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Synthesis and catalytic applications of ruthenium(II)-phosphino-oxime complexes

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In this work, the preparation of the first ruthenium complexes containing a phosphino-oxime ligand is presented. Thus, the reaction of *cis*-[$RuCl_2(DMSO)_4$] (**3**) with 2.4 equivalents of 2-$Ph_2PC_6H_4CH$=NOH (**1**) in refluxing THF led to the clean formation of the octahedral ruthenium(II) derivative *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH$=NOH$\}_2$] (**5**), whose structure was unambiguously confirmed by means of a single-crystal X-ray diffraction study. Complex **5** could also be synthesized from the reaction of dimer [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (**4**) with an excess of **1** in refluxing toluene. Treatment of **4** with 2 equivalents of **1**, in CH_2Cl_2 at r.t., allowed also the preparation of the half-sandwich Ru(II) derivative [RuCl{κ^2-(*P,N*)-2-$Ph_2PC_6H_4CH$=NOH}(η^6-*p*-cymene)][PF_6] (**6**). In addition, complexes **5** and **6** proved to be active catalysts for the rearrangement of aldoximes to primary amides, as well as for the α-alkylation/reduction of acetophenones with primary alcohols, with the former showing the best performances in both processes.

Introduction

Hybrid ligands with hard nitrogen and soft phosphorus donor sites are highly valuable in coordination chemistry and homogeneous catalysis.[1] In this context, we recently described the preparation and X-ray crystal structures of the palladium(II) complexes [$PdCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH$=NOH$\}$] and [$Pd\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH$=NOH$\}_2$][Cl]$_2$ (**A** and **B** in Fig. 1), which proved to be efficient catalyst precursors for the rearrangement of aldoximes to primary amides in water.[2,3]

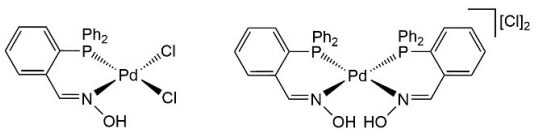

Fig. 1 Structure of the palladium(II) complexes **A** and **B**.

Remarkably, compounds **A** and **B** represent rare examples of transition metal complexes containing a phosphino-oxime as ancillary ligand. Indeed, prior to our work, only two representatives had been reported in the literature by Morris group, namely [M(COD)$\{\kappa^2$-(*P,N*)-Cy_2PCH_2CH=NOH$\}$][PF_6] (M = Rh, Ir; COD = 1,5-cyclooctadiene), both showing catalytic activity in the hydrogenation of cyclooctene.[4] Wan and co-workers also described a series of copper-catalyzed arylation reactions of amines[5] and thiols,[6] as well as palladium-catalyzed Suzuki-Miyaura cross-coupling processes,[7] employing 2-$R_2PC_6H_4CH$=NOH (R = Ph, Cy) and their respective oxides as auxiliary ligands (albeit without isolation of the corresponding metal complexes). As already indicated in our previous work, the low interest aroused by this type of ligands is quite surprising since oximes (both ketoximes and aldoximes) present a rich coordination chemistry.[8] It is also striking that, despite being commercially available from different chemical suppliers at a relatively low price,[9] there are no additional works to those of Wan and ours with the phosphino-aldoxime ligand 2-$Ph_2PC_6H_4CH$=NOH (**1**). This fact contrasts with the rich chemistry shown by its phosphino-aldehyde precursor 2-$Ph_2PC_6H_4CHO$,[10,11] and structurally related phosphino-imine ligands 2-$Ph_2PC_6H_4CH$=NR (R = aryl or alkyl group), which have been coordinated to a broad range of transition metals and have found application in multitude of catalytic transformations.[12]

Herein, we give new evidences of the enormous synthetic potential of the phosphino-oxime 2-$Ph_2PC_6H_4CH$=NOH (**1**). In particular, we describe the preparation of the first ruthenium complexes containing this ligand, and their successful application in the catalytic rearrangement of aldoximes to amides,[3] as well as in the α-alkylation/reduction of acetophenones with primary alcohols.[13]

Results and discussion

Some years ago, our group described the preparation of different five- (**C**) and six-coordinate (**D-E**) ruthenium(II)

