DOI: 10.1002/adsc.200606115

Water-Soluble Group 8 and 9 Transition Metal Complexes Containing a Trihydrazinophosphaadamantane Ligand: Catalytic Applications in Isomerization of Allylic Alcohols and Cycloisomerization of (*Z*)-Enynols in Aqueous Medium

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Received: March 17, 2006; Accepted: June 20, 2006

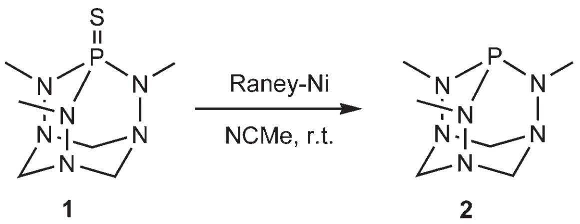
Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: An optimized synthesis of the 2,4,10-trimethyl-1,2,4,5,7,10-hexaaza-3-phosphatricyclo-[3.3.1.1^{3,7}]decane ligand (THPA) is described. It readily reacts with the dimers [{RuCl(μ-Cl)(η^6-arene)}$_2$] and [{MCl(μ-Cl)(cod)}$_2$] to yield the corresponding mononuclear complexes [RuCl$_2$(THPA)-(η^6-arene)] [arene = C_6H_6 (**4a**), *p*-cymene (**4b**), 1,3,5-$C_6H_3Me_3$ (**4c**), C_6Me_6 (**4d**)] and [MCl(THPA)(cod)] [M = Rh (**7a**), Ir (**7b**)], respectively. Treatment of **4a** and **b** with MeOTf affords the cationic derivatives [RuCl$_2$(THPA-Me)(η^6-arene)][OTf] {arene = C_6H_6 (**5a**), *p*-cymene (**5b**); THPA-Me = 1,2,4,10-tetramethyl-2,4,5,7,10-pentaaza-1-azonia-3-phosphatricyclo-[3.3.1.1^{3,7}]decane}. The arene-ruthenium(II) complexes **4a–d** and **5a** and **b** are efficient catalysts for the redox isomerization of allylic alcohols into carbonyl compounds in both THF and aqueous media. The catalytic systems can be recycled by a simple extraction process and used in up to 4 consecutive runs. All the water-soluble complexes prepared in this work are able to promote the cycloisomerization of (*Z*)-enynols to afford furans in water, the best performance being obtained with the iridium catalyst **7b**. Furthermore, **7b** has shown an excellent recyclability (10 runs). This study represents the first example of iridium-catalyzed cycloisomerization of (*Z*)-enynols.

Keywords: allylic alcohols; enynols; isomerization; P donor ligands; ruthenium; water-soluble

Introduction

Aqueous organometallic chemistry has received a great deal of attention in recent years due to the many advantages that an aqueous medium presents for both stoichiometric and catalytic processes.[1] The main interest in using water as solvent stems from its abundance, low cost and non-toxic nature, all these characteristics fulfilling the green chemistry's principles.[2] In addition, its immiscibility with many organic compounds allows the easy separation of the reaction products from the water-soluble catalyst by simple decantation or extraction processes. Moreover, the catalyst solution recovered can be re-used in further catalytic cycles, minimizing the overall cost of the processes. With the aim to develop new catalytic systems active in water, the syntheses of a great variety of water-soluble ligands, especially phosphanes, have been reported.[3] Nevertheless, the catalytic applications of most of these ligands remain limited, with the exception of aryl-sulfonated phosphines (e.g., TPPMS, TPPTS, TPPDS) which have been extensively studied in catalysis.[1,3] Recently, the cage-like water-soluble phosphine 1,3,5-triaza-7-phosphaadamantane[4] (PTA) has received an increasing attention and a variety of ruthenium and rhodium PTA-complexes have appeared to be promising catalysts in aqueous media.[5] In this context, some of us reported in 1982 the synthesis of the closely related trihydrazinophosphaadamantane ligand THPA (**2** in Scheme 1) by desulfuration of the readily available thiophosphane **1**.[6] Surprisingly, despite its great potential, the coordination chemistry of this water-soluble ligand has been completely neglected, $[Fe(CO)_4(THPA)]$ being the only transition-metal complex reported till now in the literature.[7]



Scheme 1. Synthesis of the THPA ligand **2**.

