{TOF} = 99, 200 \text{ h}^{-1}$), respectively. An
423 interesting result was the fact that the isomerisation rates are
424 strongly dependent on the nature of the arene ligand: **14** (C_6H_6)
425 ($\text{TOF} = 132 \text{ h}^{-1}$) > **15** (*p*-cymene) ($\text{TOF} = 99 \text{ h}^{-1}$) > **17** (C_6Me_6)
426 ($\text{TOF} = 29 \text{ h}^{-1}$). The catalysts remain able to promote the isomer-
427 ization reaction in water (in absence of base), which contrasts with
428 that observed in THF medium.

429 It is interesting to point out that the best isomerisation results
430 were obtained with $[\text{RuCl}_2(\text{THPA-Me})-(\eta^6\text{-C}_6\text{H}_6)](\text{OTf})$ (**18**) that
431 is still able to isomerize quantitatively 1-octen-3-ol into octan-3-
432 one within 7 h during the fourth catalytic run (yield 99%, in pres-
433 ence of $^t\text{BuOK}$). Also, quantitative catalytic isomerisation conver-

434 sion of 1-hepten-3-ol, 1-penten-3-ol and α -vinylbenzyl alcohol
435 was obtained after only 0.75–3.5 h, stressing the convenience of
436 the catalyst process and the how active and efficient can be the iso-
437 merisation reaction in aqueous media.

438 A bit later, Peris et al. [67] reported the two new NHC-water-
439 soluble complexes $\text{Cs}[\text{Ru}(\text{CO}_3)(\eta^6\text{-arene})(\text{NHC})]$, (arene = C_6Me_6
440 (**20**), *p*-cymene (**21**); NHC = *N,N'*-(methyl)(3-sulfonatopropyl)imi-
441 dazolium), which catalyze the isomerization of allylic alcohols in
442 water at 100°C . The novelty of these complexes was the incorpora-
443 tion of sulfonate groups to the hydrophilic NHC ligand. The com-
444 plex $\text{Cs}[\text{Ru}(\text{CO}_3)(\eta^6\text{-}p\text{-cymene})(\text{NHC})]$ (**21**) was found to be far
445 more active than $\text{Cs}[\text{Ru}(\text{CO}_3)(\eta^6\text{-hexamethylbenzene})(\text{NHC})]$ (**20**),
446 which is in agreement with the previously observed behavior of
447 these kinds of compounds. Nevertheless, the main advantage of
448 the use of these complexes is that the isomerization reaction can
449 be carried out in absence of basic co-catalyst, in contrast to the pre-
450 viously mentioned similar catalysts. Another interesting finding of
451 Crochet was the synthesis of $[\text{RuCl}_2(\eta^6\text{-C}_6\text{H}_5\text{OCH}_2\text{CH}_2\text{OH})(\text{L})]$
452 ($\text{L} = \text{P}(\text{OMe})_3$ (**22**) (crystal structure and selected bond distances
453 are displayed in Fig. 3), $\text{P}(\text{OEt})_3$ (**23**), $\text{P}(\text{O}^i\text{Pr})_3$ (**24**), $\text{P}(\text{OPh})_3$ (**25**),
454 PPh_3 (**26**)), which are soluble in water up to 755 g L^{-1} [68]. Com-
455 plexes are active catalysts for isomerization of allylic alcohols into
456 the corresponding ketones in aqueous medium. The best perfor-
457 mances were obtained with derivatives **22–24** (Table 3), being
458 the most activity catalyst reported to date for the isomerization
459 of aromatic or disubstituted substrates in water.

460 Joó and co-workers [65] reported that complexes $\text{Na}_4\{\text{RuCl}(\text{mtp-}$
461 $\text{ppms})_2\}_2$ (**27**), $\text{Na}_4\{\text{RuCl}(\mu\text{-Cl})(\text{C}=\text{C}=\text{CPh}_2)(\text{mtp-ppms})_2\}_2$ (**28**),
462 $\text{Na}_2\{\text{RuClCp}(\text{mtp-ppms})_2\}_2$ (**29**) and $\text{Na}\{\text{Ru}(\text{CO})\text{Cp}(\text{mtp-ppms})_2\}$ (**30**)
463 are active catalysts for the isomerization of allylic alcohols in water
464 (TOF up to 2226 h^{-1}). The catalytic activity of the four complexes
465 against several alk-1-en-3-ols was studied vs. the pH by using
466 0.1 M phosphate buffer, under an air and inert atmosphere and
467 in the temperature range of $50\text{--}80^\circ\text{C}$. However, some of them
468 are only active in presence of dihydrogen [62,63,65]. With the
469 aim of obtaining more soluble in water and cheap catalysts the
470 new complexes $[\text{RuClCp}(\text{mPTA})_2](\text{CF}_3\text{SO}_3)_2$ (**31**) and $[\text{RuCp}$
471 $(\text{mPTA})_2(\text{H}_2\text{O}-\kappa\text{O})](\text{CF}_3\text{SO}_3)_3$ (**32**) were synthesized, which showed
472 to be catalytically active for the redox isomerization of alk-1-en-3-
473 ols to the corresponding ketones in aqueous solutions and
474 aqueous-organic biphasic at 80°C [66]. Of these, compound **32** is
475 the more active (initial TOF of 162 vs. 9.6 h^{-1} for **32**) and shows



Scheme 12. Water soluble Ru complexes.

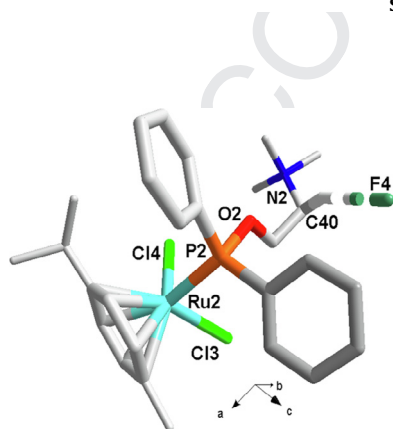


Fig. 1. Crystal structure of the complex unit of [RuCl₂(η⁶-p-cymene){k-(P)-PPh₂(OCH₂CH₂NMe₃)][SbF₆] (**13a**): monoclinic (P21/n); Ru2-P2 318(8) Å; Ru2-Cl3 2.420(6) Å; Ru2-Cl4 2.413(8) Å; Ru-pCym_{centroid} 1.714(2) Å; C39-H39B...F4 3.409(4) Å. Adapted from Ref. [64].

a sharp maximum of activity in water at pH = 4.75 by phosphate buffer. Interestingly, the derivative **32** displays a catalytic activity largely diminished in presence of phosphate buffer that decreased monotonously with increasing pH value. The study by NMR of the isomerisation reaction catalyzed by both complexes showed that components of phosphate buffer, H₂PO₄ and HPO₄²⁻ strongly interact with the ionic complex species {RuClCp(mPTA)₂}²⁺ and {RuCp(mPTA)₂(H₂O-κO)}³⁺. These results unambiguously show that the phosphate buffer is not innocent, as interacts with the catalytically active metal centre and can therefore strongly influence the catalytic properties of **31** and **32**.

A step forward was the syntheses of Ru-arene-PTA complexes like **33**, that were used by Servin et al. as ending groups on dendrimers [19,69]. The catalytic isomerization of 1-octen-3-ol into octan-3-one is carried out under vigorous stirring using 1 mol% of Ru-catalysts and 2% of Cs₂CO₃, as co-catalyst, in a mixture of water-heptane (1:1) at 75 °C.

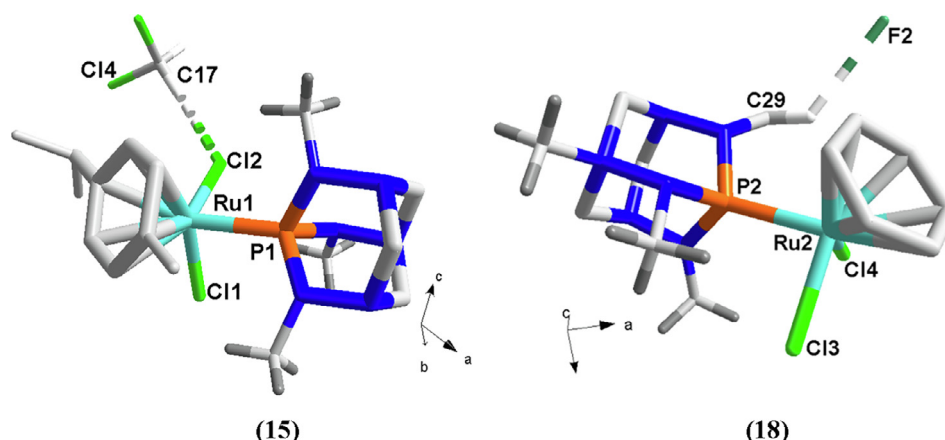


Fig. 2. Asymmetric units of the crystal structures of: $[\text{RuCl}_2(\text{THPA})(\eta^6\text{-}p\text{-cymene})\text{-CH}_2\text{Cl}_2$ (**15**): monoclinic (C12/c1); Ru2-P1 2.294(2) Å; Ru2-Cl1 2.412(2) Å, Ru2-Cl2 2.411(2) Å; Ru-*p*Cym_{centroid} 1.721(5) Å; C17-H17B...Cl2 3.751(5) Å; $[\text{RuCl}_2(\text{THPA-Me})(\eta^6\text{-C}_6\text{H}_6)\text{-OTf}$ (**18**): monoclinic (P121/c1); Ru2-P2 2.283(2) Å; Ru2-Cl3 2.400(2) Å, Ru2-Cl4 2.404(2) Å; Ru-Benzene_{centroid} 1.716(6) Å; C29-H293...F2 3.328(4) Å. Adapted from Ref. [27].

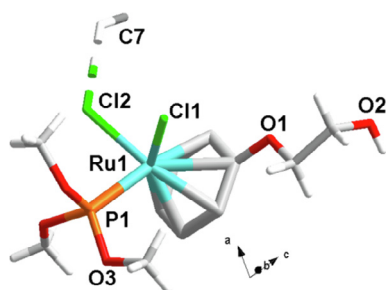


Fig. 3. Asymmetric unit of the crystal structure of: $[\text{RuCl}_2(\eta^6\text{-C}_6\text{H}_5\text{OCH}_2\text{CH}_2\text{OH})(\text{P}(\text{OMe})_3)]$ (**22**): triclinic (P-1); Ru1-P1 2.295(2) Å; Ru1-Cl1 2.414(2) Å, Ru1-Cl2 2.403(1) Å; Ru-Arene_{centroid} 1.729(0) Å; C7-H7A...Cl2 3.570(5) Å. Adapted from Ref. [68].

It is important to note that no reaction occurs in the absence of water. At the end of the reaction, a phase separation allowed an efficient recycling of the catalyst up to 4 runs. Interestingly a positive dendritic effect was clearly evident for this kind of reaction as the conversion increased from the monomer (38%) to the third generation (98%) under the same conditions. Finally, the nanoRAPTA catalyst complex **34** was obtained for the first time on an inorganic solid [70]. The resulting silica-coated ferrite nanoparticles are a magnetic, very efficient catalysts for redox isomerization of allylic alcohols. In line with the behavior of ruthenium (and rhodium) catalysts, a strong dependence on the substitution pattern of the carbon-carbon double bond was observed (TOF up to 253 h⁻¹ for aliphatic alcohols and up to 7 h⁻¹ for aromatic and di-substituted). Nevertheless, there are examples of $[\text{Ru}^{\text{II}}]$ containing nanoparticles that can isomerise even tri-substituted allylic alcohols such as 3-methyl-2-buten-1-ol into 3-methylbutanal (TOF of 4 h⁻¹, yield 92%), which is a challenging task, particularly in aqueous medium [13,61–67].

Later, two interesting dimethylbipyridine ruthenium complexes (Scheme 13) were published, which showed to be active catalysts for both redox isomerization of allylic alcohols and transfer hydrogenation of ketones [71].

These complexes are examples of the catalytic versatility of ruthenium complexes. The dichloro-bipy ruthenium complex **35** is highly efficient for the isomerization of 3-buten-2-ol in organic solvents but in water showed low activity (*t* = 4 h, *T* = 90 °C, 72%) and KOH was needed as base. Complex **36**, which contains the Me-bipy ligand, shows reverse catalytic activity for the redox isomerization and hydrogen transfer only in organic solvents.

A new approach showed as subtle differences in the electronic density on the metal produced by phosphanylferrocenecarboxamide ligands Ph₂P-fc-CONHCH_(3-n)-CH₂OH_(n) (fc = ferrocene-1,1'-diyl, *n* = 1–3) can be used to tune the abilities of the ruthenium complexes **37–45** (Scheme 14), for the isomerization of allylic alcohols [72]. The structures of, **43-CH**-Cl₂, and **44-Et**-O were determined by single-crystal X-ray diffraction (crystal structure of **43** and selected bond length are reported in Fig. 4), and show a packing by supramolecular assemblies by means of hydrogen-bond interactions between their polar hydroxyamide pendants.

Complex **40** is active in water (1,3-diphenylallyl alcohol, *t* = 20 h, 100% conversion, but lower conversions of 30 to 5% for other substrates) but particularly in 1,2-dichloroethane (Table 4), whereas for those bearing substituents at the double bond mainly in α position to the OH group, lower conversions and selectivity were achieved.

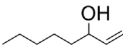

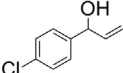
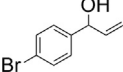
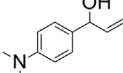
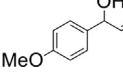
Other interesting complexes were obtained by reaction of *cis*- $[\text{RuCl}_2(\text{dmsO})_4]$ with PTA, mPTA (N-methyl-PTA) and BnPTA (N-benzyl-PTA) leading to the synthesis of complexes $[\text{RuCl}_2(\text{dmsO})_2(\text{-PTA})_2]$ (**46**) and $\{\text{RuCl}_2(\text{dmsO})_2(\text{L})_2\}^{2+}$ (L = mPTA (**47**) and BnPTA (**48**)) (Scheme 15) [73]. Compounds **46**, **47** and **48** were the first complexes with $\text{RuCl}_2\text{P}_2\text{S}_2$ coordination containing monodentate ligands to be crystallographically characterized.

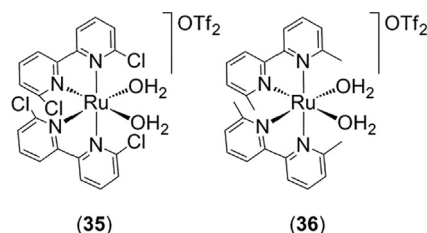
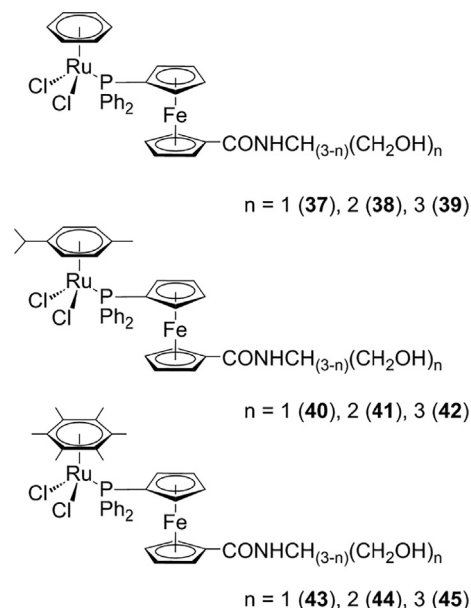
The crystal structure (crystal structure for **46** and **48**, selected distances are presented in Fig. 5) showed as the PRuP angles in these *trans*-bisphosphane complexes significantly deviate from 180° (161° in **46**, 168° in **47** and 165° in **48**). Complexes **46**, **47** and **48** were less active under mild conditions than the starting complex *cis*- $[\text{RuCl}_2(\text{dmsO})_4]$ for the transformation of allylic alcohols into the corresponding ketones, nevertheless with 100% selectivity.

New interesting Ru(II) complexes with guanidinate ligands are $[\text{RuCl}(\kappa^2\text{N,N'-C}(\text{NR})(\text{N}^i\text{Pr})\text{NH}^i\text{Pr})(\eta^6\text{-}p\text{-cymene})]$ (R = *i*Pr (**51**), 4-C₆H₄tBu (**52**), 4-C₆H₄Br (**53**), 4-C₆H₂Me₃ (**54**), 4-C₆H₄^{*i*}Pr₂ (**55**)), which were used for the redox isomerization of allylic alcohols (Scheme 16) [74]. These complexes are very active catalysts for the isomerization of allylic alcohols in the absence of base, unlike the majority of ruthenium catalysts previously described for this catalytic transformation, and have been the first ruthenium guanidinate species to be used as catalysts. Nevertheless, the achieved activity in water was lower than that observed in organic solvents (Table 5).

Compounds **52–55** represent the first examples of ruthenium complexes containing asymmetrical monoanionic guanidinate

Table 3
Isomerization of allylic alcohols in water catalyzed by complexes **22–26**.^a Data adapted from [68].

| Substrate | Entry | Catalyst [L] | Time [min] | Yield [%] | TOF [h ⁻¹] ^b |
|---|-------|--|------------|-----------|-------------------------------------|
|  | 1 | 22 [P(OMe) ₃] | 15 | 99 | 400 |
| | 2 | 23 [P(OEt) ₃] | 15 | 99 | 400 |
| | 3 | 24 [P(O ⁱ Pr) ₃] | 5 | 99 | 1200 |
| | 4 | 25 [P(OPh) ₃] | 40 | 99 | 150 |
| | 5 | 26 [PPh ₃] | 30 | 96 | 192 |
|  | 6 | 22 [P(OMe) ₃] | 10 | 99 | 600 |
| | 7 | 23 [P(OEt) ₃] | 15 | 99 | 400 |
| | 8 | 24 [P(O ⁱ Pr) ₃] | 10 | 99 | 600 |
| | 9 | 25 [P(OPh) ₃] | 60 | 96 | 96 |
| | 10 | 26 [PPh ₃] | 60 | 99 | 100 |
|  | 11 | 22 [P(OMe) ₃] | 20 | 98 | 294 |
| | 12 | 23 [P(OEt) ₃] | 30 | 97 | 194 |
| | 13 | 24 [P(O ⁱ Pr) ₃] | 30 | 98 | 196 |
| | 14 | 25 [P(OPh) ₃] | 22 h | 78 | 4 |
| | 15 | 26 [PPh ₃] | 45 | 90 | 120 |
|  | 16 | 22 [P(OMe) ₃] | 15 | 97 | 380 |
| | 17 | 23 [P(OEt) ₃] | 25 | 96 | 230 |
| | 18 | 24 [P(O ⁱ Pr) ₃] | 45 | 99 | 132 |
| | 19 | 25 [P(OPh) ₃] | 25 h | 84 | 3 |
| | 20 | 26 [PPh ₃] | 17 h | 93 | 5 |
|  | 21 | 22 [P(OMe) ₃] | 15 | 99 | 400 |
| | 22 | 23 [P(OEt) ₃] | 15 | 99 | 400 |
| | 23 | 24 [P(O ⁱ Pr) ₃] | 30 | 99 | 200 |
| | 24 | 25 [P(OPh) ₃] | 6 h | 99 | 17 |
| | 25 | 26 [PPh ₃] | 60 | 99 | 100 |
|  | 26 | 22 [P(OMe) ₃] | 10 | 97 | 582 |
| | 27 | 23 [P(OEt) ₃] | 15 | 99 | 400 |
| | 28 | 24 [P(O ⁱ Pr) ₃] | 15 | 99 | 400 |
| | 29 | 25 [P(OPh) ₃] | 24 h | 79 | 3 |
| | 30 | 26 [PPh ₃] | 24 h | 82 | 3 |

^c Turnover frequency [(mol product/mol Ru)/time].^a Reaction carried out at 75 °C using 4 mmol of appropriate allylic alcohols, 1 mol% of catalyst, 5 mol % of KO-*t*-Bu and 20 mL of water.^b GC determined.**Scheme 13.** Structures of complexes **35** and **36**.**Scheme 14.** Structures of complexes **37–45**.

crystallographically characterized (crystal structure and selected bond lengths for **52** are displayed in Fig. 6).