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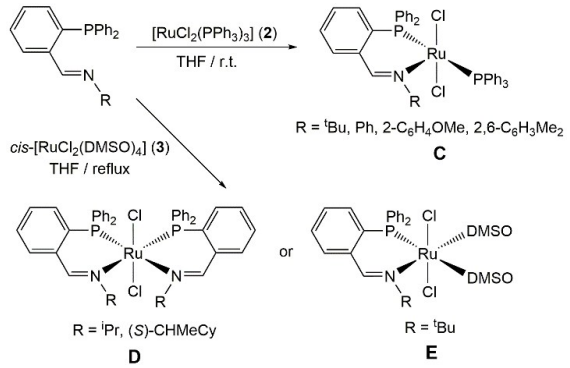
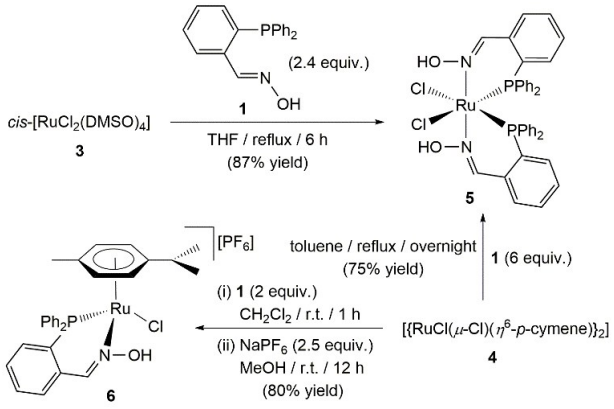
† Electronic Supplementary Information (ESI) available: Copies of the NMR spectra of the amides and alcohols synthesized in this work. CCDC 1468182 (**5**). See DOI: 10.1039/x0xx00000x

complexes containing chelated phosphino-imine 2-$Ph_2PC_6H_4CH$=NR (R = aryl or alkyl group) ligands from their reactions with compounds $[RuCl_2(PPh_3)_3]$ (**2**) and *cis*-$[RuCl_2(DMSO)_4]$ (**3**), respectively (Scheme 1).[14]



Scheme 1 Synthesis of the ruthenium(II) complexes **C**-**E**.

Based on these previous studies, we decided to explore the reactivity of $[RuCl_2(PPh_3)_3]$ (**2**) and *cis*-$[RuCl_2(DMSO)_4]$ (**3**) towards the phosphino-aldoxime 2-$Ph_2PC_6H_4CH$=NOH (**1**). In the case of complex **2**, it readily reacted with **1** in THF at r.t. to generate, regardless of the stoichiometry employed (from 1:1 to 1:4), a complex mixture of unidentified products. Unfortunately, all purification attempts by crystallization or column chromatography did not allow the separation of the products formed (extensive decomposition was observed by column chromatography). The use of other solvents (CH_2Cl_2, MeOH or toluene) or higher temperatures (refluxing conditions) did not lead to better results. In marked contrast, the treatment of *cis*-$[RuCl_2(DMSO)_4]$ (**3**) with 2.4 equiv. of **1** in refluxing THF resulted in the clean formation of the octahedral-ruthenium(II) derivative $[RuCl_2\{\kappa^2$-(P,N)-2-$Ph_2PC_6H_4CH$=NOH$\}_2]$ (**5**), which could be isolated in 87% yield (Scheme 2). It is worthy of noting that the same reaction performed with only 1 equiv. of **1** did not allow the preparation of a monophosphine complex analogous to **E** (Scheme 1). Instead, the reaction led to the formation of a mixture of **5** and the unreacted precursor **3**.



Scheme 2 Synthesis of the ruthenium(II) complexes **5** and **6**.

Complex **5** was characterized by means of spectroscopic methods (IR, Far-IR, and $^{31}P\{^1H\}$, ^1H and $^{13}C\{^1H\}$ NMR spectroscopy) and elemental analysis (details are given in the Experimental section). The spectroscopic data showed that only one of the five possible stereoisomers is formed (Fig. 2).

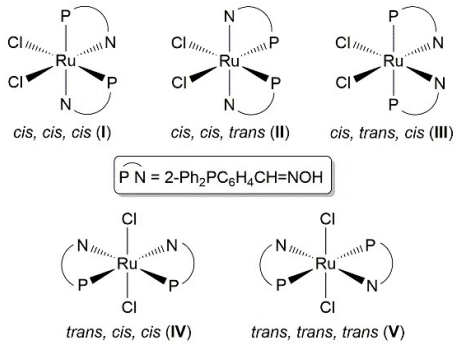


Fig. 2 Possible isomers for complex $[RuCl_2\{\kappa^2$-(P,N)-2-$Ph_2PC_6H_4CH$=NOH$\}_2]$ (**5**).