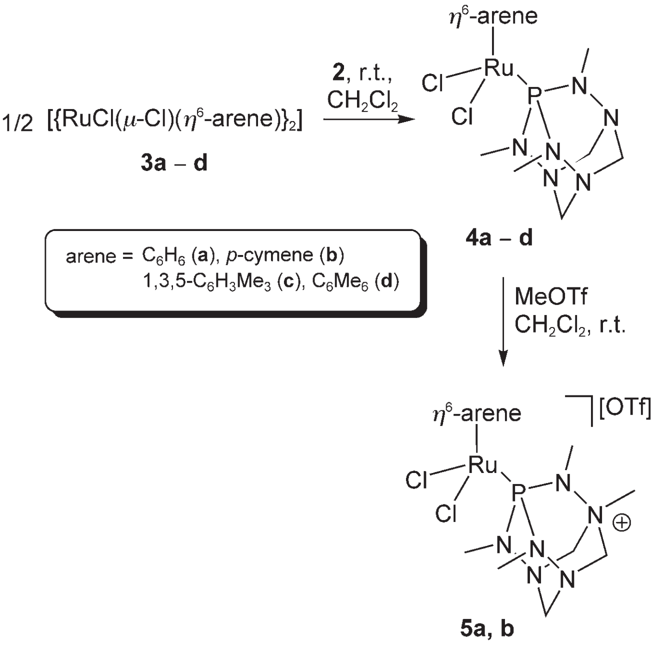
With all these precedents in mind and stimulated by the increasing demand for novel, efficient water-soluble catalysts, we decided to explore the coordination chemistry and the catalytic applications of the THPA ligand, starting from an optimized synthesis of THPA as well as the preparation of the first ruthenium, rhodium and iridium complexes containing this P donor ligand. They have proved to be soluble in organic solvents and in water, and have been successfully used to promote the catalytic isomerization of allylic alcohols into carbonyl compounds in both THF and aqueous media. They are also active catalysts in the cycloisomerization of (*Z*)-enynols into furans in aqueous media. Since only one water-soluble catalyst has been reported to date,[8] they provide new opportunities to perform this transformation in water.

Results and Discussion

Synthesis of THPA and its Water-Soluble Complexes

As commented above, the trihydrazinophosphaadamantane ligand THPA (**2**) can be easily obtained by desulfuration of the thiophosphane 4,6,9-trimethyl-5-thio-1,3,4,6,7,9-hexaaza-5-phosphatricyclo[3.3.1.1^{3,7}]-decane (**1**), which is readily accessible in a multigram-scale through the reaction of $S{=}PCl_3$ with methylhydrazine and further treatment with formaldehyde. Nevertheless, in our original preparation of **2** the desulfuration process required the use of a large excess of tri-*n*-butylphosphane, which acts both as reducing agent and solvent, as well as an extremely long reaction time (15 days), making the synthesis rather tedious.[6b] Fortunately, we recently found that this reduction step can be considerably shortened by treating **1** with Raney nickel in acetonitrile at room temperature (Scheme 1), in this case only 15 h are required.[6c] This method gives **2** as an air-stable white powder in 80 % yield.

Treatment of dimers $[\{RuCl(\mu\text{-}Cl)(\eta^6\text{-arene})\}_2]$ [arene $= C_6H_6$ (**3a**),[9] *p*-cymene (**3b**),[10] 1,3,5-$C_6H_3Me_3$ (**3c**),[9] C_6Me_6 (**3d**)[10]] with a two-fold excess of the THPA ligand **2** affords the corresponding mononuclear complexes $[RuCl_2(THPA)(\eta^6\text{-arene})]$ [arene $= C_6H_6$ (**4a**), *p*-cymene (**4b**), 1,3,5-$C_6H_3Me_3$ (**4c**), C_6Me_6 (**4d**)], isolated as air-stable orange solids in 73–85 % yield, *via* the expected cleavage of the chloride bridges (Scheme 2). Analytical and spectroscopic data confirm the proposed formulation (see Supporting Information). In particular, the P coordination of the ligand to ruthenium is clearly assessed in the $^{31}P\{^1H\}$ NMR spectra by a downfield shift of the phosphorus resonance with respect to the free ligand [$\delta = 123.4$ (**4a**), 128.1 (**4b**), 126.4 (**4c**), 126.7 (**4d**) *vs.* 101.8 (**2**)]. In addition, the structure of **4b** has been unambiguously confirmed by a single crystal X-ray diffraction study (Figure 1). The molecule displays the characteristic pseudooctahedral "three-legged piano-stool" geometry, the observed bond distances and angles around the metal comparing well to those found in the related PTA derivatives $[RuCl_2(PTA)(\eta^6\text{-}p\text{-cymene})]$[11] and $[RuCl_2(PTA)(\eta^6\text{-}C_6H_6)]$.[12]



Scheme 2. Synthesis of the ruthenium complexes **4a–d** and **5a**, **b**.