Other examples of catalysts for the isomerization of allylic alcohols in water are [Ru(η^6 -arene)Cl₂(3,5-dimethylpyrazole)] (arene = C₆H₆ (**56**), *p*-cymene (**57**), C₆Me₆ (**58**), crystal structure and most significant bond distances are indicated in Fig. 23) (Scheme 17) [75]. These complexes were less active than the Ru (IV) complexes presented in the same paper (which will be discussed later), but anyways showed interesting activity for the isomerization of 1-octen-3-ol into octan-3-one in water (TOF = 96–250 h⁻¹), which is in agreement with the scarce influence of the pyrazole-based ligands on the catalytic efficiency.

A step ahead in the family of Ru(II)-arene complexes was the synthesis of [RuCl₂(η^6 -arene)(mPPTA)]Cl (arene = C₆H₆ (**59**), *p*-cymene (**60**), 1,3,5-C₆H₃Me₃ (**61**), C₆Me₆ (**62**)), which were evaluated as potential catalysts for the redox isomerization of allylic alcohols RCH(OH)CHCH₂ (R = H, aryl, alkyl or heteroaryl group) into the corresponding carbonyl compounds RC(O)CH₂CH₃ in refluxing THF (TOF values up to 800 h⁻¹) [76].

The most active was complex **59**, which needed to be activated with K₂CO₃ (2.5 equiv. per Ru). Activity of complex **59** in water was also evaluated after adsorption onto Montmorillonite K-10 clay in the isomerization of 1-octen-3-ol, but showed lower TOF in comparison with other similar compounds (Table 6).

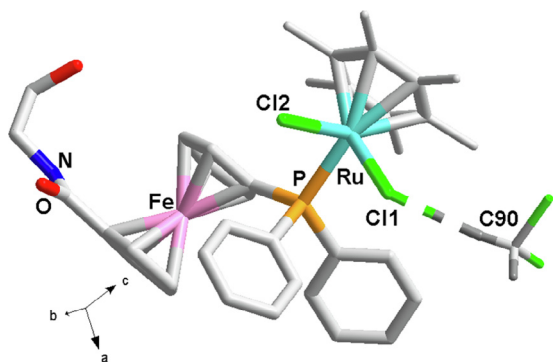


Fig. 4. Asymmetric unit of the crystal structure of $[(\eta^6\text{-C}_6\text{Me}_6)\text{RuCl}_2(\text{L-}\kappa\text{P})\cdot\text{CH}_2\text{Cl}_3$ (**43**): monoclinic (P121/c1); Ru-P 2.344(6) Å; Ru1-Cl1 2.423(6) Å; Ru-Cl2 2.423(6); Ru-Arene_{centroid} 1.723(2) Å; C90-H90B...Cl1 3.618(3) Å. Adapted from Ref. [72].

Table 4

Catalytic results achieved with complex **40** in redox isomerization of various allylic alcohols in water.^a Data adapted from [72]

| Entry | Substrate | NMR yield (%) |
|-------|-----------|---------------|
| 1 | | 17 |
| 2 | | <5 |
| 3 | | <5 |
| 4 | | <5 |
| 5 | | 29 |
| 6 | | 6 |
| 7 | | 100 |

^a Conditions: substrate (1.0 mmol), catalyst **40** (2 mol. %) and KOBu-t (5 mol. %) in water (4 mL) at 80 °C for 20 h. The reaction mixture was extracted with chloroform (2 mL) before analysis. The results are an average of two independent runs.

A new development was achieved with preparation of Ru(II) complexes $[\text{RuX}\{\kappa^2\text{-N,N'-hpp}\}(\eta^6\text{-arene})]$ [arene = *p*-cymene, X

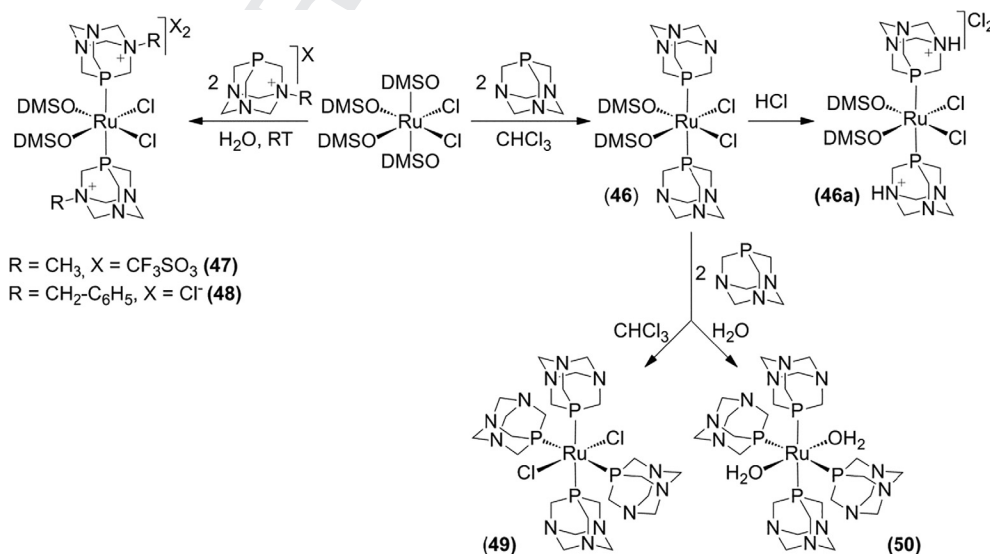
= Cl (**63**, crystal structure, selected distances are presented in Fig. 7), Br (**64**), I (**65**); arene = C₆Me₆, X = Cl (**66**) [77]. The complexes display some activity for the isomerization of 1-octen-3-ol in THF and THF/H₂O, nevertheless were useful for the isomerization of allylbenzene estragole into the industrially relevant 1-propenylbenzene anethole, with a *trans* selectivity of up to 95% (Scheme 18).

A brilliant bottom-up design of a Ru(*p*-cymene) complex was realized by the Kathò research group [78]. The water soluble complex $[\text{RuCl}_2(\text{PTA})(\eta^6\text{-}p\text{-cymene})]$ (**67**) was synthesized and its catalytic activity studied for the transposition in aqueous media of allylic alcohols from 1-propen- to 1-octen-3-ol (TOF from 96 to 396; $n(\text{Ru}) = 10^{-5}$ mol; $[\text{substrate}]/[\text{Ru}] = 200$; $V(\text{substrate}) = 310$ μL; $V(\text{H}_2\text{O}) = 3$ mL; $T = 75$ °C). The isomerization of oct-1-en-3-ol to octan-3-one could be achieved only in buffer solutions at pH >10 or in the presence of alkali metal carbonates. Notably, aqueous solutions containing complex **67** + 2 eq Na₂CO₃ can be reused in the biphasic isomerization of 1-octen-3-ol for at least five times without a significant loss of the catalytic activity. When H₂ is included in the reaction at neutral pH the isomerization of 1-octen-3-ol is accompanied by hydrogenation to octan-3-ol.

When **67** was reacted with CO₃²⁻ the highly active catalyst $[\text{Ru}(\eta^2\text{-CO}_3)(\text{PTA})(\eta^6\text{-}p\text{-cymene})]$ (**68**) was obtained, which shows that the carbonate is required in the reaction for obtaining the real catalytic species and not only as a base, being **68** significantly more active than the prepared in situ **67** + CO₃²⁻ system. The crystal structure of this interesting complex was determined by single crystal X-ray diffraction (crystal structure and selected bond distances are shown in Fig. 8).

Aqueous solutions of **68** are close to neutral pH, so this catalyst can be applied in case of base-sensitive substrates. The authors proposed a mechanism for the reaction (Scheme 19) that includes the formation of the carbonate complex, which is partially substituted by the deprotonated oxygen of the allylic alcohols. The carbonate is totally substituted in the next reaction step leading to the final isomerization of the substrate and to the regeneration of the active species.

Despite of the large amount of PTA-Ru complexes synthesized and used time ago [17] the complexes $[\text{RuClCp}(\text{PTA})_2]$ (**69**) and $[\text{RuClCp}^*(\text{PTA})_2]$ (**69a**) [79] (crystal structure, selected bond lengths are presented in Fig. 9) were never evaluated as catalyst for isomerization of allylic alcohols in water [80].



Scheme 15. Synthesis of Ru(II) complexes containing triazaphosphaadamantanes.

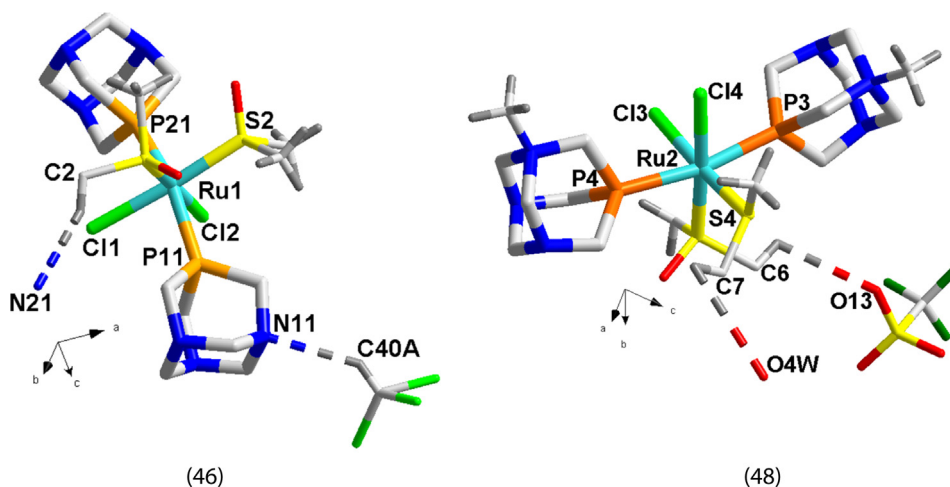
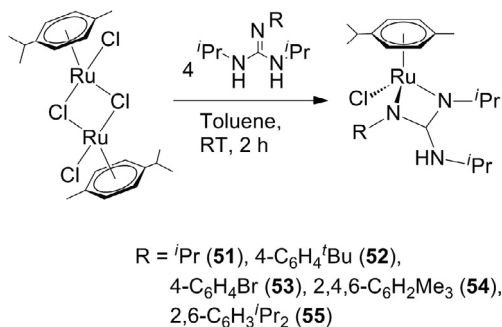


Fig. 5. Asymmetric unit of the crystal structure of: *cis-cis-trans*-[RuCl₂(dmsO)₂(pta)₂].CHCl₃ (**46**): triclinic (P-1); Ru1-P11 2.387(2) Å; Ru2-P21 2.362(2) Å; Ru1-Cl1 2.449(2) Å; Ru1-Cl2 2.429(2); C2-H2A...N21 3.420(9) Å; C40A-H40A...N11 3.464(2) Å. *cis-cis-trans*-[RuCl₂(dmsO)₂(pta-Me)₂].(CF₃SO₃)·H₂O (**48**): triclinic (P-1); Ru2-P3 2.365(3) Å; Ru2-P4 2.377(3) Å; Ru1-Cl3 2.433(3) Å; Ru1-Cl4 2.441(4); C6-H6B...O13 3.251(2) Å; C7-H7B...O4w 3.226(5) Å. Adapted from Ref. [73].



Scheme 16. Synthesis and structure of complexes **51–55**.

Complex **69a** was not soluble enough in water and did not display any particular activity in water under the evaluated reaction conditions. In contrast, complex **69** showed to be an excellent catalyst for the isomerization of linear allylic alcohols at neutral pH.

The catalytic activity of **69** was compared with its protonated derivative [RuClCp(HPTA)₂]₂Cl₂ (**69b**) and DMSO derivative (**69c**) (crystal structure and selected bond lengths are displayed in Fig. 10).

The complex **69** is more active for the isomerization of allylic alcohols in clean water than **69b** under an air atmosphere (91%, t = 2 h), while this trend is the opposite in aqueous phosphate buffer (69%, t = 3 h). This fact was previously observed by the authors for similar complexes [65]. The presence of phosphate in the reaction media diminishes the conversion yield. The complex **69** showed different catalytic activity depending on the size of the isomerized allylic alcohol (Fig. 11).

The experiments carried out with the aim of understanding this behavior showed that the real active catalyst for the reaction is not **69** but the aqua complex {RuCp(H₂O-κO)(PTA)₂}⁺, which is generated spontaneously when **69** is dissolved in clear water by the substitution of the Cl⁻ by a water molecule. The experimental data obtained made possible to propose the coexistence of two catalytic processes with different mechanisms (Scheme 20), both useful for the isomerization of allylic alcohols, which justify that the observed catalytic activity under air that is higher than under N₂, where only one mechanism is active.

To obtain more information on catalytic properties of Cp-piano-stool Ru(II) complexes with PTA derivatives, the complex [RuClCp(HdmoPTA)(PPh₃)](OSO₂CF₃) (**70**) and their dimetallic derivatives [RuClCp(PPh₃)-μ-dmoPTA-1κP:2κ²N,N'-MCl₂] (M = Ni (**71**), Co (**72**), Zn (**73**)) (Scheme 21) were evaluated as catalyst for the isomerization in water under Ar and ambient atmosphere of 1-hexen-3-ol, 1-hepten-3-ol and 1-octen-3-ol, being this later the allylic alcohols more deeply studied [81].

Complex **70** showed to be a more active catalyst for the isomerization of allylic alcohols in water than their derivative dimeric complexes both under air and inert atmosphere. Also, this complex showed better catalytic activity for the isomerization of 1-octen-3-ol than their parent complexes **31** [66], **32** [66] and **69** [79], in phosphate buffer than in water. The possible coexistence of two different catalytic cycles, both useful for the isomerization of allylic alcohols under air but only one of those operating under Ar, could explain the higher catalytic activity observed under air in contrast with that under inert atmosphere. Similarly also, the real possible catalytically active specie was found to be the aqueous complex {Ru(OH₂-κO)Cp(HdmoPTA)(PPh₃)₂}²⁺ (**74**), which is generated in

Table 5
Catalytic isomerization of 1-octen-3-ol into 1-octen-3-one using complexes (**51–53**) as catalysts.^a Data derived from [74].

| Entry | Catalyst | Amn of Ru, mol% | Solvent | Time [min] | Yield [%] ^b | Temp °C |
|-------|-----------|-----------------|--------------------|------------|------------------------|---------|
| 1 | 51 | 1 | THF | 15 | >99 | 80 |
| 2 | 52 | 1 | THF | 15 | >99 | 80 |
| 3 | 53 | 1 | 1,2-Dichloroethane | 20 | 99 | 80 |
| 4 | 53 | 1 | MeOH | 3 h | 52 | 80 |
| 5 | 53 | 1 | H ₂ O | 3 h | 15 | 80 |
| 6 | 53 | 1 | THF | 24 h | 92 | 50 |

^a Reaction performed under N₂ atmosphere using 4 mmol of 1-octen-3-ol (0.2 M solutions).

^b Yields determined by GC.

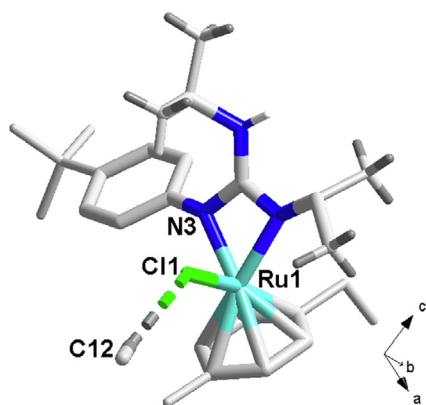
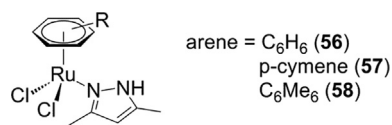


Fig. 6. Asymmetric unit of the crystal structure of $[\text{RuCl}\{\kappa^2\text{N,N}'\text{-C}(\text{N}(4\text{-C}_6\text{H}_4\text{tBu}))(\text{N}^{\text{TPr}})\text{NH}^{\text{TPr}}\}(\eta^6\text{-p-cymene})]$ (**52**): monoclinic ($C2/c$); Ru1-Cl1 2.415(1) Å; Ru1-N3 2.085(3) Å; C12-H12...Cl1 3.510(4) Å. Adapted from Ref. [74].



Scheme 17. Structures of complexes **56–58**.