The presence of a single singlet signal in the $^{31}P\{^1H\}$ NMR spectrum of **5** at δ_P 51.9 ppm allowed to discard the all *cis* stereoisomer **I**. On the other hand, the Far-IR spectrum showed two $\nu_{Ru\text{-}Cl}$ absorptions at 322 and 263 cm^{-1}, consistent with a *cis* dichloride complex.[15] Consequently, isomers **IV**, *i.e.* the analogue of complexes **D** previously obtained in the reaction of **3** with phosphino-imines 2-$Ph_2PC_6H_4CH$=NR (^{i}Pr, (*S*)-CHMeCy), and **V** were ruled out (a single $\nu_{Ru\text{-}Cl}$ absorption would be expected for these stereoisomers).[14b,15] Concerning the ^1H and $^{13}C\{^1H\}$ NMR spectra, the former showed broad signals at 8.52 and 11.27 ppm for the CH=N and OH protons of the phosphino-aldoxime ligand, and the latter the inequivalence of the phenyl rings of the PPh_2 units, along with a characteristic singlet signal for the iminic CH=N carbon at δ_C 154.5 ppm. Since these spectroscopic data did not allow to distinguish between stereoisomer **II** and **III**, to determine unambiguously the stereochemistry of **5**, an X-ray diffraction study was carried out. X-ray quality crystals were obtained by slow diffusion of diethyl ether into a saturated solution of the complex in THF. An ORTEP diagram of the molecule, along with selected structural parameters, is shown in Fig. 3. The ruthenium atom is in a slightly distorted octahedral environment with the two chloride ligands and PPh_2 units each mutually *cis* oriented (Cl(1)-Ru-Cl(2) = 84.28(3)° and P(1)-Ru-P(2) 98.21(3)°), and the oxime groups mutually *trans* disposed (N(1)-Ru-N(2) 171.9(1)°), *i.e.* the *cis,cis,trans* stereoisomer **II** was formed in the reaction. The observed bond distances for the aldoxime units (C(7)-N(1) 1.279(4) Å, C(27)-N(2) 1.273(4) Å, N(1)-O(1) 1.404(3) Å and N(2)-O(2) 1.395(4) Å) were almost identical to those previously found in the solid-state crystal structures of the palladium(II) complexes $[PdCl_2\{\kappa^2$-(P,N)-2-$Ph_2PC_6H_4CH$=NOH$\}]$ (**A** in Fig. 1; C-N = 1.27(1) Å and N-O = 1.39(1) Å) and $[Pd\{\kappa^2$-(P,N)-2-$Ph_2PC_6H_4CH$=NOH$\}_2][Cl]_2$ (**B** in Fig. 1; C-N = 1.275(4) Å and N-O = 1.389(5) Å).[2] On the other hand, the close proximity of the hydroxyl-oxime functions to the chloride ligands enabled the establishment of intramolecular hydrogen bonds between both groups.[16] The distances and angles of the O(1)-H(1o)···Cl(1) and O(2)-H(2o)···Cl(2) contacts (O(1)-H(1o) = 1.030 Å, H(1o)-Cl(1) = 1.979 Å, O(1)-Cl(1) = 2.974 Å and O(1)-H(1o)-Cl(1) = 161.37°; O(2)-H(2o) = 0.849 Å, H(2o)-

Cl(2) = 2.122 Å, O(2)-Cl(2) = 2.940 Å and O(2)-H(2o)-Cl(2) = 161.62°) indicate, according with the Jeffrey´s terminology,[17] that the intensity of these H-bond interactions is moderate (mostly electrostatic).