It is well-known that the *N*-protonated or alkylated forms of PTA can also act as ligands, the affinity for water of the resulting cationic complexes being enhanced when compared to that of the neutral counter-

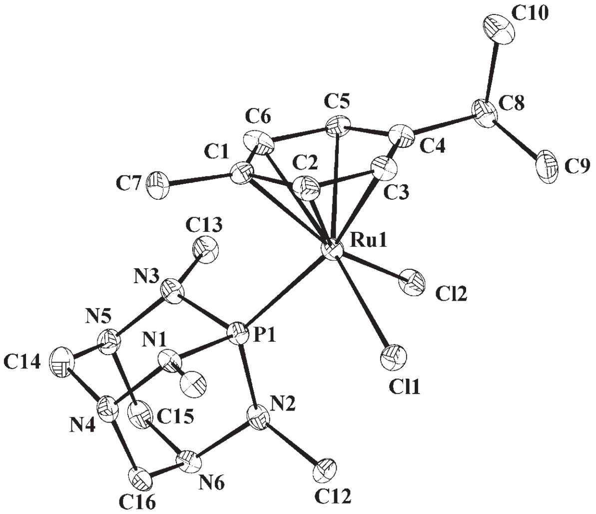


Figure 1. ORTEP-type view of the structure of [RuCl$_2$(THPA)(η^6-*p*-cymene)] (**4b**). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): Ru–Cl(1) = 2.4121(19); Ru–Cl(2) = 2.4110(17); Ru–P = 2.294(2); Cl(1)–Ru–Cl(2) = 88.03(7); Cl(1)–Ru–P = 89.70(7); Cl(2)–Ru–P = 88.14(7); P–N$_{(average)}$ = 1.706 (±0.01); N–N$_{(average)}$ = 1.432 (±0.01); N–CH$_{2(average)}$ = 1.475 (±0.01); N–CH$_{3(average)}$ = 1.474 (±0.01).

parts.[5] In this context, we have found that treatment of [RuCl$_2$(THPA)(η^6-arene)] [arene = C$_6$H$_6$ (**4a**), *p*-cymene (**4b**)] with a large excess of methyl triflate leads to the high-yield formation (70–89%) of the cationic complexes [RuCl$_2$(THPA-Me)(η^6-arene)][OTf][13] [arene = C$_6$H$_6$ (**5a**), *p*-cymene (**5b**)], as the result of the selective methylation of one of the bridgehead nitrogen atoms of the tricyclic ligand skeleton (Scheme 2). The structure of **5a** has been unequivocally confirmed by an X-ray diffraction study (see Figure 2), the main structural parameters within the ligand framework remaining almost unchanged when compared to those found in the neutral complex **4b**.[14]

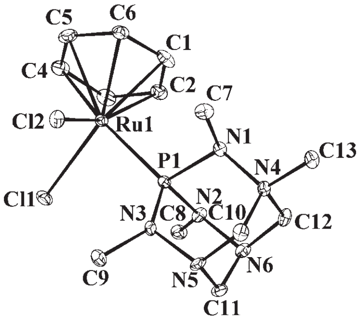
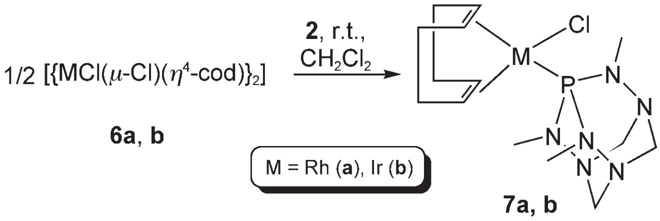


Figure 2. ORTEP-type view of the structure of the cation [RuCl$_2$(THPA-Me)(η^6-C$_6$H$_6$)]$^+$ (**5a**). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): Ru–Cl(1) = 2.4025(18); Ru–Cl(2) = 2.4005(19); Ru–P = 2.2791(18); Cl(1)–Ru–Cl(2) = 87.83(7); Cl(1)–Ru–P = 87.52(6); Cl(2)–Ru–P = 89.39(6); P–N$_{(average)}$ = 1.701 (±0.04); N–N$_{(average)}$ = 1.472 (±0.02); N–CH$_{2(average)}$ = 1.481 (±0.05); N–CH$_{3(average)}$ = 1.459 (±0.03).