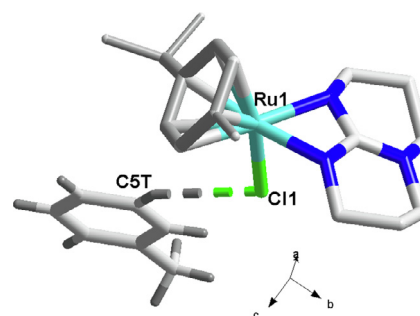
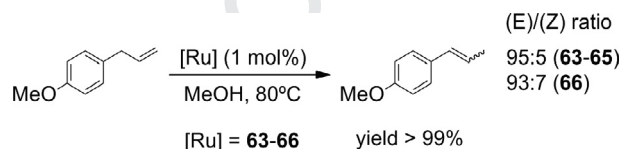


Fig. 7. Asymmetric unit of the crystal structure of $[\text{RuCl}\{\kappa^2\text{-(N,N}'\text{-hpp)}\}(\eta^6\text{-p-cymene})] 1/2\text{C}_7\text{H}_8$ (**63**): monoclinic ($P2_1/c$); Ru1-Cl1 2.421(7) Å; Ru-arene_{centroid} 1.659(4) Å; C5T-H5T...Cl1 3.733(8) Å. Adapted from Ref. [77].



Scheme 18. Isomerization of estragole to anethole catalyzed by **63–66**.

aqueous solution by the substitution of the Cl⁻ by a water molecule anion in **70**.

It was also noticed that dimetallic complexes **71–73** decompose in the catalytic reaction releasing the {MCl₂} (M = Ni, Co, Zn) and Cl⁻, which, in turn, hinders the formation of the catalytically active aqua species and therefore, reducing the catalytic conversion of the substrates.

Going ahead with the aim of determining additional characteristics of the catalytic properties for the isomerization of allylic alcohols of the piano-stool Ru-water derivatives of $[\text{RuClCp}(\text{PTA})_2]$, the complex $[\text{RuCp}(\text{H}_2\text{O}-\kappa\text{O})(\text{PTA})_2](\text{CF}_3\text{SO}_3)$ (**75**), in which the Cl⁻ is substituted by a H₂O molecule (Scheme 22), was synthesized, studied and was fully characterized by single crystal X-ray diffraction (Fig. 12, including selected distances) [82].

Similarly, to **69**, aqueous complex **75** was evaluated for the isomerisation of linear allylic alcohols from 3-buten-2-ol to 1-octen-3-ol under both an inert and air atmosphere, showing to be more active than **69** (Fig. 13). The studies with this complex were not limited to water, but also other solvents such as the substrates themselves, in which **75** is soluble, mixtures of substrate/water, MeOH and mixtures of MeOH/water were used (Fig. 14).

Again, the catalytic isomerization conversion was found to be dependent on the size of the substrate but in this case also a clear dependence on the amount of water in the reaction was observed.

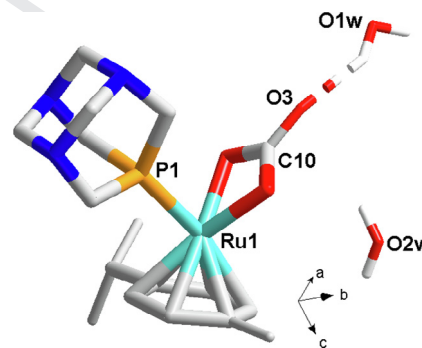


Fig. 8. Asymmetric unit of the crystal structure of $[\text{Ru}(\eta^2\text{-O}_2\text{CO})(\text{pta})(\eta^6\text{-p-cymene})]\cdot 2\text{H}_2\text{O}$: (**68**) orthorhombic ($P2_12_12_1$); Ru1-P1 2.309(5) Å; Ru-arene_{centroid} 1.681(4) Å; O3-H11...O1w 2.763(3) Å. Adapted from Ref. [78].

A threshold of water is needed for obtaining the optimal conversion, and it varies along the series of the terminal, linear allylic alcohols tested (from 3-buten-2-ol to 1-octen-3-ol). Additionally, it was determined that the required amount of water is much larger than that expected to obtain conversion whether water molecules were involved stoichiometrically in the reaction. This fact was not previously evidenced and is not possible to be included

Table 6

Isomerization of 1-Octen-3-ol into 1-Octen-3-one catalyzed by complex $[\text{RuCl}_2(\eta^6\text{-C}_6\text{H}_6)(\text{mPTA})\text{Cl}]$ (**59**) in different solvents.^a Data derived from [76].

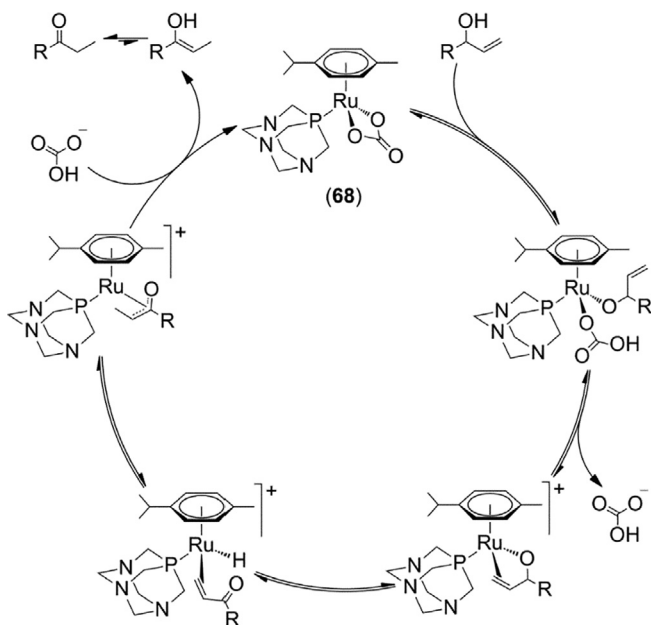
| Entry | Solvent | ϵ^b | Time [min] | Yield [%] ^c | TOF (h ⁻¹) ^d |
|-------|--------------------|--------------|------------|------------------------|-------------------------------------|
| 1 | 1,4-Dioxane | 2.3 | 2 h | 100 | 100 |
| 2 | Toluene | 2.4 | 2.5 h | 100 | 80 |
| 3 | THF | 7.6 | 35 | 100 | 343 |
| 4 | 1,2-Dichloroethane | 10.4 | 45 | 100 | 267 |
| 5 | Ethanol | 24.6 | 1 h | 100 | 200 |
| 6 | Methanol | 32.7 | 1 h | 100 | 200 |
| 7 | Water | 80.1 | 24 h | 100 | 8 |

^a Reaction performed under N₂ atmosphere at 75 °C using 4 mmol of 1-octen-3-ol (1 M in the appropriate solvent), [1-octen-3-ol]:[Ru]:[K₂CO₃] = 100:0.5:1.25.

^b Dielectric constant of the solvent at 25 °C.

^c Yields determined by GC (uncorrected GC areas).

^d Turnover frequencies (mol product/mol Ru)/time) were calculated at the time indicated in each case.



Scheme 19. Suggested mechanism for the redox isomerization of allylic alcohols catalyzed by **68**.

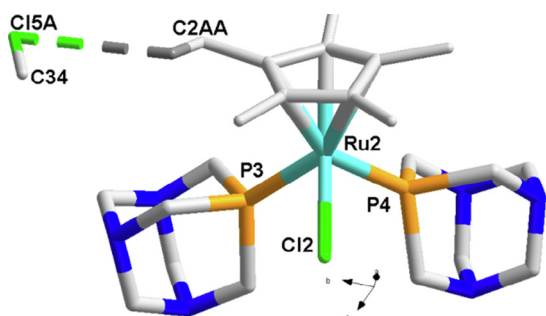


Fig. 9. Asymmetric unit of the crystal structure of $[\text{RuCp}^*(\text{PTA})_2\text{Cl}]$ (**69a**): triclinic (P-1); Ru2-P3 2.284(2) Å; Ru2-P4 2.285(2) Å; Ru1-Cl2 2.465(2) Å; Ru-Cp_{centroid} 1.857(6) Å; C2AA-H2AC...C15A 3.937(6) Å. Adapted from Ref. [79].

easily in previously proposed mechanism for this reaction. Stabilization of reaction intermediates by water looked as key step in the reaction.

With the aim of obtaining information on how water molecules interact with complex $[\text{RuCp}(\text{H}_2\text{O}-\kappa\text{O})(\text{PTA})_2]^+$ this complex and the intermediate formed by reaction with 1-propen-3-ol (**76**) in water were studied by neutron diffraction by using the method published by the Romerosa team previously. It is an atomistic approach for obtaining information about the conformation and dynamics of complex molecules in aqueous solution, which combines experimental techniques (NMR; Fig. 15) and total neutron scattering) and computational approaches (AIMD and EPSR simulations) to obtain detailed microscopic insight into the solvation structure of the observed intermediate species [83].

The obtained results supported that the coordination of allyl alcohol to $[\text{RuCp}(\text{PTA})_2]^+$ occurs in an *exo*- η^2 -C=C-Ru conformation after the substitution of the water ligand on the metal center.

Analysis of the neutron data combined with AIMD simulations indicated that changes in the hydroxyl group orientation of the reactive complex occurs upon solvation. A peculiar directional interaction of the most stable isomer **76a** (Scheme 23) with surrounding water molecules leads to the formation of stable intramolecular chains of water molecules. The formation of water chains is linked to the stabilization of only isomer **76a**. The existence of water chains linked to the intermediate is supported by the strong similarity between the water molecule positions predicted using neutron scattering (Fig. 16A) and the AIMD simulations (Fig. 16B).

Although the overall flexibility of the water chain increases when continuing the simulations at reactive temperature, its motif and substrate conformation are conserved. This differs when the simulation is carried out in methanol, where no hydrogen bond network linking the substrate to the PTA ligand is formed and the substrate conformation changes rotating around the allyl C=C bond, which leads to a potentially less favorable position for isomerization for the alkyl hydrogen atom with respect to the catalytic ruthenium centre.

Finally, the catalytic isomerization of 1-propen-3-ol by $[\text{RuCp}(\text{H}_2\text{O}-\kappa\text{O})(\text{PTA})_2]^+$ in water showed a very low conversion, even at 80 °C (ca. 12%), in contrast with longer linear allylic alcohols described previously. Therefore, the results suggest that the conformation taken by the substrate could be affected by the water environment. The solvation process as a whole (as described by the authors' AIMD simulations on water solutions) is the responsible of the intermediate formed, rather than the coordination or interaction of some water molecules. Consequently, a large number of water molecules is needed around the intermediate to promote the formation of the most reactive intermediate isomer.

As introduced before, the ability of **69** and **75** to catalyze the isomerization of terminal, linear allylic alcohols also are dependent

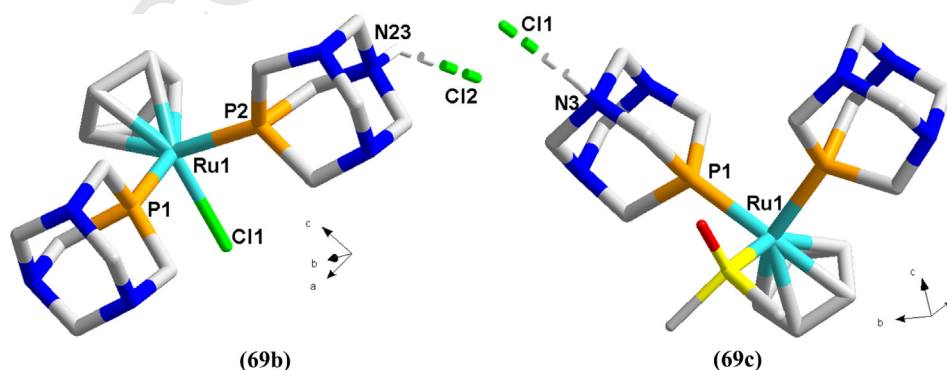


Fig. 10. Asymmetric units of the crystal structures of: $[\text{RuClCp}(\text{HPTA})_2]_2 \cdot 2\text{H}_2\text{O}$ (**69b**): triclinic (P-1); Ru1-P1 2.253(2) Å; Ru1-P2 2.2251(2) Å; Ru1-Cl1 2.462(2) Å; Ru-Cp_{centroid} 1.851(5) Å; N23-H23...Cl2 3.144(7) Å; $[\text{RuCp}(\text{DMSO}-\kappa\text{S})(\text{HPTA})_2]\text{Cl}_3 \cdot 2\text{H}_2\text{O}$ (**69c**): orthorhombic (*Pnma*); Ru1-P1 2.280(8) Å; Ru1-S1 2.260(2) Å; Ru-Cp_{centroid} 1.887(4) Å; N3-H1N...Cl1 3.070(3) Å Adapted from Ref. [80].

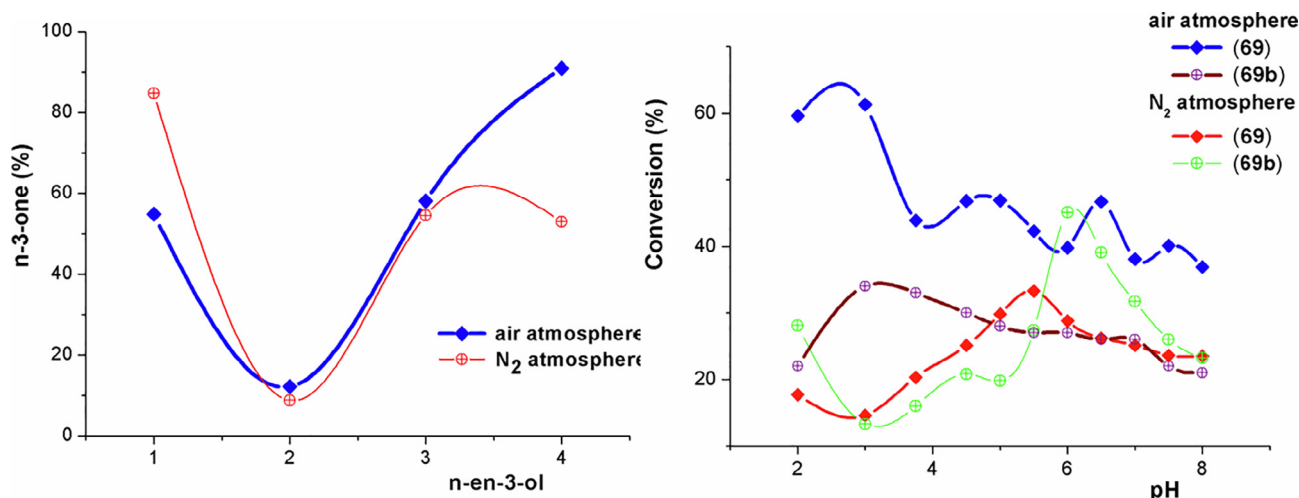
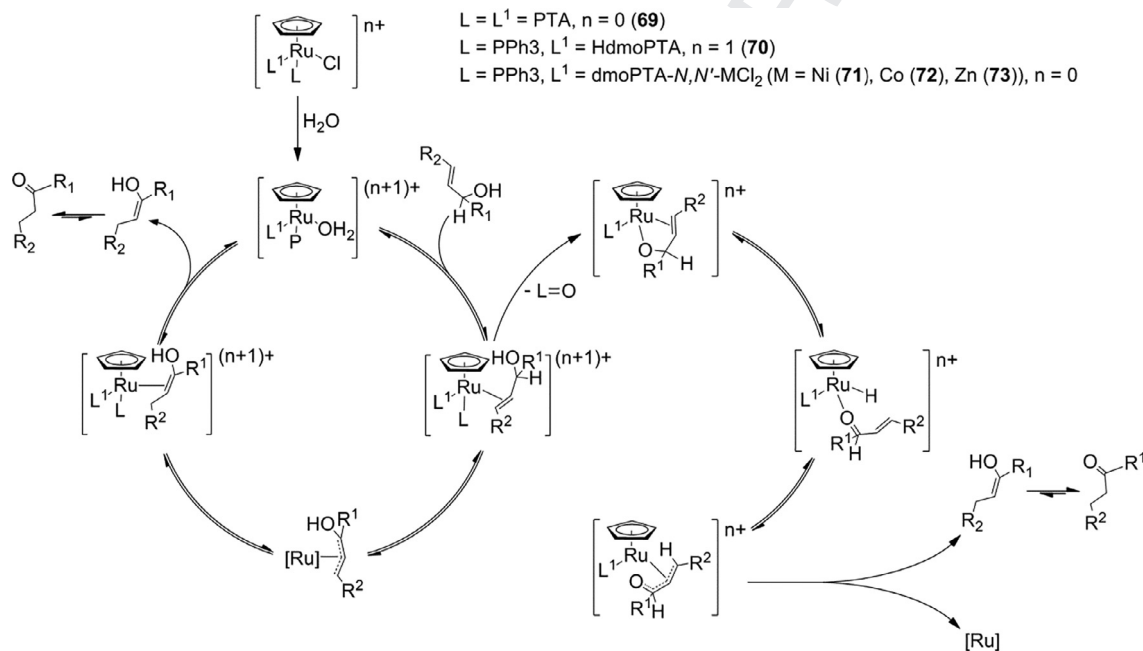
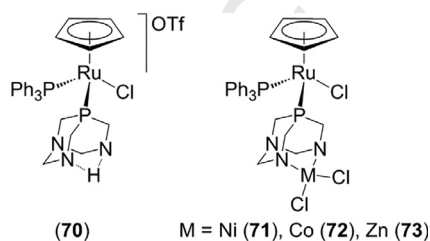


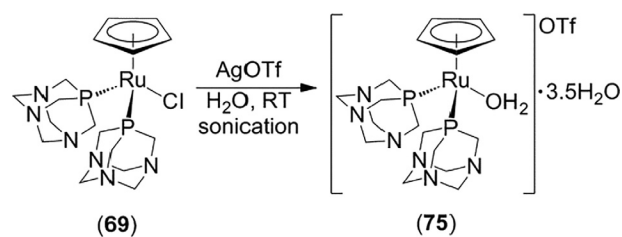
Fig. 11. (left) Isomerization of allylic alcohols ($H_2C=CHOHR$ with $R = CH_3(CH_2)_n$, $n = 1-4$) catalyzed by **69** in water at $80^\circ C$, at 2 h under air (bold line) and N_2 (thin line) atmospheres. (right) Isomerization of 1-octen-3-ol catalyzed by **69** (blue line) and **69b** (red line) vs. pH: 1-octen-3-ol (1.15 mmol), **69** or **69b** (0.015 mmol), 0.1 M aqueous phosphate buffer (5 mL), $80^\circ C$, 2 h, under air- and N_2 atmospheres. Adapted from Ref. [80].



Scheme 20. Proposed mechanism for the isomerization of allylic alcohols catalyzed by Ru(II)-phosphaadamantane complexes in water.



Scheme 21. Structure of complexes **70-73**.



Scheme 22. Synthesis of **75** from **69**.