The coordination chemistry of the THPA ligand has been extended to Group 9 metals. Thus, the mononuclear derivatives [RhCl(THPA)(cod)] (**7a**) and [IrCl(THPA)(cod)] (**7b**), could be readily synthesized (68–86% isolated yields) from the reactions of **2** with the dimeric precursors [{RhCl(μ-Cl)(cod)}$_2$][15] (**6a**) and [{IrCl(μ-Cl)(cod)}$_2$][16] (**6b**), respectively (Scheme 3). The formation of the neutral iridium complex **7b** is noteworthy since it has been reported that, under similar reaction conditions, dimer **6b** reacts with the related PTA ligand to afford the cationic derivative [Ir(PTA)$_3$(cod)][Cl] exclusively.[17] Compounds **7a**, **b** have been characterized by means of elemental analyses, multinuclear NMR spectroscopy (details are given in the Supporting Information) and, in the case of the rhodium complex **7a**, by single-crystal X-ray diffraction methods (see Figure 3).



Scheme 3. Synthesis of the rhodium and iridium complexes **7a**, **b**.

All the complexes prepared in this work are soluble in common organic solvents (CH$_2$Cl$_2$, acetone, etc) and, as expected, are also soluble in water, making

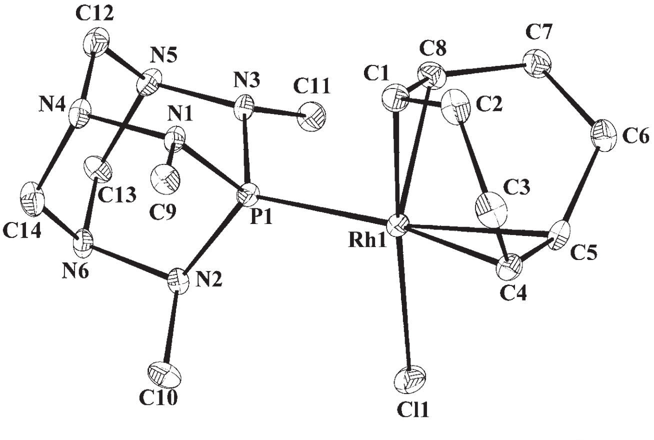
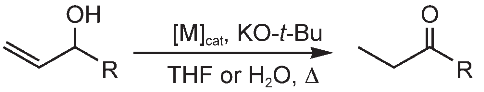


Figure 3. ORTEP-type view of the structure of [RhCl(THPA)(cod)] (**7a**). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): Rh–Cl = 2.3716(14); Rh–P = 2.2489(13); P–Rh–Cl = 95.25(5); P–N$_{(average)}$ = 1.696 (±0.01); N–N$_{(average)}$ = 1.463 (±0.02); N–CH$_{2(average)}$ = 1.475 (±0.01); N–CH$_{3(average)}$ = 1.461 (±0.01).

them suitable for catalytic studies both in organic and aqueous media.[18]

Isomerization of Allylic Alcohols into Ketones in Organic and Aqueous Media

The isomerization of allylic alcohols promoted by transition metal complexes represents a straightforward synthetic route to the corresponding saturated carbonyl compounds (Scheme 4).[19] This process, which proceeds with a total atom economy, can be catalyzed by Group 8, 9 and 10 metal derivatives,[19] and in particular by cyclopentadienyl-ruthenium complexes,[20] some of which are extremely efficient.[20b,d,e] Despite the great interest in the catalytic isomerization of allylic alcohols in synthesis, efforts to develop such a reaction in aqueous medium are still scarce.[21,22] In the context of our ongoing interest in studying this synthetically useful transformation in aqueous media,[21d–g] we have explored the catalytic activity of the THPA-based complexes.



Scheme 4. Catalytic isomerization of allylic alcohols.

First, the catalytic activity of the neutral arene-ruthenium(II) complexes **4a–d** has been checked in the isomerization of 1-octen-3-ol into octan-3-one using THF as solvent (Table 1). In a typical experiment, 4 mmol of substrate, 1 mol% of catalyst, 5 mol% of KO-*t*-Bu and 20 mL of THF were heated at 75 °C and the reaction was monitored by GC analyses. Under these conditions, **4a–d** showed very high activities, the conversion being in all cases complete after only 5 min (entries 1–4; TOF = 1200 h^{-1}). In contrast, the neutral rhodium and iridium derivatives (**7a**, **b**) are, under the same reaction conditions, much less efficient (entries 5 and 6) requiring 17 and 2.5 h, respectively, to reach similar yields. Remarkably, at a lower catalyst loading (0.2 mol%), the results obtained using the ruthenium complexes **4a–d** are strongly dependent on the arene ligand. Thus, while the benzene and *p*-cymene derivatives (**4a**, **b**) remain very efficient (entries 7–8 in Table 1), a slow reaction or an incomplete conversion have been observed for the mesitylene (**4c**) and hexamethylbenzene complexes (**4d**), respectively (entries 9 and 10).[23]