762 on substrate. For both complexes TON and TOF decreases as the
763 length of alcohol increases, but not linearly: they reach a minimum
764 for 1-hexen-3-ol. The next step performed by the authors was the
765 assessment of **69** and **75** in the isomerization of the rigid allylic

alcohol 2-cyclohexenol into cyclohexanone in water and biphasic
media (Fig. 17) [84]. Unexpectedly, complex **75** showed an excel-
lent catalytic activity for the studied conversion both in water
(TON = 647) and in biphasic of cyclohexene/ H_2O , which allows to

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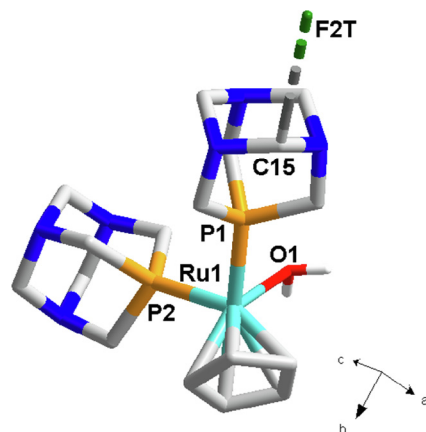


Fig. 12. Crystal structure of the complex unit of $[\text{RuCp}(\text{H}_2\text{O}-\kappa\text{O})(\text{PTA})_2](\text{CF}_3\text{SO}_3) \cdot 3.5\text{H}_2\text{O}$ (**75**): triclinic (P-1); Ru1-P1 2.265(5) Å; Ru1-P2 2.261(4) Å; Ru1-O1 2.177(1) Å; Ru-Cp_{centroid} 1.837(3) Å; C15-H15A...F2T 3.690(3). Adapted from Ref. [82].

recycle the catalyst up to 7 times. (TON = 3420) (Fig. 18). In contrast, but as expected, chloride complex **69** showed a lower but also good activity in water (TON = 95) and in biphasic TON = 100).

The catalytic reaction intermediate $[\text{RuCp}(\text{PTA})_2(\eta^2\text{-C}_6\text{H}_9\text{OH})](\text{CF}_3\text{SO}_3)$ (**77**) was synthesized and spectroscopically characterized by NMR (Fig. 19).

A new surprising result was that both complexes **69** and **75** isomerise 2-cyclo-hexenol also in dry MeOH. Therefore, and in contrast with that observed with linear allylic alcohols, water is

not needed for obtaining the largest isomerization conversion. In this case, the previously described mechanism for the isomerization of linear allylic alcohols (Scheme 20) could be valid.

3.1.2. Ru(IV) complexes

Catalytic isomerization of allylic alcohols into carbonyl compounds in aqueous media catalyzed by Ru(IV)-complexes has scarcely been studied until recent times, being the main contributions provided by Gimeno's Group (Scheme 24) initially and further by Cadierno and Crochet group. The first contributions of these teams to this chemistry were the complexes $[\text{Ru}(\eta^3:\eta^2:\eta^3\text{-C}_{12}\text{H}_{18})\text{Cl}_2]$ ($\text{C}_{12}\text{H}_{18}$ = dodeca-2,6,10-triene-1,12-diyl) (**78**) [85,86], $[\{\text{RuCl}(\mu\text{-Cl})(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\}_2]$ ($\text{C}_{10}\text{H}_{16}$ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (**79**), $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{L})]$ (L = CO (**80**), PR_3 (**81**), CNR (**82**), NCR (**83**)), $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}(\text{NCMe})_2][\text{SbF}_6]$ (**84**) [36] and $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}(\kappa^2\text{O},\text{O}-\text{CH}_3\text{CO}_2)]$ (**85**) [87].

A very active catalyst for redox isomerization of allylic alcohols (TOF of 1500–2000 h^{-1} with Cs_2CO_3 , and 300–2000 h^{-1} without Cs_2CO_3) is obtained from the complex $[\text{Ru}(\eta^3:\eta^2:\eta^3\text{-C}_{12}\text{H}_{18})\text{Cl}_2]$ (**78**) under relatively mild conditions (N_2 atmosphere at 75 °C) in H_2O and 0.2 M of the corresponding allylic alcohol [85,86]. The catalyst can be recycled at least three runs (0.2 M in water, 0.2 mol% and 0.4 mol% of Cs_2CO_3) but shows a strong dependence on the substitution of the carbon-carbon double bond, as observed by other metal catalysts.

Under similar reaction conditions the complex $[\{\text{RuCl}(\mu\text{-Cl})(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\}_2]$ (**79**) showed a similar behavior upon substitution of the allyl alcohol carbon-carbon double bond, leading to TOF values of 1500–2000 h^{-1} with Cs_2CO_3 , and 750–3000 h^{-1}

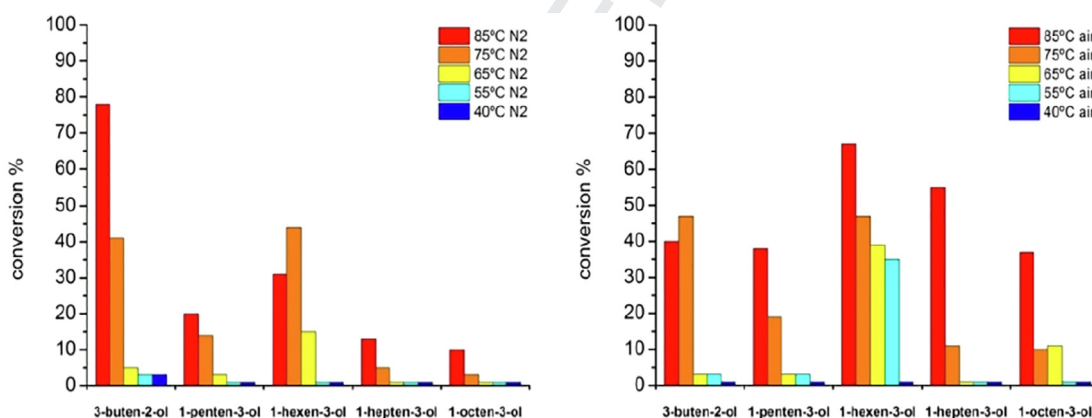


Fig. 13. Selectivity in the conversion (%) in water into the corresponding ketones of an equimolar mixture of allylic alcohols from 3-buten- to 1-octen-3-ol catalyzed by **75** (0.2 mol% against the overall content of alcohols) under N_2 at 40, 55, 65, 75 and 85 °C, at 2 h.

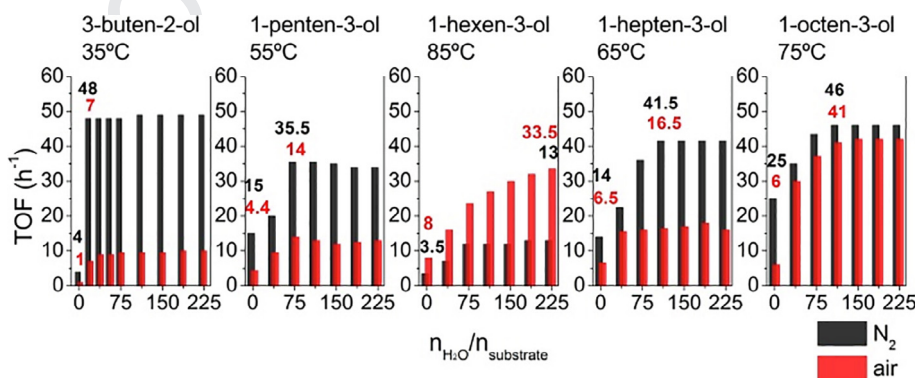


Fig. 14. TOF at 2 h reaction time of the catalytic isomerization of 3-buten-2-ol to 1-octen-3-ol by **75** (1 mol %) vs. molar ratio of water at the lowest temperature which reactions occur.

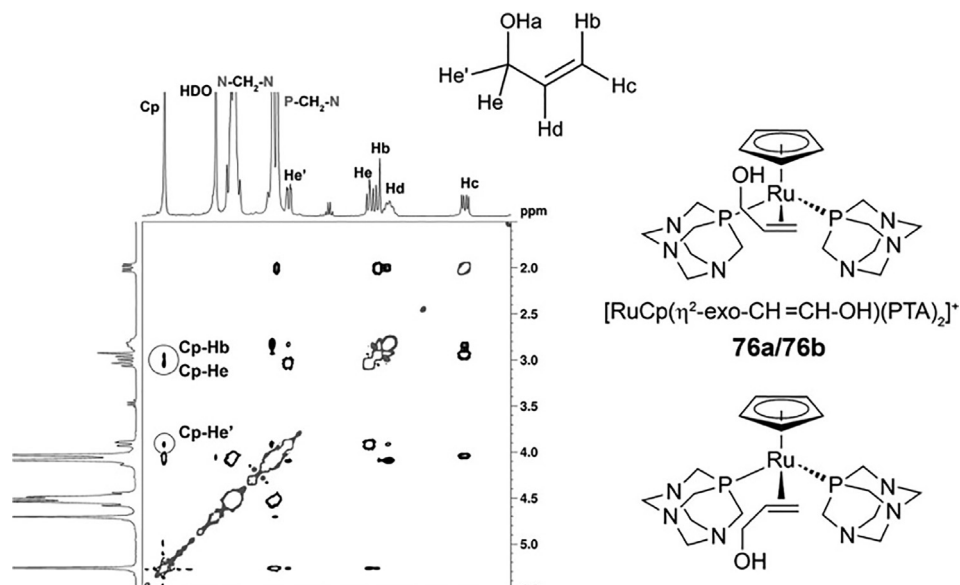
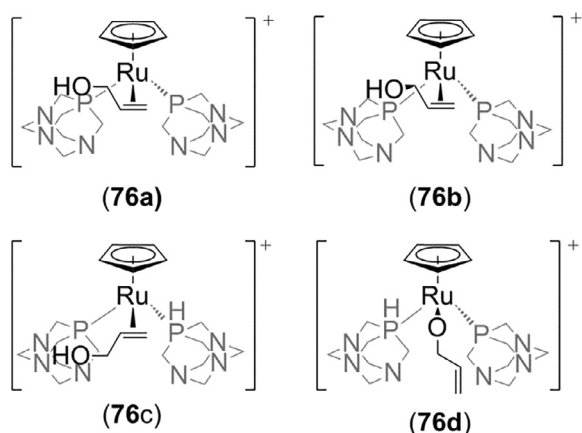


Fig. 15. ¹H-¹H NOESY of **76** in D₂O. Adapted from Ref. [83]



Scheme 23. Calculated minimum structures of **76**.

without Cs₂CO₃. As observed for [Ru(η³:η²:η³-C₁₂H₁₈)Cl₂] (**78**), complex **79** can be recycled four times and is capable of catalyzing the allylic alcohol isomerization, even in the presence of competing conjugated dienes. Both complexes were considered the most active catalysts in aqueous medium reported to date.

Further, the complex [Ru(η³:η³-C₁₀H₁₆)Cl(κ²-N,O-O-CH₃CO₂)] (**85**) was reported as a new highly efficient catalyst in water and ionic liquids (crystal structure and selected bond distances are displayed in Fig. 20). The complex **85** displays a good catalytic activity for the quantitative isomerization of 1-octen-3-ol into 3-octan-3-one under mild conditions (N₂ atmosphere, 20 mL of H₂O, 75 °C, 1 mol%) and, remarkably, at temperature close to room temperature (35 °C, 5 mL H₂O, 1 mol%) in a time as short as 35 min. It is readily recoverable and remains active up to five runs (in 1.5 or 2 h), leading to cumulative TON values of 495 in water and 487 in ionic liquid (BMIM)(BF₄) [87]. The catalytic isomerisation activity of **85** of allyl alcohols different to 1-octen-3-ol is similar to that observed for **78** and **79** (TOF of 710–6000 h⁻¹).

Other interesting compounds are the complexes [Ru(η³:η³-C₁₀H₁₆)Cl₂L] [L = pyrazole (**86**), 3-methylpyrazole (**87**), 3,5-dimethylpyrazole (**88**), 3-methyl-5-phenylpyrazole (**89**), 2-(1H-pyrazol-5-yl)phenol (**90**), 6-azauracile (**91**), and 1H-

indazol-3-ol (**92**) [89]. Complex **90** reacts with NaOH to give rise to the chelated complex [Ru(η³:η³-C₁₀H₁₆)Cl(κ²-N,O-2-(1H-pyrazol-yl)phenoxy)] (**93**). Crystal structures, for example, of **91** (Fig. 21 shows crystal structure and selected bond lengths) confirmed the composition of the complexes.

Diffusion-NMR experiments revealed that **93** is in an equilibrium between monomer and dimer species depending on the temperature, concentration, and coordinating properties of the solvent (Scheme 25). Complex **91** is highly active catalyst for the isomerization of 1-octen-3-ol into octan-3-one, with a catalytic activity that was among the best reported to the publication date and under mild reaction conditions (Table 7).

An interesting system for isomerizing allylic alcohols to α,β-unsaturated alcohols is the complex [Ru(η³:η³-C₁₀H₁₆)Cl₂L] (C₁₀H₁₆ = 2,7-dimethyl octa-2,6-diene-1,8-diyl) (L = imidazole (**94**), benzimidazole (**95**)) and N-methylimidazole (**96**), which were found to be precursors of catalytic species for the redox isomerization of allylic alcohols in pure water [90]. These complexes induce the catalytic isomerization of a wide variety of primary and secondary allylic alcohols into the corresponding carbonyl compounds, being complex **95** (crystal structure, selected bond distances are indicated in Fig. 22) one of the most efficient catalyst reported for the isomerization of 1-octen-3-ol in water (0.02 mol % cat/substrate, 5 min, room temperature; TOF = 60 000 h⁻¹), remaining active up to seven cycles in a biphasic system.

The proposed mechanism involves the interaction of the starting complex with a water molecule to generate the catalytic species (Scheme 26). In the first step of the mechanism the hydride is transferred back to the substrate. A possible inconvenience is that a too acidic water ligand would make difficult the protonation of the hydroxo-ligand during the second half of the process. The donor properties of the N-ligand determine: the acidity of the water ligand, the concentration of the hydroxo active species, and the Lewis acid properties of the ruthenium center, which make it suitable for accepting the hydride [90].

DFT calculations supported that the hydroxo-complexes derived from **94–96** species could be formed in water and that the fact that non-coordinated N–H group of imidazole remains

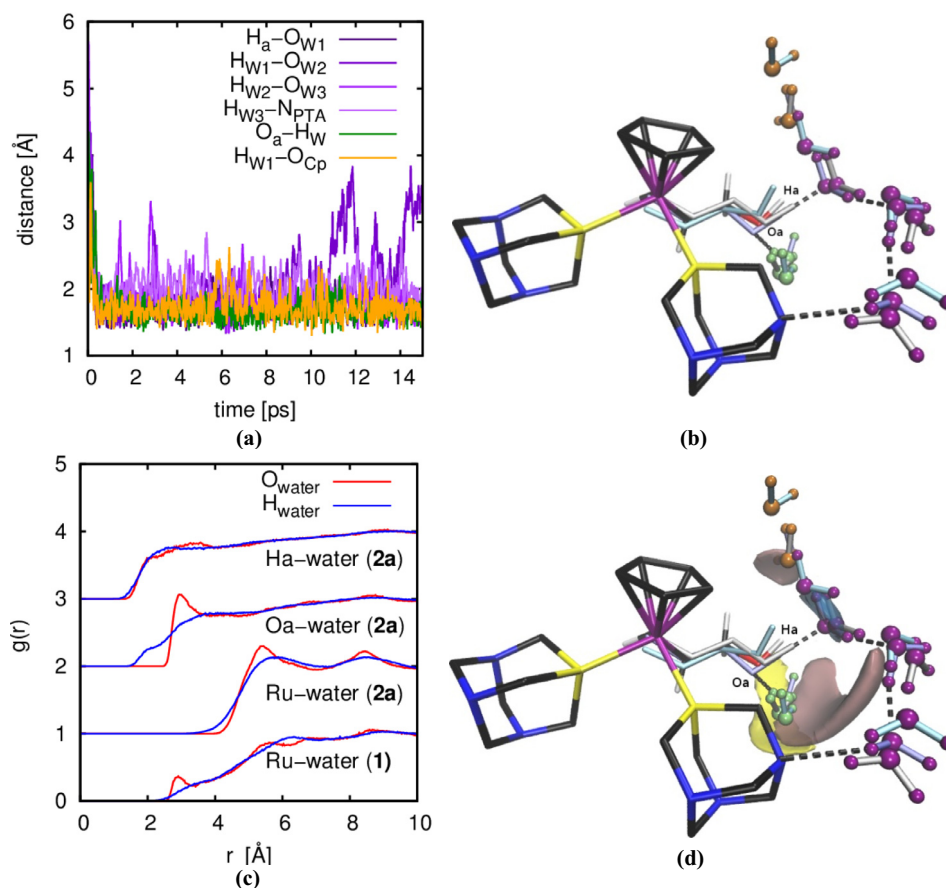


Fig. 16. AIMD and EPSR results for **76a**. (a) Distance evolution during an AIMD simulation for relevant water molecules forming a water chain (purple) and connection to the Cp water network (orange), as well as the water molecule coordinating to the allylic hydroxyl oxygen Oa (green) for **76a**. (b) Overlay of snapshots of **76a** after 6 (violet), 8 (silver) and 10 ps (cyan) including three bridging water molecules (purple spheres), the secondary water coordinating to the Oa (green spheres) and the water molecule linking the water chain to Cp (orange spheres). Comparison of AIMD and results for **76a**. (c) Atom-atom radial distribution function (RDF) for water (O_{water} in red, H_{water} in blue) around the ruthenium atom in catalyst **75** and catalyst with substrate in configuration **76a**. For the latter, also the RDFs for water around the allylic hydroxyl group (Oa, Ha) are shown. (d) Overlay of AIMD snapshots of left panel with EPSR results of right panel. Spatial Density Functions show areas of water probability >50% in the range 1–2 Å (blue), >25% at 2.7–3.5 Å (pink), and >15% at 3.5–4.5 Å (yellow) distance from Ha. Adapted from Ref. [83].

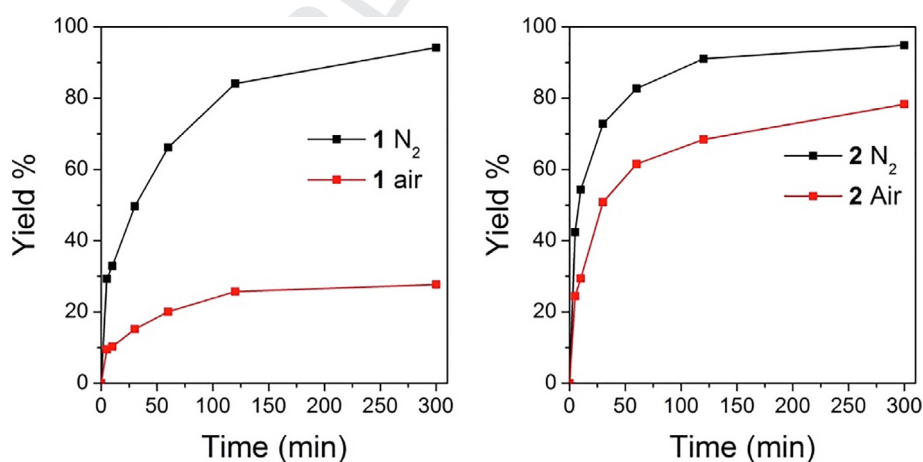


Fig. 17. Conversion of 2-cyclohexenol to cyclohexanone catalyzed by **69** and **75** (H₂O, 70 °C, [Ru] 1 mol%). Yields determined by GC. Adapted from Ref. [84].

unchanged, acting as a spectator ligand during the whole catalytic cycle. The catalytic hydroxo complex acts as the α -N-H groups and participate in the mechanisms of a conventional bifunctional catalysis. Therefore, a water molecule plays the same role than the β -N-H protic group of the 1,3-azole ligands. Nevertheless, β -NH groups

have an important role in the proposed mechanism as they help the catalytic process entails hydrogen transfers to and from the catalyst. The authors propose that a good catalyst for the isomerization of allylic alcohols in water should be able to perform efficiently both hydrogen transfers to and from the catalyst.

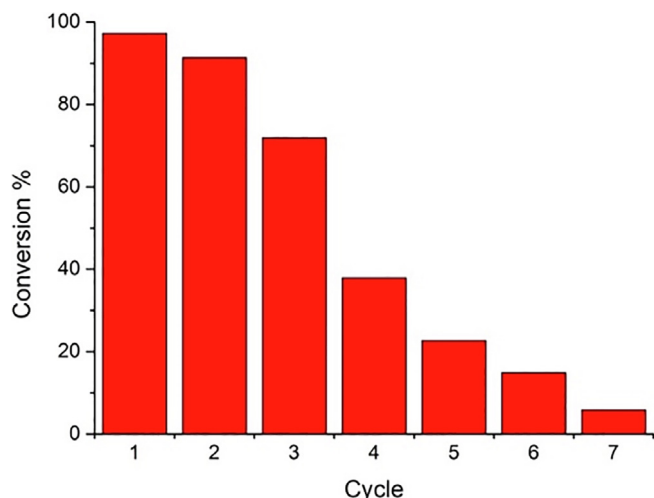


Fig. 18. Isomerization of 2-cyclohexanol catalyzed by **75** in biphase (H₂O/cyclohexane (1:1), at 70 °C, [Ru] 0.1 mol%, 3 h/cycle) in successive recycling runs. Adapted from Ref. [84].

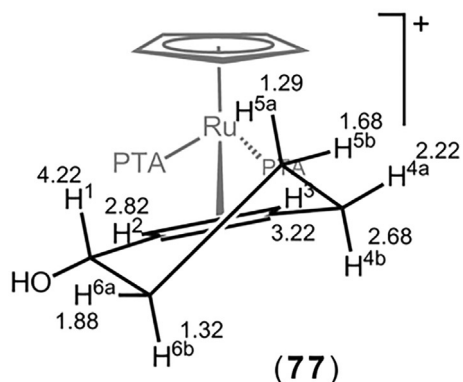
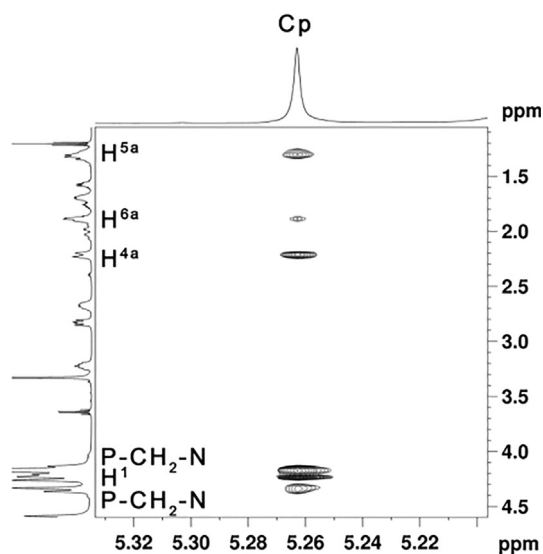
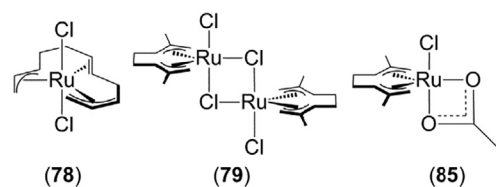


Fig. 19. ROE cross peaks between Cp and H¹, H^{4a}, H^{6a} and H^{5a}. Bottom: proposed structure for **77** containing hydrogen chemical shifts of the 2-cyclohexenol ligand. Adapted from Ref. [84].



Scheme 24. Structures of complexes **78**, **79** and **85**.

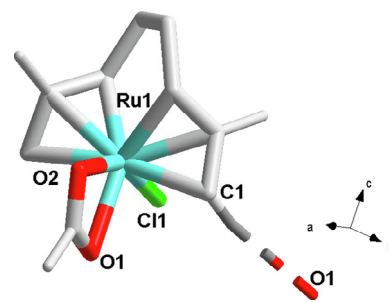


Fig. 20. Asymmetric unit of the crystal structure of [Ru(η^3 : η^3 -C₁₀H₁₆)Cl(κ^2 O,O-CH₃CO₂)] (**85**): orthorhombic (Pbca); Ru1-Cl1 2.386(3) Å; Ru1-O1 2.205(6) Å; Ru1-O2 2.095(7) Å; C1-H2...O1 3.450(2) Å. Adapted from Ref. [87].

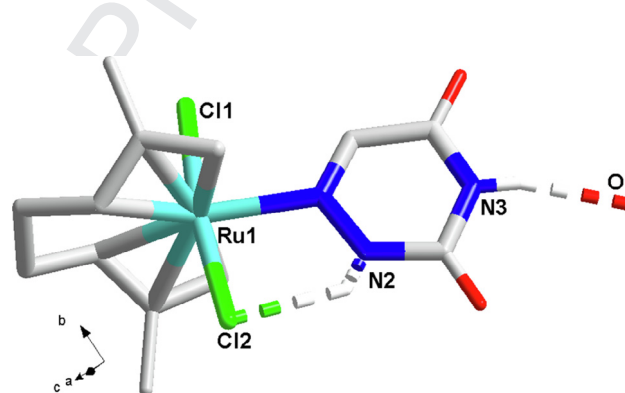


Fig. 21. Asymmetric unit of the crystal structure of [Ru(η^3 : η^3 -C₁₀H₁₆)Cl₂(6-azauracile)] (**91**): monoclinic (P121/c1); Ru1-Cl1 2.399(2) Å; Ru1-Cl2 2.406(2) Å; N2-H2...Cl2 2.986(5) Å; N3-H3...O1 2.828(5) Å. Adapted from Ref. [89].

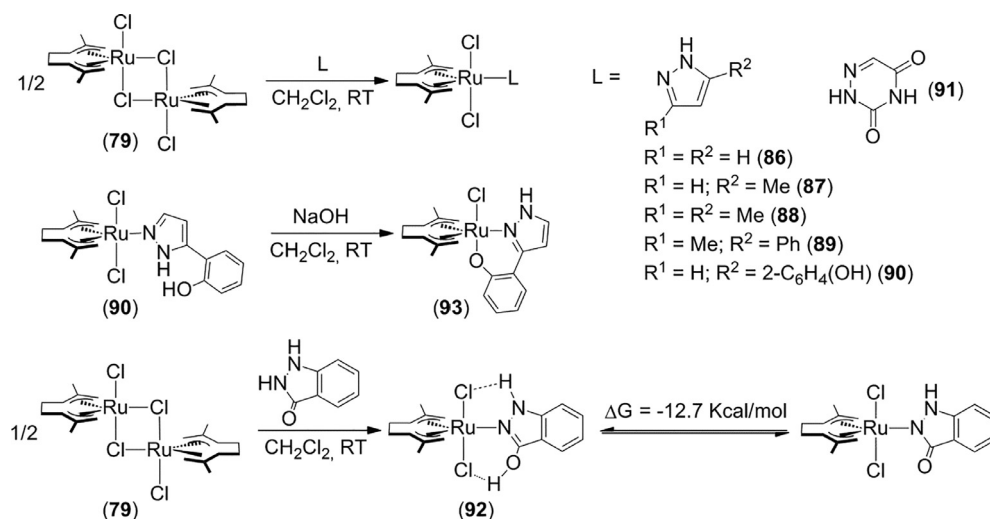
New valuable knowledges on how isomerization of allylic alcohols is catalyzed by Ru(IV) complexes were obtained by studying the catalytic properties of complexes [Ru(η^3 : η^3 -C₁₀H₁₆)Cl₂L] (C₁₀H₁₆ = 2,7-dimethylocta-2,6-diene-1,8-diyl; L = pyrazole (**97**), 3-methylpyrazole (**98**), 3,5-dimethylpyrazole (**99**), 3-methyl-5-phenylpyrazole (**100**), 2-(1H-pyrazol-3-yl)phenol (**101**), indazole (**102**)) [75]. Crystal structures of **99** and **102** are displayed in Fig. 23 with selected bond lengths and angles, showing the similar mono-coordination of the imidazole derivatives.

The complex **97** showed to be the most active for a large variety of substrates. The isomerization conversion is working also in THF, that require base as a co-catalyst, but in water is faster, taking 10–60 min to obtain the complete isomerization at 75 °C with only 0.2 mol% catalyst (TOF = 750–3000 h⁻¹). The isomerization of 1-octen-3-ol occurs at 35 °C in 60 min with 1 mol% catalyst. Up to that moment Rh(I) catalysts were the most efficient in water in the absence of base [91].

The ESI mass spectrometry provided the needed information to establish that when dissolved the complex **97** is involved in an equilibrium (Scheme 27). This conclusion was also supported by CID experiments, being used as reference for theoretical descriptions. DFT theoretical calculations suggested that the overall isomerization implies two hydrogen-transfer steps from the

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Also, they suggest that the high catalytic activity of the complex **95** is due to the donor properties of the benzimidazole ligand. The final conclusion points out the importance of a water molecule that acts as the cooperating ligand.



Scheme 25. Synthesis of complexes 86–93 and the keto-enolic equilibrium involving 79 and 92.

Table 7
Isomerization of 1-octen-3-ol into octan-3-one^a catalyzed by complex 91.

| Entry | Solvent | T °C | mol % of 3 | mol % of KO ^t Bu | time | Yield ^b | TOF (h ⁻¹) ^c |
|-------|------------------|------|------------|-----------------------------|--------|--------------------|-------------------------------------|
| 1 | THF | 75 | 0.2 | | 24 h | 99 | 21 |
| 2 | THF | 75 | 0.2 | 0.4 | 40 min | 99 | 743 |
| 3 | H ₂ O | 75 | 0.2 | | 10 min | 99 | 2970 |
| 4 | H O | 35 | 1 | | 3 h | 99 | 33 |

^a Reactions performed under a nitrogen atmosphere using 1 mmol of 1-octen-3-ol (0.2 M).

^b Yield of octan-3-one determined by gas chromatography.

^c Turnover frequencies [(mol of product/mol of ruthenium)/time] were calculated at the time indicated in each case.

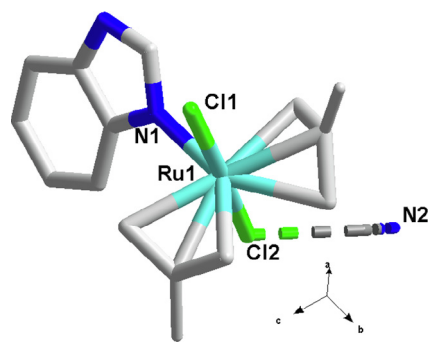


Fig. 22. Asymmetric unit of the crystal structure of [Ru(η³:η³-C₁₀H₁₆)Cl₂(benzimidazole)] (95): orthorhombic (Pbca); Ru1-Cl1 2.413(5) Å; Ru1-Cl2 2.436(5) Å; Ru1-N1 2.179(2) Å; N2-H2N...Cl2 3.274(2) Å. Adapted from Ref. [90].

substrate to the catalyst and subsequent transfer back to the substrate.

A very exciting step forward is the use of the isomerization of allylic alcohols in water, which was accomplished with ruthenium complexes 85, with enzymes [92]. Enantioselective isomerization of racemic allylic alcohols was possible by using a catalytic system obtained by combining a ruthenium(IV)-catalyst with an enantioselective enzymatic ketone reduction mediated by KREDs (KREDs = ketoreductases) in a concurrent process in aqueous medium. The enantioselective catalytic system is active under mild reaction conditions, employing commercially and readily available catalytic systems, and without external coenzymes or cofactors, coexisting metal catalyst and biocatalyst from the beginning. This procedure provides enantiomerically pure alcohols with high efficiency (85% conversion) (Table 8). The process is efficient and

simple, the only adjustment before KRED and cofactor addition requires a slight decrease on the temperature, both the metal catalyst and biocatalyst coexisting and working simultaneously from the beginning.

A more classical approach to develop a better catalytic system for the isomerization of allylic alcohols was provided by Cadierno et al in 2017 [77]. The complex [RuCl{κ²-N,N'-hpp}(η³:η³-C₁₀H₁₆)] (103) (C₁₀H₁₆ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (Hhpp = 1,3,4,6,7,8-hexahydro-2H-pyrimido[1,2-a]pyrimidine), which was obtained as showed in Scheme 28, contains a bicyclic guanidine chelating the metal.

Complex 103 is one of the most active catalyst for the isomerization of allylic alcohols (TOF up to 5940 h⁻¹), being also active for the isomerization of anethole (95% conversion). This complex was the first example of the application of metal guanidinate complexes in aqueous catalysis. Similarly, to the parent Ru(II) complexes presented previously, compound 103 isomerizes catalytically the estragole into the industrially relevant anethole, quite fast and with trans selectivity.

The isomerization of allylic alcohols was coupled with the chemoselective addition of organolithium or organomagnesium reagents to the in situ formed ketones, in route to tertiary alcohols, employing Deep Eutectic Solvents (DESs) as environmentally friendly reaction media (Scheme 29) [93]. The transformation formally involves: (i) the reduction of a C=C double bond, (ii) the oxidation of a secondary carbinol moiety, and (iii) a chemoselective C-C bond formation. These three steps allow the addition of Grignard and organolithium reagents at room temperature and the presence of air to the transiently formed ketones. The resulting conversion is excellent (up to 99%) at room temperature and under air in the last step, with no concomitant reduction or enolisation processes, and with high atom economy. The process takes place

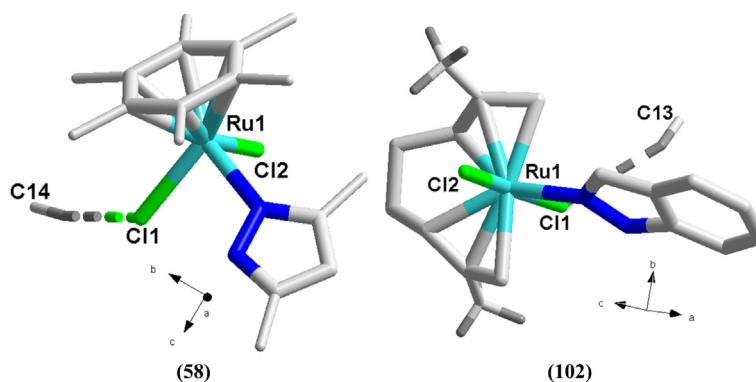
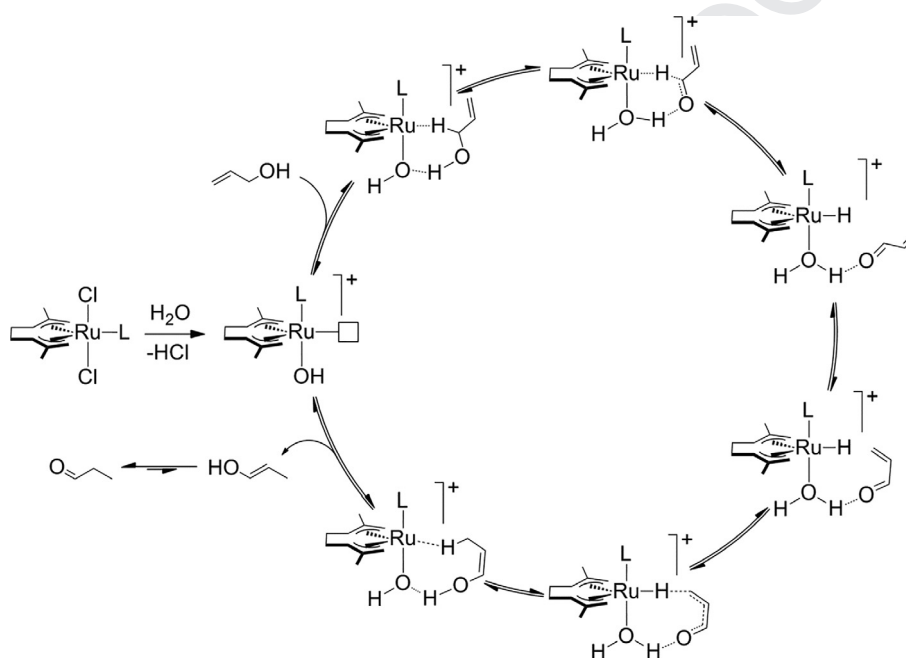
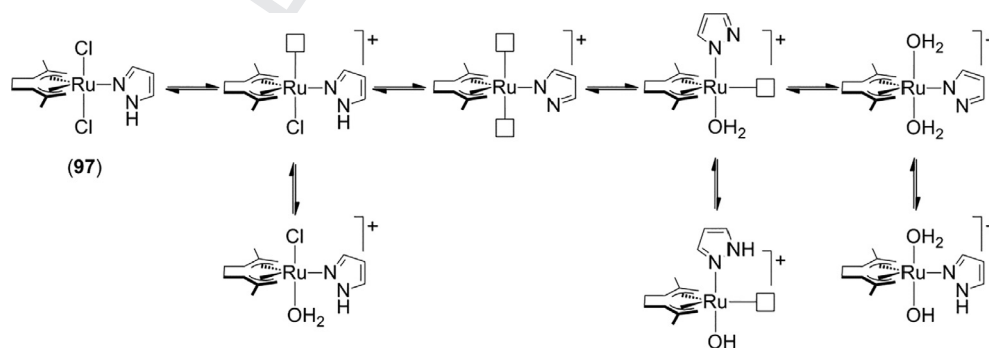


Fig. 23. Asymmetric units of the crystal structures of: (left) $[\text{Ru}(\eta^6\text{-C}_6\text{Me}_6)\text{Cl}_2(3,5\text{-dimethylpyrazole})]$ (**58**): monoclinic (C12/c1); Ru1-C11 2.413(1) Å; Ru1-C12 2.411(1) Å; Ru-arene_{centroid} 1.700(3) Å C14-H14A...Cl1 3.713(6) Å. (right) $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2\text{L}]$ (**102**): monoclinic (C1c1); Ru1-C11 2.406(4) Å; Ru1-C12 2.417(2) Å; C13-H13...Cl1 3.648(3) Å. Adapted from Ref. [75].