Table 1. Comparison of the different THPA-based catalysts in the isomerization of 1-octen-3-ol into octan-3-one in THF.[a]

Entry	Catalyst	mol% Metal	Time	Yield [%]	TOF $[h^{-1}]$[b]
1	**4a**	1	5 min	100	1200
2	**4b**	1	5 min	100	1200
3	**4c**	1	5 min	100	1200
4	**4d**	1	5 min	100	1200
5	**7a**	1	17 h	99	6
6	**7b**	1	2.5 h	99	40
7	**4a**	0.2	15 min	100	2000
8	**4b**	0.2	30 min	100	1000
9	**4c**	0.2	1.25 h	100	400
10	**4d**	0.2	3 h	14	23

[a] Reactions carried out at 75 °C using 4 mmol of 1-octen-3-ol, 20 mL of THF, the catalyst and KO-*t*-Bu (base/catalyst ratio = 5).

[b] Turnover frequency ((mol product/mol catalyst)/time) was calculated at the time indicated in each case.

The most active catalysts, namely the ruthenium complexes **4a** and **4b**, have also been successfully employed in the isomerization of 1-hepten-3-ol (R = *n*-Bu), 1-hexen-3-ol (R = *n*-Pr), 1-penten-3-ol (R = Et) and α-vinylbenzyl alcohol (R = Ph) into the corresponding carbonyl compounds (Table 2). Notably, the quantitative conversion of α-vinylbenzyl alcohol into propiophenone can be achieved in only 5 min using a catalyst loading of 1 mol% (TOF = 1200 h^{-1}). This result is one of the best reported for this substrate.[19]

Table 2. Isomerization of various allylic alcohols catalyzed by **4a**, **b** in THF.[a]

Substrate	Catalyst	mol% Ru	Time	Yield [%]	TOF $[h^{-1}]$[b]
1-hepten-3-ol	**4a**	0.2	1.5 h	100	333
1-hepten-3-ol	**4b**	0.2	1.33 h	100	375
1-hexen-3-ol	**4a**	0.2	1.25 h	100	400
1-hexen-3-ol	**4b**	0.2	1 h	100	495
1-penten-3-ol	**4a**	0.2	1.5 h	100	333
1-penten-3-ol	**4b**	0.2	1.67 h	100	300
α-vinylbenzyl alcohol	**4a**	1	5 min	100	1200
α-vinylbenzyl alcohol	**4b**	1	5 min	100	1200

[a] Reactions carried out at 75 °C using 4 mmol of the corresponding allylic alcohol, 20 mL of THF, the catalysts and KO-*t*-Bu (Base/Ru ratio = 5).

[b] Turnover frequency [(mol product/mol Ru)/time] were calculated at the time indicated in each case.

Taking advantage of the hydro-solubility of our THPA-based catalysts, we extended the catalytic study to an aqueous medium. Firstly, we checked the catalytic activities of the neutral ruthenium complexes **4a–d** in the isomerization of 1-octen-3-ol into octan-3-one using water as solvent (Table 3). In order to compare the results with those obtained in THF, the experiments were carried out under the same experimental conditions, i.e., at 75 °C using 4 mmol of sub-

Table 3. Isomerization of 1-octen-3-ol into octan-3-one in water using the THPA-based Ru catalysts.[a]

Entry	Catalyst	With KO-*t*-Bu[b]			Without KO-*t*-Bu		
		Yield [%]	Time	TOF[c]	Yield [%]	Time	TOF[c]
1	**4a**	99	45 min	132	100	1 h	100
2	**4b**	99	1 h	99	100	1.25 h	80
3	**4c**	99	2 h	50	98	3.5 h	28
4	**4d**	100	3.5 h	29	71	9 h	8
5	**5a**	99	1 h	99	13	6 h	2
6	**5b**	99	30 min	200	96	5 h	19

[a] Reactions carried out using 4 mmol of 1-octen-3-ol, 20 mL of water, 1 mol% of catalyst.

[b] With 5 mol% of KO-*t*-Bu.