Scheme 26. Proposed catalytic mechanism for the isomerization of allylic alcohols catalyzed by complexes **94–96**.



Scheme 27. Equilibrium cationic species of aqueous solutions of **97** detected by ESI-MS at $t = 0$ and 1.5 h. Adapted from Ref. [91].

954 starting from allylic alcohols completely soluble in DESs mixtures
955 but reaction can be performed also in water with good conversions.

956 A final finding provided by Gimeno et al. showed that the cluster
957 $[\text{Ru}_3^{\text{III,III,III}}\text{O}(\text{CH}_3\text{CO}_2)_6(\text{H}_2\text{O})_3] \cdot 2\text{H}_2\text{O}$ (**104**) (Scheme 30) (crystal
958 structure and selected bond distances are displayed in Fig. 24) dis-

954 plays catalytic activity for the isomerization of allylic alcohols in
955 presence of NaHCO_3 [94].

956 The crystal structure of **104** displays 2D supramolecular net-
957 works extended through multiple hydrogen bonds which can be
958 simplified to hexagonal plane (hcb) topological net. The catalytic

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Table 8
Isomerisation of α -vinylbenzyl alcohol catalyzed by the Ru(IV) complexes in the phosphate buffer of KREDs.^a

| Entry | Complex | Mol% [Ru] | t (h) | c (%) ^b |
|----------------|-----------|-----------|-------|--------------------|
| 1 | 79 | 1 | 7.5 | >99 |
| 2 | 85 | 1 | 2.5 | >99 |
| 3 | 85 | 1 | 2.5 | >99 |
| 4 ^c | 85 | 1 | 2.5 | >99 |
| 5 ^c | 95 | 1 | 5 | >99 |
| 6 ^d | 85 | 1 | 2.5 | >99 |
| 7 ^e | 85 | 1 | 2.5 | 99 |
| 8 ^f | 85 | 1 | 24 | 70 |
| 9 | – | – | 24 | 2 |

^a Reaction conditions: α -vinylbenzyl alcohol (1 mmol) under Ar atmosphere at 50 °C, 1 mol% Ru(IV) catalyst, in 5 mL of KH_2PO_4 buffer 125 mM (1.25 mM MgSO_4) pH 7.0. Previously, buffer solution was degassed with Ar.

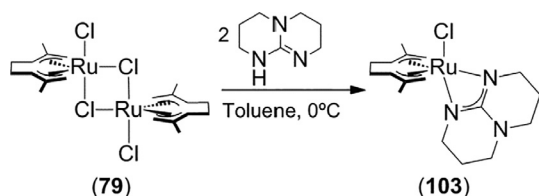
^b Calculated by GC.

^c Addition of 20 vol% of *i*-PrOH.

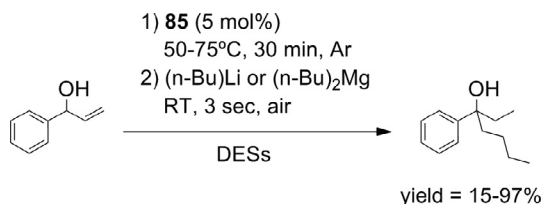
^d Experiment performed in the presence of different commercially available KREDs.

^e Experiment performed using 10 mM NADPH.

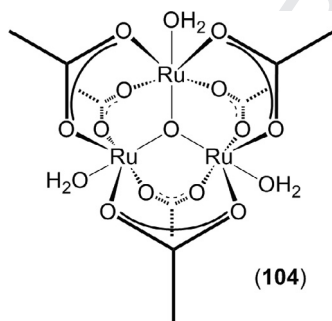
^f Experiment performed using 1 mM NADP



Scheme 28. Synthesis of **103**.



Scheme 29. Sequential isomerization and alkyl addition of 1-phenylprop-2-en-1-ol.



Scheme 30. Structure of **104**.

isomerization required to be performed at 80 °C in the three solvents: DMF, EtOH and water. Under the same reaction conditions the best conversion was obtained in DMF (Table 9). Additionally, the isomerization conversion was dependent linearly on the size of the allylic alcohols with the order of 3-buten-2-ol > 1-penten-3-ol > 1-hexen-3-ol > 1-hepten-3-ol > 1-octen-3-ol. This complex also showed to be active for the hydration of nitriles in water.

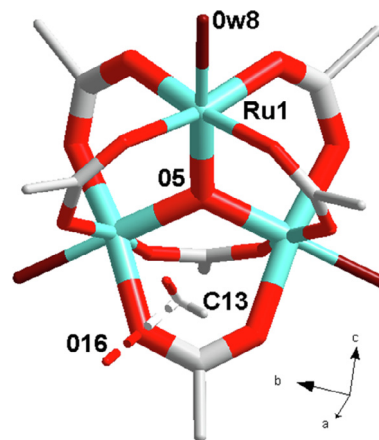


Fig. 24. Asymmetric unit of the crystal structure of $[\text{Ru}_3(\text{CH}_3\text{CO}_2)_6(\text{H}_2\text{O})_3]\cdot 2\text{H}_2\text{O}$ (**104**): monoclinic ($C2/c$); $\text{Ru}-\text{O}_{1\text{average}} = 1.905 \text{ \AA}$; $\text{C}13-\text{H}1\cdots\text{O}17$ 2.347(0), $\text{C}13-\text{H}1\cdots\text{O}16$ 2.329(0) \AA . Adapted from Ref. [94].

3.2. Catalysts containing other metals

3.2.1. Rhodium complexes

Rhodium is one of the rarest and most expensive valuable metals but it is also one of the most useful in catalysis and in chemistry in general. It has an electronic configuration $[\text{Kr}]4d^85s^1$ and exhibits mainly the principal oxidation states of +1 and +3. Rh-complexes are active catalyst for the asymmetric hydrogenation of prochiral enamides, for example in the successful commercial Monsanto *L*-DOPA (a drug for curing Parkinson's disease) process [95]. Hydroformylation of alkenes to synthesize linear and branched aldehydes with high selectivity [96], hydrosilylation crosslinking of silicone rubber [97] and carbonylation of alkenes in supercritical CO_2 /ionic liquid system [98], play an important role as industrial homogeneous catalysis. A great variety of rhodium complexes useful for the catalytic isomerisation of allyl alcohols are prepared from $\text{RhCl}_3\cdot\text{H}_2\text{O}$ (Scheme 31) [99–101].

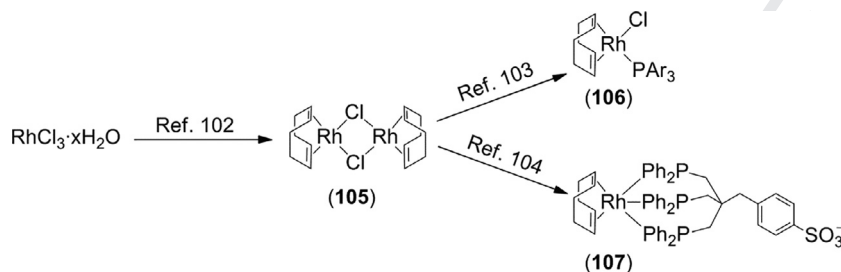
In 1981 Sasson and coworkers [102] presented the isomerization of 1-octen-3-ol in benzene/water catalyzed by 2% mol RhCl_3 . It was observed that under the reaction condition the metal was partially extracted into the organic phase by the help of onium salt. Further studies showed that under biphasic conditions (water/toluene), 0.02% mol of $[\text{RhCl}(\text{COD})(\text{PAR}_3)]$ ($\text{COD} = \text{cycloocta-1,5-diene}$; $\text{PAR}_3 = o-, m-$ and $p-(\text{Ph})_n\text{P}(\text{C}_6\text{H}_4-\text{COOH})_{3-n}$) catalyzes the isomerization of 1-octen-3-ol with optimal conversions [99,100]. The obtained results supported that complex $[\text{RhCl}(\text{COD})(\text{Ph}_2\text{P}(\text{C}_6\text{H}_4-2-\text{COOH}))]$ (**108**) is more active (96% vs 30–54%, after 1 h) than the other checked complexes. On the base of the IR and ^1H NMR data, equilibria were proposed (Scheme 32a) between intramolecular oxidative addition reductive-elimination in the complex and that produced when the complex and product is extracted into organic layers (Scheme 32b).

From the study and comparison of the obtained results (Scheme 32) some general conclusions were extracted: (i) in the absence of a phase transfer catalyst the allylic alcohol hardly reacted; (ii) the rate depended on both the location and the number of carboxyl groups in the phosphine ligand; (iii) the formation of the hydride complex **109** favors the isomerization process; (iv) the rate of isomerization process is directly proportional upon increasing pH probably due to the presence of the anion $\{\text{RhCl}(\text{COD})(\text{Ph}_2\text{PC}_6\text{H}_4-2-\text{COO})\}^-$ into the organic substrate-containing layer; (v) the sole function of the phase transfer agent is metal extraction; (vi) the quaternary phosphonium ion is more efficient than the corresponding ammonium salt due to the lower basicity of diphosphine ligands which facilitates olefin insertion into Rh-

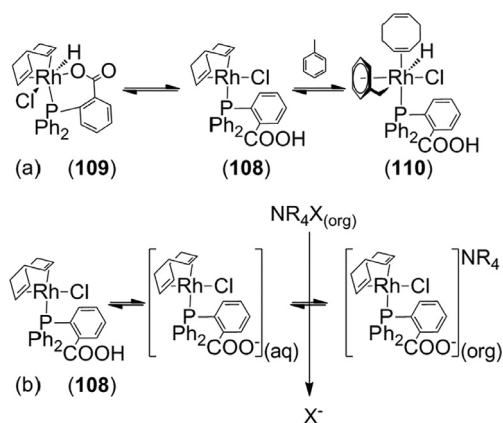
Table 9
Isomerization of allylic alcohols catalyzed by the triruthenium oxo-cluster **104**. Data derived from [97].

| Entry | Substrate | Solvent | Base | Temp °C | Time [min] | TOF (h ⁻¹) | Yield [%] |
|-------|---------------|------------------|---------------------------------|---------|------------|------------------------|-----------|
| 1a | 1-Buten-3-ol | DMF | NaHCO ₃ | 80 | 45 | 1.8 | 97 |
| 2e | 1-Octen-3-ol | EtOH | NaHCO ₃ | 80 | 60 | 1.3 | 95 |
| 3a | 1-Buten-3-ol | H ₂ O | NaHCO ₃ | 80 | 48 | 0.1 | 5 |
| 3b | 1-Penten-3-ol | H ₂ O | NaHCO ₃ | 80 | 24 | 0.1 | 2 |
| 3c | 1-Hexen-3-ol | H ₂ O | NaHCO ₃ | 80 | 12 | 0.1 | 1.5 |
| 3d | 1-Hepten-3-ol | H ₂ O | NaHCO ₃ | 80 | 24 | 0 | 0 |
| 3e | 1-Octen-3-ol | H ₂ O | NaHCO ₃ | 80 | 24 | 0.03 | 1 |
| 4a | 1-Penten-3-ol | DMF | Na ₂ CO ₃ | RT | 48 | 0.01 | 0.6 |

Reaction performed under N₂ atmosphere in Schlenk tube using 1.2 mmol% (Ru) of catalyst and 1 mmol of substrate. TOF = mmol of product/mmol of catalyst (based on Ru)/h.



Scheme 31. Synthesis of complexes **105**–**107**.



Scheme 32. Formation of rhodium hydride **109** and **110** (a) and extraction of the metal complex into organic layer (b).

H bond hydride complexes [96]; (vii) The presence of toluene as a solvent can facilitate the formation of hydride species **110**, indeed, the isomerisation under these reaction conditions is faster than in benzene; (viii) water does not play a part in the isomerisation process, justifying that the isomerisation of 1-octen-3-ol to 3-octanone can be interpreted in terms of a metal-hydride-addition-elimination mechanism (Scheme 32).

In conclusion, the position of the hydrophilic functions, the nature of organic groups linked to the coordinating phosphorous centre and the nature of the counter-cation are contributing factors to improve catalytic activity, as was observed in other metal-catalyzed-isomerisation systems commented earlier. Using a similar strategy, Bellefon et al. [60] described an active catalyzed process in water/n-heptane and water/methanol for the isomerisation of primary and secondary alcohols bearing the C=C bond in a terminal or inner position (Table 10). The catalyst was obtained in situ by reaction of RhCl₃ (and Rh₂(SO₄)₂) with the sodium salt of sulfonated triphenylphosphine (TPPTS).

Differences in TOF were observed as a function of the length of a hydrocarbon chain from C₄ to C₈. Thus, the values decrease from

Table 10
TOF values of rhodium-TPPTS catalysts for isomerization of allylic alcohols in water/n-heptane.

| Substrate | Rh-precursor | TOF (h ⁻¹) |
|-----------|---|------------------------|
| | RhCl ₃ | 3.2 |
| | RhCl ₃ | 3.1 |
| | RhCl ₃ | 4.8 |
| | Rh ₂ (SO ₄) ₃ | 2520 |
| | RhCl ₃ | 540 |
| | RhCl ₃ | 36 |
| | Rh ₂ (SO ₄) ₃ | 490 |
| | Rh ₂ (SO ₄) ₃ | 30 |

2520 to 30 h⁻¹ when the hydrocarbon chain length increases for lineal allylic alcohols (Table 10); clearly the catalytic activity depends on the substrate size. The allyl alcohol bearing the C=C bond in its terminal position is the most reactive substrate (vide

supra). Therefore, primary alcohols are less reactive than secondary alcohols [37,60].

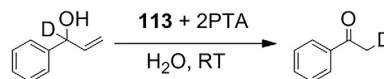
In this line of work, Bianchini et al. published the first zwitterionic rhodium complex [Rh(sulphos)(COD)] (sulphos = NaO₃S(C₆H₄)CH₂C(CH₂-PPh₂)₃) (**107**) [101,103] (Scheme 31) as a catalyst for the isomerization of both allylic and homoallylic alcohols in *n*-octane/water (100 °C, 1 h). The activity of this complex was as high as 100 equiv. of 1-propen-3-ol that was converted to propanal after 1 h at 100 °C. By simple phase separation, the aldehyde product (ca. 99% in *n*-octane) was separated from the catalyst, which was recycled three times with TOF values of 490, 430 and 390 h⁻¹, respectively. The observed deactivation (ca. 10%) after each run was proposed to be due to partial incorporation of active metal into the carbonyl complex [(sulphos)Rh(CO)₂].

Increasing the steric hindrance and hydrocarbon backbones of the allylic moiety (e.g. 2-buten-1-ol or 3-methyl-2-buten-1-ol) resulted in a progressive decay of the catalytic efficiency reaction. The isomerization of cycloocta-1,5-diene to cycloocta-1,3-diene in water-MeOH-*n*-octane at 100 °C in 1 h. was also observed. Finally, a π -allyl metal hydride mechanism was proposed as the responsible key of the catalytic process (Scheme 33).

Two years later, in 2003, Knight and Schull [104] reported the aqueous phase isomerization of cinnamyl-, crotyl-alcohol and 2-cyclohexene-1-ol catalyzed by the water-soluble rhodium complexes [Rh(cod)₂]BF₄ (**111**) and {[Rh(cod)(*p*-TPPMP)₂]⁺ (*p*-TPPMP = *para*-triphenylphosphine monophosphonate) (**112**).

The product of the reaction of [Rh(COD)(CH₃CN)₂](BF₄) (**113**) (5 mol%) with 2 equivalents of PTA proved to be an efficient catalyst for the redox isomerization of secondary allylic alcohols in water at ambient temperature and neutral pH [91]. However, some primary alcohols can also be isomerized into the corresponding aldehydes. The highest conversions (54–39%) were found in the range from neutral to basic pH, decreasing sharply in acid media.

The catalytic process is sensitive towards steric hindrance of the allylic alcohols. In general, to achieve that the C=C bonds present a



Scheme 34. Deuterated allylic alcohol isomerisation catalyzed by **103**.

higher degree of substitution; higher temperatures are needed, although full conversion cannot always be achieved. A deuterium labeling mechanistic study was made, which suggested that the isomerisation process proceeded by an enone-centered mechanism (Scheme 34). A 1,3-hydrogen shift takes place intramolecularly and a consecutive formation of Rh-aldol, -enone, and -enol intermediates may take place (Scheme 4a).

Interestingly, a supramolecular M₄L₆ (M = Ga³⁺, L = bis-catecholamide naphthalene) host has been shown to encapsulate a variety of cationic rhodium catalysts. The Rh-Ga₄L₆ system is able to have a supramolecular control over the catalytic isomerization of allylic alcohols. For example, the cation complex {(PMe₃)₂Rh(D₂O)₂}⁺ (**114**) in 10% in D₂O isomerises allyl alcohols with 95% yield after 0.5 h at 25 °C. When catalyst was encapsulated [114 ⊂ Ga₄L₆] a selective isomerization into propionaldehyde was produced.

A very interesting finding was provided by Pombeiro's group [105]. The water-soluble rhodium complexes [Rh(CO)(PTA)₄]Cl (**115**), [RhCl₂(PTA)₄]Cl (**116**) and [RhH(PTA)₄] (**117**) (crystal structure, selected bond lengths for **115** and **116** are showed in Fig. 25) are catalytically active for the isomerisation and controlled condensation of 1-propen-3-ol in water under ambient conditions to provide *n*-propanal (in low proportion), and 3-hydroxy-2-methylpentanal or 2-methyl-2-pentenal in quantitative yields, at lower or higher concentrations of the base (NaOH), respectively (Scheme 35). The catalytic activity remains the same for three runs.

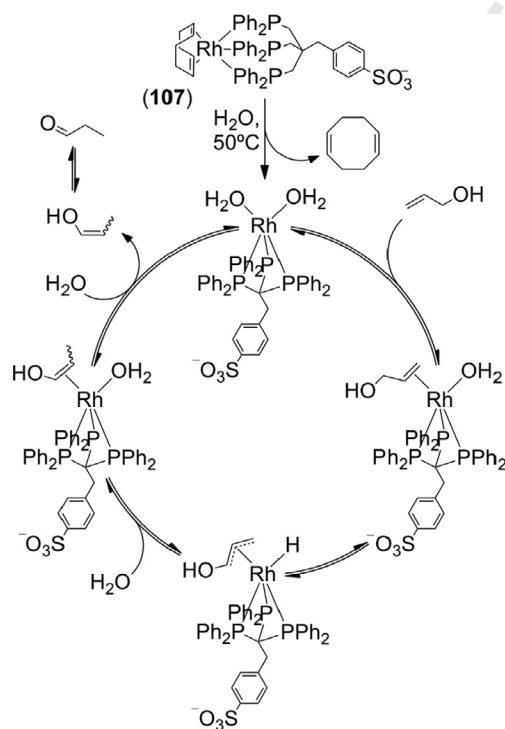
3.2.2. Nickel complexes

The organometallic chemistry of nickel has a rich history dating back to more than 100 years ago. Despite this, new reactions are still being developed at a rapid pace. At present, nickel chemistry seems to be well poised to provide an increasing number of new reactions of isomerization of olefins by migration of the double bonds [106–108] and is extended to the coupling of olefins with aldehydes that provide allylic or homoallylic alcohol derivatives [109–111].

In contrast, the Ni-catalytic isomerisation of allyl alcohols has not received much attention. In fact, to our knowledge, the catalyzed isomerisation of allyl alcohol has been studied in CH₂Cl₂ [112], xylene [106], HCN/CF₃COOH:benzene [113] and methanol/xylene [114] but only one example in the presence of water was found.

Monflier et al. [115] established the catalytic activity of Ni⁰/diphosphino/acid systems for the irreversible catalytic isomerization of geraniol and prenol in water/toluene (Table 11). The catalyst suffered progressive deactivation due to formed aldehydes citronellal and isovalaldehyde, which was found to reversibly coordinate to Ni⁰ to form non-catalytic species. From the obtained results two conclusions can be extracted from the reaction in biphasic conditions: (i) In absence of co-solvent the dehydration of geraniol into prenol was the major reaction, citronellal being obtained in very poor yield (3%). In absence of nickel-catalyst, a proton-assisted dehydration of geraniol. (ii) In presence of DMF as a co-solvent and irrespectively of the acid used, citronellal is selectively formed with 86% yield in contrast with the 3% yield obtained when DMF was not introduced in the reaction.

Regardless of the high solubility of **XV** in water, the presence of a co-solvent does not suppress the proton-catalyzed side reaction that produces **XVII**.



Scheme 33. Proposed π -Allyl metal hydride mechanism for the isomerization of 1-propen-3-ol to propanal catalyzed by [Rh(sulphos)(COD)] (**107**).

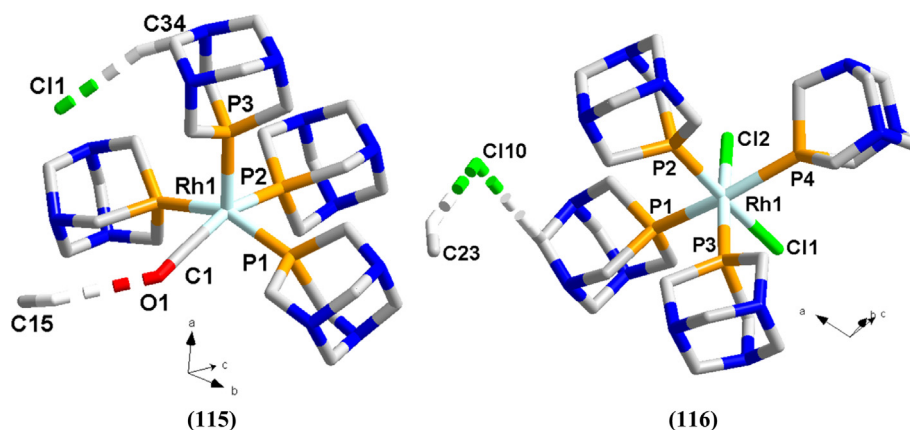
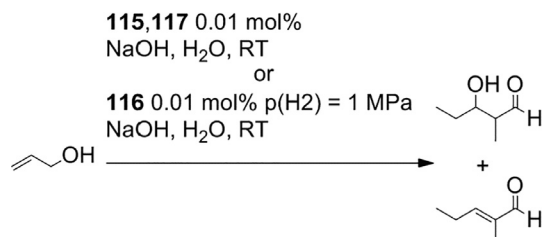


Fig. 25. Asymmetric units of the crystal structures of: (a) $[\text{Rh}(\text{CO})(\text{PTA})_4]\text{Cl}$ (**115**): monoclinic ($P121/m1$); Rh1-CO 1.921(2) Å; (Rh1-P)_{average} 2.368 Å; C15-H15B...OC 3.680(2) Å; C34-H34B...Cl1 3.712(1) Å; (b) $[\text{RhCl}_2(\text{PTA})_4]\text{Cl}$ (**116**): monoclinic ($C12/c1$); Rh1-Cl1 2.419(1) Å; Rh1-Cl2 2.420(8) Å; (Rh1-P)_{average} 2.346 Å; C23-H23A...Cl10 3.745(4) Å. Adapted from Ref. [105].



Scheme 35. Condensation of allyl alcohol to 3-hydroxy-2-methylpentanal and 2-methyl-2-pentenal catalyzed by **115–117**.

Nickel-hydride complexes can be formed by protonation of the water-soluble zerovalent nickel complex $[\text{Ni}(\text{TPPTS})_3]$ and $[\text{Ni}(\text{DPPBTS})_x]$ similarly to $[\text{Ni}(\text{PPh}_3)]$ (**118**) and $[\text{Ni}(\text{DPPB})_2]$ (**119**) in acidic homogeneous medium [108]. In this line, the proposed mechanism for catalyst deactivation suggest an active hydride-nickel (a), an alkyl- (b) and π -allyl-nickel species (c), which are produced by allyl alcohol insertion into the hydride-nickel species (Scheme 36). Apart from certain structural limitations an allylic alcohol may serve as a direct synthon for an enolate anion. The

complex $[(\text{Cy}_3\text{P})_2\text{NiCl}_2]$ (**120**) proved to be a good catalyst for the isomerization of allylic lithium alkoxides to the corresponding enolates. This compound provided much higher regioselectivity and was more capable of isomerising highly substituted double bond that is not catalytically isomerized by rhodium complexes [116,117].

3.2.3. Palladium complexes

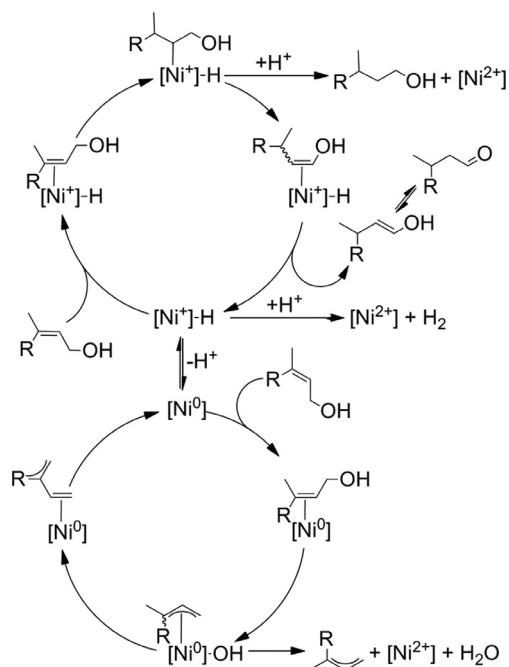
Interestingly, the unique complexes containing Pd(II) active in catalytic isomerization of allylic alcohols in water is constituted by a sulfonated tetrahydrosalen (sulfosalan, HSS) [118]. This complex, $[\text{Pd}(\text{HSS})]$ (**121**) (Scheme 37), showed outstanding activity in hydrogenation and redox isomerization of allylic alcohols in water and in water/organic biphasic systems (for oct-1-en-3-ol, TOF (hydrogenation) = 1580 h^{-1} , TOF (redox isomerization) = 400 h^{-1}). To understand the reaction DFT calculations were performed, which revealed that the molecular hydrogen (H_2) is activated heterolytically, resulting in a Pd(II)-hydride complex, $[\text{Pd}(\text{H})(\text{HSS}-\text{Hphen})]$, in which one of the phenolate oxygens is protonated (Scheme 38).

Table 11

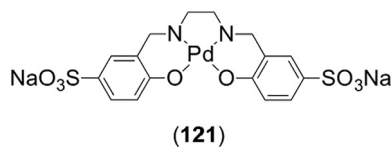
Ni-catalyzed $(\text{Ni}(\text{COD})_2 + \text{DPPBTS})$ isomerization of geraniol and prenol in water:toluene at 110 °C (DPPBTS = 1,4-bis(diphenylphosphino)butane).

| Acid (equiv.) | Substrate | Time (h) | Yield (mol-%) | Sel. (mol-%) | Sel. (mol-%) |
|------------------|-----------|----------|---------------|--------------|--------------|
| TFA | Geraniol | 0.5 | 1 | 10 | 90 |
| TFA | Geraniol | 2 | 1 | 3 | 97 |
| TFA | Geraniol | 16 | 3 | 5 | 95 |
| TFA ^a | Geraniol | 0.5 | 8 | 80 | 16 |
| TFA ^a | Geraniol | 2 | 13 | 86 | 10 |
| TFA ^a | Geraniol | 16 | 14 | 74 | 15 |
| HCl ^a | Geraniol | 0.5 | 8 | 88 | 11 |
| HCl ^a | Geraniol | 2 | 13 | 86 | 10 |
| HCl ^a | Geraniol | 16 | 14 | 74 | - |
| TFA ^a | Prenol | 0.5 | 11 | 47 | 53 |
| TFA ^a | Prenol | 2 | 12 | 38 | 62 |
| TFA ^a | Prenol | 16 | 12 | 22 | 78 |

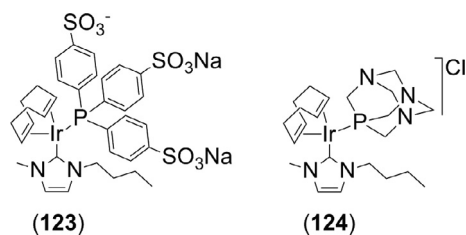
^a With dimethylformamide, TFA: trifluoroacetic acid.



Scheme 36. Proposed mechanism for the isomerization of allylic alcohols by Ni complexes in presence of water.



Scheme 37. Structure of sulfosalan complex **121**.



Scheme 38. Structures of **123** and **124**.

1160 Despite of hex-1-en-3-one and hex-2-en-3-ol were not
1161 observed experimentally, the DFT calculated free energies do not
1162 exclude the contribution of this compounds to the overall reaction.
1163 Though, [Pd(HSS)] did not catalyze the redox isomerization of
1164 allylic alcohols in the absence of H₂, on all theoretical levels, calcu-
1165 lations show the preference of ketone formation over alcohol pro-
1166 duction. Nevertheless, the solution model prefers unequivocally
1167 the formation of hexan-3-ol, as found experimentally. This com-
1168 plex was found to be active in both redox isomerization of allylic
1169 alcohols and hydrogenation under mild conditions, with somewhat
1170 higher activity in hydrogenation than in redox isomerization, being
1171 also active for various C–C coupling.

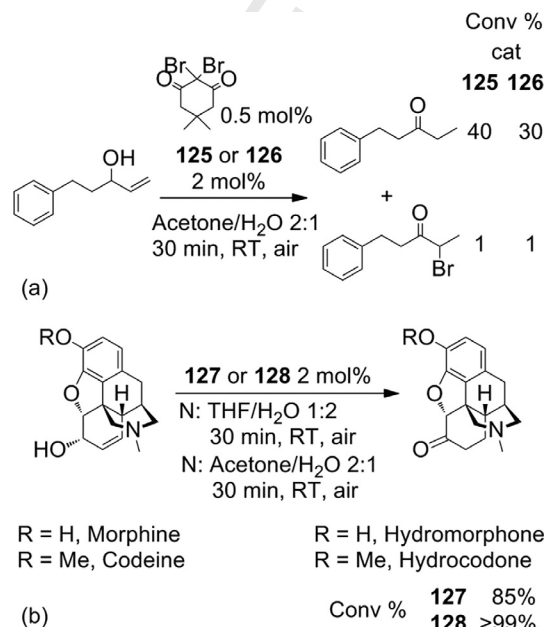
3.2.4. Osmium complexes

1172 The only example of Os complexes catalytically active in the
1173 isomerization of allylic alcohols is [OsCl(κ²-(N,N')-hpp)
1174 (η⁶-pcymene)] (**122**) (hpp = 1,3,4,6,7,8-hexahydro-2H-pyrimido[1
1175 ,2-a]pyrimidine (hpp), bicycle guanidine chelating the metal) [77].
1176

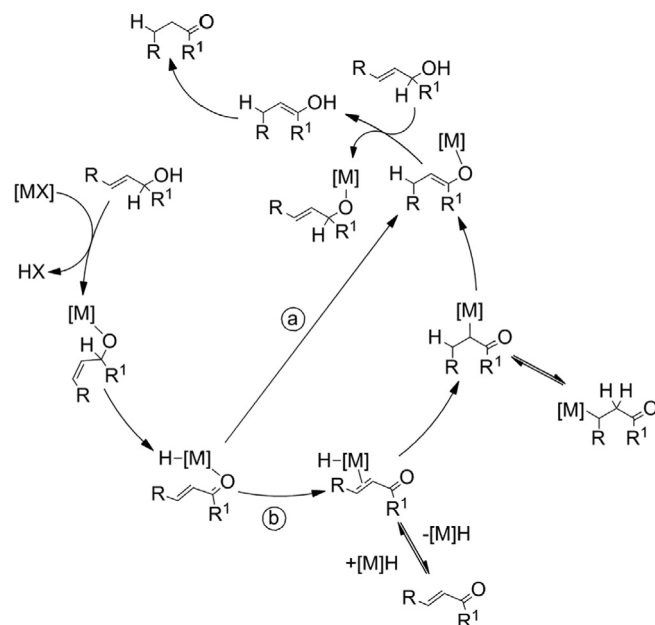
1177 These complexes were synthesized similarly to previously dis-
1178 cussed Ru(II) and Ru(IV) complexes. As indicated the Ru(IV) com-
1179 plexes were the most stable but also the Os complexes showed
1180 to be active, but with significant lower conversion, also in the iso-
1181 merization process of estragole.

3.2.5. Iridium complexes

1182 In 2014 Kathó and Joó team published the Ir(I) complexes [Ir
1183 (NHC)(η⁴-cod)(L)] (NHC = bmim, emim; L = Cl⁻, H₂O, mTPPMS-
1184 Na, mTPPTS-Na₃, PTA) [119]. Among them, are particularly inter-
1185 esting the complexes Na₂[Ir(bmim)(η⁴-cod)(mTPPTS)] (**123**) and
1186



Scheme 39. a) isomerization of 5-phenylpent-1-en-3-ol catalyzed by **125** and **126** in the presence of 2,2-dibromo-5,5-dimethyl-1,3-Cyclohexanedione; b) isomerization of morphine and codeine catalyzed by **127** and **128**.



Scheme 40. Proposed mechanisms for the isomerization of allylic alcohols with Ir complexes **125–128**.