[c] Turnover frequency [(mol product/mol Ru)/time], in h^{-1}, was calculated at the time indicated in each case.

strate, 1 mol% of ruthenium, 5 mol% of KO-*t*-Bu and 20 mL of water.[24] Thus, as previously observed in THF, the reaction rates were found to be strongly dependent on the nature of the arene ligand, following the order: C_6H_6 (TOF = 132 h^{-1}) > *p*-cymene (TOF = 99 h^{-1}) > mesitylene (TOF = 50 h^{-1}) > hexamethylbenzene (TOF = 29 h^{-1}) (entries 1–4). Under the same conditions, the cationic ruthenium complexes **5a**, **b** are also active showing similar catalytic performances as those of their neutral counterparts **4a**, **b** (entries 5 and 6 *vs.* 1 and 2 in Table 3). It is interesting to note that both the neutral (**4a–d**) and cationic (**5a**, **b**) complexes remain able to promote the isomerization of allylic alcohols in the absence of base, in contrast with that observed in THF. This fact can be attributed in part to the higher polarity of water *vs.* THF which favors the dissociation of the Ru–Cl bond in complexes **4** and **5**.[25] Nevertheless, in the presence of base better catalytic efficiencies are observed. The most active catalysts, i.e., **4a**, **b** and **5a**, **b**, have also been checked in the isomerization of 1-hepten-3-ol, 1-hexen-3-ol, 1-penten-3-ol and α-vinylbenzyl alcohol in water (Table 4). In all the cases almost quantitative conversions were observed after only 0.75–3.5 h, pointing out the generality of this catalytic transformation in aqueous media.

The catalyst recycling has also been investigated using the isomerization of the 1-octen-3-ol into octan-3-one as a model reaction. Thus, we have found that, after a simple extraction process with hexane and diethyl ether (details are given in the Experimental Section), the catalysts **4a–b** and **5a–b** can be re-used in 2–4 subsequent cycles (see Table 5). The best results were obtained using the cationic complex **5a** which, in the fourth run, is still able to isomerize quantitatively 1-octen-3-ol into octan-3-one within 7 h.

Cycloisomerization of (*Z*)-Enynols into Furans in Aqueous Media

The synthesis of furans is of particular interest since they can be found in many naturally occurring compounds being also key structural units in several important pharmaceuticals as well as in flavor and fragrance compounds.[26] Furthermore, furans are useful and versatile building blocks in organic synthesis.[27] One of the most attractive synthetic routes for functionalized furan derivatives is based on the transition-metal-catalyzed cycloisomerization of (*Z*)-2-en-4-yn-

Table 4. Isomerization of various allylic alcohols catalyzed by **4a**, **b** and **5a**, **b** in water.[a]

Substrate	Catalyst	mol% Ru	Time	Yield [%]	TOF [h^{-1}][b]
1-hepten-3-ol	**4a**	1	1 h	98	98
1-hepten-3-ol	**4b**	1	1.5 h	99	66
1-hepten-3-ol	**5a**	1	1.5 h	95	63
1-hepten-3-ol	**5b**	1	45 min	99	132
1-hexen-3-ol	**4a**	1	2 h	96	48
1-hexen-3-ol	**4b**	1	2.5 h	98	39
1-hexen-3-ol	**5a**	1	1.17 h	99	85
1-hexen-3-ol	**5b**	1	1.5 h	96	64
1-penten-3-ol	**4a**	1	45 min	99	132
1-penten-3-ol	**4b**	1	2.5 h	96	38
1-penten-3-ol	**5a**	1	1.5 h	97	65
1-penten-3-ol	**5b**	1	3.5 h	100	26
α-vinylbenzyl alcohol	**4a**	2	2.5 h	95	19
α-vinylbenzyl alcohol	**4b**	2	2 h	99	50
α-vinylbenzyl alcohol	**5a**	2	45 min	97	129
α-vinylbenzyl alcohol	**5b**	2	2 h	99	50

[a] Reactions carried out at 75 °C using 4 mmol of the corresponding allylic alcohol, 20 mL of H_2O, the catalysts and KO-*t*-Bu (Base/Ru ratio = 5).

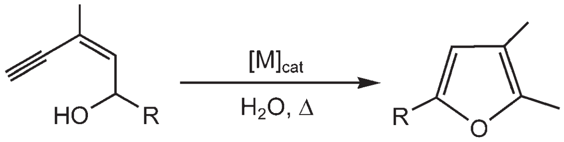
[b] Turnover frequency [(mol product/mol Ru)/time] was calculated at the time indicated in each case.

Table 5. Recycling of the catalysts **4a**, **b** and **5a**, **b** in the isomerization of 1-octen-3-ol into octan-3-one.[a]

Catalyst	Cycle	Time	Yield [%]
4a	1	45 min	99
	2	3 h	99
	3	4 h	4
5a	1	1 h	99
	2	2.5 h	99
	3	4.75 h	99
	4	7 h	99
	5	13.5 h	32
4b	1	1 h	99
	2	2 h	99
	3	5 h	83
5b	1	30 min	99
	2	2 h	99
	3	6 h	95

[a] Reactions carried out at 75 °C using 4 mmol of 1-octen-3-ol, 20 mL of H_2O, 1 mol% of catalyst and 5 mol% of KO-*t*-Bu.