Table 12

Transition metal complexes useful for the catalytic isomerization of allylic alcohols in water and some of their most significant catalytic features.

| Compound | TOF (h ⁻¹) | TON | Temp (°C) | Conv (%) | Substrate | Ref |
|---|------------------------|--------------------|-----------|----------|--|-----------|
| [Ru(H ₂ O) ₆](tos) ₂ (1) | 1.5 ^j | 18 ^j | 45 | >90 | 1-Penten-3-ol | [25–27] |
| [RuCl ₂ (PPh ₃) ₃] (2) | 15.67 ⁱ | 50 ⁱ | 45 | 99 | (E)-1-(4-Methoxy-phenyl) hex-2-en-1-ol | [58,59] |
| <i>cis,cis</i> -[RuCl ₂ (dmso) ₂ (phen)] (3) | 45.9 ^j | 290 | 135 | >95 | 1-Buten-3-ol | [40,62] |
| [RuCl ₂ (1-butyl-3-methylimidazolin-2-ylidene)(η ⁶ -p-cymene)] (4) | 167.3 ⁱ | 251 | 80 | 93 | 1-Octen-3-ol | [65] |
| [RuCl(1-butyl-3-methylimidazolin-2-ylidene)(PTA)(η ⁶ -p-cymene)] (5) | 135 | 89.1 ^j | 80 | 95.6 | 1-Octen-3-ol | [63] |
| [RuCl ₂ (η ⁶ -C ₆ H ₆)[P(CH ₂ OH) ₃]] (6) ^a | 600 | 625 | 75 | 100 | 3-Buten-2-ol | [64] |
| [RuCl ₂ (η ⁶ -p-cymene)[P(CH ₂ OH) ₃]] (7) ^a | 782 | 200 | 75 | 100 | 3-Buten-2-ol | [64] |
| [RuCl ₂ (η ⁶ -C ₆ Me ₆)[P(CH ₂ OH) ₃]] (8) ^a | 29 | 193 | 75 | 100 | 1-Octen-3-ol | [64] |
| [RuCl(η ⁶ -C ₆ H ₆)[P(CH ₂ OH) ₃] ₂]Cl (9) ^a | 6 | 191 | 75 | 100 | 1-Octen-3-ol | [64] |
| [RuCl ₂ (η ⁶ -p-cymene)[P(CH ₂ OH) ₃] ₂]Cl (10) ^a | 5 | 183 | 75 | 100 | 1-Octen-3-ol | [64] |
| [RuCl(η ⁶ -C ₆ Me ₆)[P(CH ₂ OH) ₃] ₂]Cl (11) ^a | 4 | 186 | 75 | 100 | 1-Octen-3-ol | [64] |
| [RuCl ₂ (η ⁶ -p-cymene)[P(OCH ₂ CH ₃) ₃]] (12) | 46 | 115 ⁱ | 35 | 99 | 1-Octen-3-ol | [13] |
| [RuCl ₂ (η ⁶ -p-cymene){κ-(P)-PPh ₂ (OCH ₂ NMe ₃) ₃][SbF ₆] (13a) | 594 ⁱ | 396 | 75 | 99 | 1-Octen-3-ol | [66] |
| [RuCl ₂ (η ⁶ -p-cymene){κ-(P)-PPh ₂ (OCH ₂ NMe ₃) ₃][SbF ₆] (13b) | 396 ⁱ | 792 ⁱ | 75 | 99 | 1-Octen-3-ol | [66] |
| [RuCl ₂ (THPA)(η ⁶ -C ₆ H ₆)] (14) + KOBu ^t | 132 | 99 ^j | 75 | 99 | 1-Octen-3-ol | [28] |
| [RuCl ₂ (THPA)(η ⁶ -p-cymene)] (15) + KOBu ^t | 99 | 99 ^j | 75 | 99 | 1-Octen-3-ol | [28] |
| [RuCl ₂ (THPA)(η ⁶ -1,3,5-C ₃ H ₃ Me ₃)] (16) + KOBu ^t | 50 | 100 ⁱ | 75 | 99 | 1-Octen-3-ol | [28] |
| [RuCl ₂ (THPA)(η ⁶ -C ₆ Me ₆)] (17) + KOBu ^t | 29 | 101.5 ^j | 75 | 100 | 1-Octen-3-ol | [28] |
| [RuCl ₂ (THPA-Me)(η ⁶ -C ₆ H ₆)] (18) + KOBu ^t | 99 | 99 ^j | 75 | 99 | 1-Octen-3-ol | [28] |
| [RuCl ₂ (THPA-Me)(η ⁶ -p-cymene)] (19) + KOBu ^t | 200 | 100 ⁱ | 75 | 99 | 1-Octen-3-ol | [28] |
| Cs[Ru(CO ₃)(η ⁶ -C ₆ Me ₆)(N,N'-(CH ₃) ₂ (C ₃ H ₅ SO ₃) ₂ imidazolium)] (20) | 250 ⁱ | 250 | 100 | 99 | 2-Propen-1-ol | [69] |
| Cs[Ru(CO ₃)(η ⁶ -p-cymene)(N,N'-(CH ₃) ₂ (C ₃ H ₅ SO ₃) ₂ imidazolium)] (21) | 99 ⁱ | 928 | 100 | 86 | 1-Hexen-3-ol | [69] |
| [RuCl ₂ (η ⁶ -CH ₃ OCH ₂ CH ₂ OH)[P(OMe) ₃]] (22) + KOBu ^t | 100 ⁱ | 400 | 75 | 99 | 1-Octen-3-ol | [71] |
| [RuCl ₂ (η ⁶ -C ₆ H ₅ OCH ₂ CH ₂ OH)[P(OEt) ₃]] (23) + KOBu ^t | 100 ⁱ | 400 | 75 | 99 | 1-Octen-3-ol | [71] |
| [RuCl ₂ (η ⁶ -C ₆ H ₅ OCH ₂ CH ₂ OH)[P(OiPr) ₃]] (24) + KOBu ^t | 100 ⁱ | 1200 | 75 | 99 | 1-Octen-3-ol | [71] |
| [RuCl ₂ (η ⁶ -C ₆ H ₅ OCH ₂ CH ₂ OH)[P(OPh) ₃]] (25) + KOBu ^t | 100 ⁱ | 150 | 75 | 99 | 1-Octen-3-ol | [71] |
| [RuCl ₂ (η ⁶ -C ₆ H ₅ OCH ₂ CH ₂ OH)(PPh ₃) ₂] (26) + KOBu ^t | 96 ^j | 192 | 75 | 99 | 1-Octen-3-ol | [71] |
| Na ₄ [(RuCl(mtppps) ₂)] (27) | 50 | 100 ⁱ | 50 | 38 | 1-Octen-3-ol | [67] |
| Na ₄ [(RuCl(μ-Cl)(C=C=CPh ₂)(mtppps) ₂)] (28) | 100 | 100 ⁱ | 80 | 99 | 1-Octen-3-ol | [67] |
| Na ₂ [(RuClCp(mtppps) ₂)] (29) | 2226 | 1113 ^j | 80 | 99 | 1-Octen-3-ol | [67] |
| Na[(Ru(CO)Cp(mtppps) ₂)] (30) | 10 | 10 ^j | 50 | 25 | 1-Octen-3-ol | [67] |
| [RuClCp(mPTA) ₂](CF ₃ SO ₃) ₂ (31) | 18.7 | 37.4 ^j | 80 | 50% | 1-Octen-3-ol | [68] |
| [RuCp(mPTA) ₂ (H ₂ O-κ O)](CF ₃ SO ₃) ₂ (32) | 47 | 931 | 80 | 94% | 1-Octen-3-ol | [68] |
| 5-G ₃ (33) + Cs ₂ CO ₃ ^b | 12.25 ⁱ | 382 ⁱ | 75 | 98 | 1-Octen-3-ol | [19,72] |
| RAPTA-functionalized magnetic nanoferrites (34) | 253 | 63.25 ^j | 150 | 99 | 1-Octen-3-ol | [73] |
| <i>cis</i> -[Ru(6,6'-Cl ₂ bipy) ₂ (H ₂ O) ₂](OTf) ₂ (35) + KOBu ^t | 180 ⁱ | 720 ⁱ | 90 | 72 | 3-Butene-2-ol | [74] |
| [(η ⁶ -p-cymene)RuCl ₂ (2-κP)] (40) + KOBu ^t P: (Diphenylphosphanyl)-1-[N-(bis(hydroxymethyl)methyl)carbamoyl]ferrocene | 2.5 ⁱ | 50 ⁱ | 80 | 100 | 1,3-Diphenylallyl alcohol | [75] |
| [RuCl ₂ (dmso) ₂ (PTA) ₂] (46) + Sodium formate ^c | 26.5 ^j | 26.5 ^j | 80 | 53 | 1-Octen-3-ol | [76] |
| [RuCl ₂ (dmso) ₂ (mPTA) ₂]Cl ₂ (47) + Sodium formate ^c | 22.5 ^j | 22.5 ^j | 80 | 45 | 1-Octen-3-ol | [76] |
| [RuCl ₂ (dmso) ₂ (BnPTA) ₂][OTf] ₂ (48) + Sodium formate ^c | 32.5 ^j | 32.5 ^j | 80 | 65 | 1-Octen-3-ol | [76] |
| [RuCl(κ ² N,N'-C(N(4-C ₆ H ₄ Br))(N'Pr)NH'Pr)(η ⁶ -p-cymene)] (53) | 5 ^j | 15 ^j | 80 | 15 | 1-Octen-3-ol | [77] |
| [Ru(η ⁶ -C ₆ H ₆)Cl ₂ (3,5-dimethylpyrazolyl)] (56) | 96 | 480 ⁱ | 75 | 1 | 1-Octen-3-ol | [78] |
| [Ru(η ⁶ -p-cymene)Cl ₂ (3,5-dimethylpyrazolyl)] (57) | 185 | 370 ⁱ | 75 | 1 | 1-Octen-3-ol | [78] |
| [Ru(η ⁶ -C ₆ Me ₆)Cl ₂ (3,5-dimethylpyrazolyl)] (58) | 250 | 500 ⁱ | 75 | 1 | 1-Octen-3-ol | [78] |
| [RuCl ₂ (η ⁶ -C ₆ H ₆)(PTA-Me)Cl] (59) | 8 | 192 ⁱ | 75 | 100 | 1-Octen-3-ol | [79] |
| [RuCl ₂ (PTA)(η ⁶ -p-cymene)] (67) ^d | 184 | 184 ⁱ | 80 | 100 | 1-Octen-3-ol | [81] |
| [Ru(η ₂ -CO ₃)(PTA)(η ⁶ -p-cymene)] (68) | 396 | 264 ⁱ | 75 | 99 | 1-Octen-3-ol | [81] |
| [RuClCp(PTA) ₂] (69) | 19 | 95 | 70 | 95 | 2-Cyclohexenol | [82,87] |
| [Ru[RuClCp(HdmoPTA)(PPh ₃)](OSO ₂ CF ₃) (70) | 4 ⁱ | 12 ⁱ | 80 | 100 | 1-Octen-3-ol | [84] |
| [RuClCp(PPh ₃)-μ-dmoPTA-1κP:2κ ² N,N'-CoCl ₂] (71) | 1.1 ^j | 6.4 ^j | 80 | 53 | 1-Octen-3-ol | [84] |
| [RuClCp(PPh ₃)-μ-dmoPTA-1κP:2κ ² N,N'-NiCl ₂] (72) | 0.9 ^j | 5.3 ^j | 80 | 44 | 1-Octen-3-ol | [84] |
| [RuClCp(PPh ₃)-μ-dmoPTA-1κP:2κ ² N,N'-ZnCl ₂] (73) | 0.6 ^j | 3.8 ^j | 80 | 32 | 1-Octen-3-ol | [84] |
| [RuCp(H ₂ O-κO)(PTA) ₂](CF ₃ SO ₃) (75) ^e | >333 | 3420 | 70 | 99 | 2-Cyclohexenol | [85,87] |
| [Ru(η ³ :η ² :η ³ -C ₁₂ H ₁₈)Cl ₂] (C ₁₂ H ₁₈ = dodeca-2,6,10-triene-1,12-diyl) (78) | 2000 | 500 ⁱ | 75 | 100 | 1-Hexen-3-ol | [88] |
| [(RuCl(μ-Cl)(η ³ :η ³ -C ₁₀ H ₁₆)) ₂] (79) | 3000 | 500 ⁱ | 75 | 100 | 1-Hexen-3-ol | [37] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl(κ ² O, OCH ₃ CO ₂)] (85) | 6000 | 495 | 75 | >99 | 1-Octen-3-ol | [90] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (6-azauracile)] (91) | 2970 | 495 ⁱ | 75 | 99 | 1-Octen-3-ol | [92] |
| [Ru(η ₃ :η ₃ -C ₁₀ H ₁₆)Cl ₂ (imidazole)] (C ₁₀ H ₁₆ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (94) | 1500 | 500 ⁱ | 75 | 99 | 1-Octen-3-ol | [93] |
| [Ru(η ₃ :η ₃ -C ₁₀ H ₁₆)Cl ₂ (benzimidazolyl)] (95) | 6000 | 691 | 75 | >99 | 1-Octen-3-ol | [93] |
| [Ru(η ₃ :η ₃ -C ₁₀ H ₁₆)Cl ₂ (N-methylimidazolyl)] (96) | 1300 | 433 ⁱ | 75 | 99 | 1-Octen-3-ol | [93] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (C ₁₀ H ₁₆ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (97) | ≈2900 | ≈483 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (98) | ≈2700 | ≈450 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (99) | ≈2700 | ≈450 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (100) | ≈1900 | ≈475 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (101) | ≈1900 | ≈475 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [Ru(η ³ :η ³ -C ₁₀ H ₁₆)Cl ₂ (pyrazolyl)] (102) | ≈1900 | ≈475 ⁱ | 75 | >99 | 1-Octen-3-ol | [78] |
| [RuCl(κ ² -N,N'-hpp)(η ₃ :η ₃ -C ₁₀ H ₁₆)] (103) | 5940 | 495 ⁱ | 80 | 99 | 1-Penten-3-ol | [80] |
| [Ru ₃ (^{II,III,III})O(CH ₃ CO ₂) ₆ (H ₂ O) ₃]·2H ₂ O (104) + NaHCO ₃ | 0.1 | 4.8 ^j | 80 | 5 | 1-Buten-3-ol | [97] |
| [Rh(sulphos)(COD)] (sulphos = NaO ₃ S(C ₆ H ₄)CH ₂ C(CH ₂ -PPh ₂) ₃) (107) ^k | 490 | 270 ⁱ | 100 | 99 | Propen-3-ol | [105,106] |
| Rh ₂ (SO ₄) ₃ + TPPTS ^l | 2520 | 120 ⁱ | 70 | 100 | 1-Buten-3-ol | [62] |
| {[Rh(cod)(p-TPMP) ₂]}* (p-TPMP = para-triphenylphosphine monophosphonate) (112) | 3.6 ⁱ | 58 ^j | 100 | 58 | 2-Cyclohexene-1-ol | [107] |

(continued on next page)

Table 12 (continued)

| Compound | TOF (h ⁻¹) | TON | Temp (°C) | Conv (%) | Substrate | Ref |
|--|------------------------|------------------|-----------|----------|------------------------|-------|
| [Ni(COD) ₂] + dppbts + Triflic acid ^a + butane-1,2-diol | 3.2 ^j | 51 ^j | 110 | 72 | Geraniol | [118] |
| [Pd(HSS)] (121) (HSS: sulfosalan + Na-phosphate buffer + 9 atm H ₂) | 400 | 400 ^j | 80 | 20 | 1-Octen-3-ol | [121] |
| [OsCl(κ ² -(N,N')-hpp)(η ⁶ -p-cymene)] (122) (hpp = 1,3,4,6,7,8-hexahydro-2H-pyrimido [1,2-a]pyrimidine ^b) | 50 | 88 ^j | 80 | 25 | 1-Octen-3-ol | [80] |
| Na ₂ [Ir(bmim)(η ⁴ -cod)(mTPPTS)] (123) | 100 | 100 ^j | 80 | 100 | But-1-en-3-ol | [119] |
| [Ir(bmim)(η ⁴ -cod)(PTA)]Cl (124) | 28 ^j | 28 ^j | 80 | 28 | 1-Octen-3-ol | [119] |
| [(Cp [*] IrCl ₂) ₂] (125) ⁱ | 200 ^j | 100 ^j | RT | >99 | 5-Phenylpent-1-en-3-ol | [122] |

^a mixture H₂O/*n*-heptane; Vorg/Vaq = 1.

^b H₂O:Heptane 1:1.

^c H₂O:Toluene 3:1.

^d pH >11.

^e H₂O:Cyclohexane 1:1.

^f Heptane: H₂O 2:1.

^g H₂O:Toluene 2:1.

^h Solvent: THF.

ⁱ Acetone:H₂O 2:1.

^j Calculated from the reference, TOF calculated for the first cycle.

^k Water:*n*-octane 1:1.

[Ir(bmim)(η⁴-cod)(PTA)]Cl (124), which catalyze the hydrogenation of alkenoic and oxo acids in aqueous solution but also the isomerization of alk-1-en-3-ols to the corresponding ketones at 80 °C in water. The isomerization reaction occurs without external reducing agent such as H₂. Under an argon atmosphere the reactions were fully selective to the corresponding ketone or aldehyde. Complex 6 was observed to be sensitive to the presence of phosphate buffer in the reaction medium as observed for other systems such as those catalyzed by Ru(II) complexes, as previously mentioned. It is interesting to point out that complex 6 catalyze the decomposition of aqueous formate to H₂ and bicarbonate.

The first Ir(III) complexes with catalytic properties for isomerization of allylic alcohols in water were presented in 2016 [120]. These complexes, [Cp^{*}Ir(H₂O)₃]SO₄ (125), [(Cp^{*}Ir)₂(OH)₃]OH (126), [(Cp^{*}IrCl₂)₂] (127) and [(Cp^{*}IrI₂)₂] (128) are commercially available and not too much expensive. These complexes are able to isomerize primary and *sec*-allylic alcohols under very mild reaction conditions. XAS and MS spectroscopy suggested that the process requires to be previously activated by a halide.

Allylic alcohols with mono-, di-, and trisubstituted double bonds were isomerized in water and in some cases even at room temperature and under air with excellent conversions and TOF in temperature range from 60 °C to 100 °C and variable time from 0.5 h to more than 48 h. It is important to stress that natural allylic alcohols like morphine were isomerized in mild conditions under air in a short time (Scheme 39).

The study of the reactions suggest that the catalytic isomerization process fits better with a mechanism via enone intermediates in which is formed in the first process step an {Ir@(allyl alkoxy)} intermediate (Scheme 40). Nevertheless, to justify the isotopic distribution on the final compound to different pathways in this mechanism (a and b) must be considered. Experiments of XAS and MS showed that the mechanism is the same for all alcohols studied but subtle changes in the reaction conditions and with the structure of the alcohols are produced.

4. Conclusions and perspective

The isomerization of allylic alcohols mediated by water soluble homogeneous transition metal catalysts offers a versatile and elegant route to various substituted aldehydes and ketones. Only recently, have significant advances been made in the use of water as an isomerisation reaction media despite the fact that for more than 60 years the isomerisation of allylic alcohols to ketones has

been studied. As a result, there is economic interest in eco-benign catalyzed isomerisation of allylic alcohols in water. Generally, water in the reaction media provides larger yield, reactivity and mild reaction conditions than in dry solvents. Additionally, the catalyst recycling that is possible in water and water/organic systems and the facility of separation of the products, made the isomerisation in water an economical and eco-benign synthetic procedure.

Nevertheless, at the moment only Ru, Rh and Ni, Pd, Os and Ir complexes have been shown to be catalytically active for the isomerisation of allylic alcohols in water. The isomerization process usually is strongly dependence upon the substitution on the C=C allyl alcohol bond. The reaction becomes more difficult as the number of substituents increases on the double bond. Nevertheless, interesting and useful catalyzed isomerisation processes of substituted allyl alcohols were presented (a comparison of all the catalysts mentioned in this review is reported in Table 12). The isomerisation mechanisms in water have been proposed to be the same as those in organic solvents in the base of several elegant studies. Excellent indications have been obtained concerning the inter-/intra-molecular characteristics of the isomerization but it is very clear that in many reported examples, complementary studies are necessary to allow in depth understanding of their mechanism.

There are no examples for asymmetric allylic alcohol isomerization in water catalyzed only by metal complexes, but it can be expected that a novel and more efficient generation of catalysts will be developed soon. Such derivatives could allow a routine use in synthesis of this economical and powerful transformation, especially for the multistep preparation of natural as well as non-natural, products. The synthetic processes in water catalyzed by aqueous organometallic chemistry has broad applications and a bright future.

Uncited reference

[88].

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ccr.2019.04.012>.

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