1-ols (see Scheme 5), which are readily available starting materials.[28] Palladium,[29] gold[30] and especially ruthenium[31] catalysts have been successfully used to promote such a transformation. However, only one example has been performed in aqueous medium, the study being limited to the commercially available enynol (*Z*)-3-methylpent-2-en-4-yn-1-ol (R = H).[8] With these precedents in mind, we decided to explore the catalytic activity in water of our THPA-based complexes in such a cyclization process.



Scheme 5. Catalytic cycloisomerisation of (*Z*)-enynols.

The catalytic cycloisomerization reactions have been performed at 80 °C using 5 mmol of the enynol, 1 mol% of catalyst and 1 mL of water. Under these conditions, all the complexes synthesized, i.e., **4a–d**, **5a**, **b** and **7a**, **b**, were found to be able to convert (*Z*)-3-methylpent-2-en-4-yn-1-ol into 2,3-dimethylfuran (R = H; Scheme 5) with good yields. The results, which are summarized in Table 6, clearly evidence the higher efficiency of the iridium derivative **7b** with respect to its ruthenium (**4a–d/5a**, **b**) and rhodium (**7a**) counterparts, leading to a complete conversion of the substrate within only 1 h (96% yield of 2,3-dimethylfuran; determined by GC). Moreover, catalyst **7b** has shown an excellent recyclability allowing its use in 10 consecutive runs with only a slight decrease of the activity (Table 7). The recycling process can be performed by distillation of the 2,3-dimethylfuran under reduced pressure, or by a biphasic extraction of the product with hexane (details are given in the Experimental Section).

Table 6. Cycloisomerization of (*Z*)-enynols.[a]

R	Catalyst	Time	Yield [%]
H	**4a**	5 h	78
H	**4b**	5 h	93
H	**4c**	5 h	92
H	**4d**	5 h	77
H	**5a**	5 h	98
H	**5b**	6 h	92
H	**7a**	6 h	51
H	**7b**	1 h	96
Et	**7b**	30 min	99
n-Pr	**7b**	30 min	99
$CH_2CH{=}CH_2$	**7b**	30 min	99
$CH_2C(Me){=}CH_2$	**7b**	1 h	99
$C{\equiv}CSiMe_3$	**7b**	4.5 h	81

[a] Reactions carried out at 80 °C using 5 mmol of enynol, 1 mol% of catalyst and 1 mL of H_2O.

Table 7. Recycling of **7b** in the cycloisomerization of (*Z*)-3-methylpent-2-en-4-yn-1-ol.[a]

Cycle	Time [h]	Yield [%]
1	1	98
2	1.5	96
3	2	96
4	2	96
5	2.5	98
6	2.75	97
7	2.75	98
8	3.25	92
9	3.5	93
10	4	96

[a] Reactions carried out at 80 °C using 5 mmol of (*Z*)-3-methylpent-2-en-4-yn-1-ol, 1 mol% of **7b** and 1 mL of H_2O.

In order to evaluate the scope of the reaction, the cycloisomerization of (*Z*)-5-methylhept-4-en-6-yn-3-ol (R = Et), (*Z*)-6-methyloct-5-en-7-yn-4-ol (R = *n*-Pr), (*Z*)-6-methylocta-1,5-dien-7-yn-4-ol (R = $CH_2CH{=}CH_2$), (*Z*)-5-methyl-1-trimethylsilylhept-4-ene-1,6-diyn-3-ol (R = $C{\equiv}CSiMe_3$) and (*Z*)-2,6-dimethylocta-1,5-dien-7-yn-4-ol [R = $CH_2C(Me){=}CH_2$] catalyzed by the iridium derivative **7b** has been investigated (Table 6). For all these enynols, high conversions into the corresponding furans are achieved in 0.5–4.5 h. These results evidence the compatibility of the process with the presence of an additional alkene or alkyne functionality on the enynols. Only the isomerization of 5-methylhept-4-ene-1,6-diyn-3-ol (R = $C{\equiv}CH$), known to be a problematic substrate,[31b] has failed.

Conclusions

The syntheses of the first ruthenium, rhodium and iridium complexes containing the trihydrazinophosphaadamantane ligand THPA (**2**) have been described and the first catalytic studies are reported. All the complexes prepared, which are soluble in water as well as in common organic solvents, have shown a good activity in the catalytic isomerization of allylic alcohols into the corresponding ketones both in THF and water, the best results being obtained with the benzene and *p*-cymene ruthenium complexes **4a**, **b** and **5a**, **b**. Both neutral [$RuCl_2$(THPA)(η^6-arene)] (**4**), and cationic [$RuCl_2$(THPA-Me)(η^6-arene)][OTf] (**5**) ruthenium complexes as well as rhodium and iridium [MCl(THPA)(cod)] (M = Rh, Ir) (**7**) derivatives have shown to be efficient catalysts for the cycloisomerization of (*Z*)-2-en-4-yn-1-ols providing a general synthetic approach to functionalized furans in aqueous media. The best performances in terms of activity and recyclability (up to 10 cycles) have been obtained using the iridium catalyst **7b**. It is worthy of mention that this study represents the first example of an iridium-catalyzed cycloisomerization of (*Z*)-2-en-4-yn-1-ols.

In summary, we have demonstrated that the readily available trihydrazinophosphaadamantane THPA (**2**) is a suitable water-soluble ligand for the solubilization of transition metal catalysts in aqueous phase, representing an appealing alternative to the well-known and widely used 1,3,5-triaza-7-phosphaadamantane (PTA) ligand.

Experimental Section

General Remarks

The manipulations were performed under an atmosphere of dry nitrogen using vacuum-line and standard Schlenk techniques. Solvents were dried and distilled under nitrogen before use. GC and GC/MSD measurements were made on a Hewlett–Packard HP6890 apparatus (Supelco Beta-Dex^{TM} 120 column; 30 m, 250 μm) and a Agilent 6890N instrument coupled to a 5973 mass detector (HP-5MS column; 30 m, 250 μm), respectively.

Synthesis of THPA (2)

To a suspension of Ni-Raney (10 g) in 250 mL of acetonitrile, S=P($NMeNCH_2$)$_3$ (**1**) (0.75 g, 3.2 mmol) was added and the mixture stirred at room temperature overnight. After filtration, the solution was evaporated to dryness affording a white solid which was used without further purification. Yield: 0.52 g (80%). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 101.8 (s); ^1H NMR ($CDCl_3$): δ = 5.24 (d, 3H, $^2J_{HH}$ = 12.4 Hz, CH_2), 4.38 (d, 3H, $^2J_{HH}$ = 12.4 Hz, CH_2), 2.77 (d, 9H, $^3J_{PH}$ = 15.6 Hz, NMe); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 67.9 (d, $^3J_{PC}$ = 2.8 Hz, CH_2), 38.8 (d, $^2J_{PC}$ = 16.8 Hz, NMe).

General Procedure for the Catalytic Isomerization of Allylic Alcohols

Under an inert atmosphere, the catalyst precursor (0.2, 1 or 2 mol%), potassium *tert*-butoxide (1, 5 or 10 mol%), the allylic alcohol (4 mmol) and 20 mL of THF or deoxygenated water were introduced into a Schlenk tube fitted with a condenser. Then, the mixture was heated at 75 °C. The reaction was monitored by GC and GC/MSD, each 5 min during the first hour and then, the interval time was increased progressively.

Recycling procedure: After cooling the aqueous reaction mixture, the product was extracted twice with 20 mL of hexane and twice with 15 mL of diethyl ether. Then, traces of organic solvent were eliminated at reduced pressure. Substrate (4 mmol) was added and the mixture was heated again at the indicated temperature.

General Procedure for the Catalytic Cycloisomerization of (*Z*)-Enynols

Under an inert atmosphere, the catalyst precursor (1 mol%), the enynol (5 mmol) and 1 mL of deoxygenated water were introduced into a sealed tube. Then, the mixture was heated at 80 °C and the reaction was monitored by GC and GC/MSD.

Recycling procedure: After cooling the reaction mixture, the product was distilled at reduced pressure. Substrate (5 mmol) was added to the resulting aqueous solution and the mixture was heated again at the indicated temperature. The recycling can also be performed by successive extractions of the product with hexane.

Crystal Structure Determination

Crystallographic data for **4b**, **5a** and **7a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications Nos. CCDC 602040, 602039 and 602041, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44–1223/336–033; E-mail: deposit@ccdc.cam.ac.uk].

Supporting Information

Preparation and characterization of compounds **1**, **4**, **5** and **7**. Details of X-ray diffraction analyses of **4b**, **5a** and **7a**.

Acknowledgements

We are indebted to the Ministerio de Ciencia y Tecnología (MCyT) of Spain (Project BQU2003–00255) and the Gobierno del Principado de Asturias (Project PR-01-GE-6) for financial support. P.C. and V.C. thank the MCyT and the European Social Fund for "Ramón y Cajal" contracts. M.Z. thanks the Ministry of Science and Information Society Technologies Poland for financial support (Grant No. 3T09 A 158 29). A.E.D.A., M.Z. and J.P.M. thank the LEA (Laboratoire Européen Associé, Toulouse-Lodz) for financial support.

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