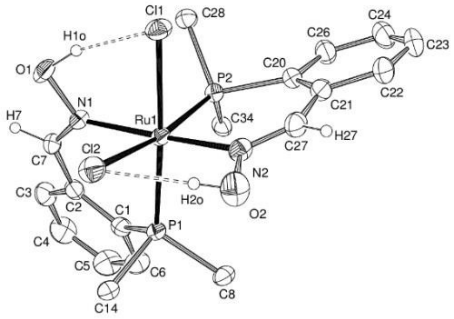


Fig. 3 ORTEP diagram of the structure of complex **5** showing the crystallographic labelling scheme. Phenyl groups of the PPh_2 fragments and hydrogen atoms, except those on O(1), O(2), C(7) and C(27), have been omitted for clarity. Thermal ellipsoids are drawn at 30% probability level. Selected bond lengths (Å): Ru-Cl(1) 2.4782(8), Ru-Cl(2) 2.4914(8), Ru-P(1) 2.2724(7), Ru-P(2) 2.2881(8), Ru-N(1) 2.056(3), Ru-N(2) 2.050(3), C(7)-N(1) 1.279(4), C(27)-N(2) 1.273(4), N(1)-O(1) 1.404(3), N(2)-O(2) 1.395(4). Selected bond angles (°): Cl(1)-Ru-Cl(2) 84.28(3), P(1)-Ru-P(2) 98.21(3), N(1)-Ru-N(2) 171.9(1), P(1)-Ru-N(1) 87.76(7), P(2)-Ru-N(2) 92.01(8), C(2)-C(7)-N(1) 126.5(3), C(7)-N(1)-Ru 135.0(2), C(7)-N(1)-O(1) 110.6(3), O(1)-N(1)-Ru 114.3(2), C(21)-C(27)-N(2) 127.8(3), C(27)-N(2)-Ru 133.4(2), C(27)-N(2)-O(2) 109.9(3), O(2)-N(2)-Ru 115.9(2).

As shown in Scheme 2, complex *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**) could be alternatively synthesized by reacting the arene-ruthenium(II) dimer [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (**4**) with an excess (6 equiv.) of the phosphino-aldoxime ligand 2-$Ph_2PC_6H_4CH{=}NOH$ (**1**) in refluxing toluene (75% isolated yield).[18] Dimer **4** also readily reacted with 2 equiv. of **1**, in dichloromethane at r.t., to generate the cationic species [RuCl{κ^2-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH$}(η^6-*p*-cymene)][Cl]. This complex was isolated as the corresponding hexafluorophosphate salt **6** in 80% yield after Cl^-/PF_6^- counter-anion exchange with a methanolic solution of $NaPF_6$. Characterization of **6** was straightforward by following its analytical and spectroscopic data (details are given in the Experimental section). Key spectroscopic features are: (*i*) ($^{31}P\{^1H\}$ NMR) a singlet resonance at δ_P 38.9 ppm, consistent with the coordination of the PPh_2 unit to the metal ($\Delta\delta$ = 53 ppm with respect to the free ligand), and (*ii*) (^1H and $^{13}C\{^1H\}$ NMR) the presence of characteristic resonances for the aldoxime CH=NOH protons and carbon at δ_H 8.90 (dd, $^4J_{PH}$ = 13.5 Hz, $^4J_{HH}$ = 2.1 Hz, CH=N) and 12.54 (d, $^4J_{HH}$ = 2.1 Hz, OH) ppm, and δ_C 172.0 (d, $^3J_{PC}$ = 8.2 Hz) ppm, respectively.

The catalytic potential of the new ruthenium complexes *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**) and [RuCl{κ^2-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH$}(η^6-*p*-cymene)][PF_6] (**6**) was subsequently explored. In particular, given the good results obtained with the palladium(II) derivatives **A** and **B** (Fig. 1) in the rearrangement of aldoximes to primary amides in water,[2] we initially focused on this catalytic transformation. It should be mentioned at this point that, despite several late-transition metal catalysts able to promote rearrangement of aldoximes to amides are already known,[3] examples active in aqueous media still remain scarce.[19] To our delight, employing the same experimental conditions to those used previously with palladium (pure water, 100 °C and a metal loading of 5 mol%),[2] both complexes were able to promote the rearrangement of commercially available (*E*)-benzaldoxime, providing benzamide in ≥ 85% yield (entries 1 and 2 in Table 1). The best results were obtained with the octahedral derivative **5**, which was able to generate benzamide in 94% GC-yield after only 5 h (entry 1). In the reaction, the substrate was totally consumed and only a small amount of the intermediate benzonitrile (*ca.* 5%) was present in the crude.[20] The catalytic activity found for complex **5** compares favorably with that of the palladium complexes **A** and **B**, which required 24 h to generate the amide in similar yields.[2] Reduction of the catalyst loading to 3 mol% still produced benzamide in 93% GC-yield, although in this case the reaction rate decreased considerably (entry 3). The same happened when the reaction was carried out at 80 °C (entry 4). Compared with the arene-ruthenium(II) complexes **F-H** (Fig. 4), which are the only ruthenium catalysts active in pure water previously reported in the literature, the effectiveness of **5** was very similar to that of **F-G** (98% GC-yield of benzamide after 5-6 h of heating at 100 °C with 5 mol% of Ru)[19b,e] and slightly lower to that of **H** (93% GC-yield of benzamide after 7 h of heating at 100 °C with 3 mol% of Ru).[19c] As expected, a blank experiment in the absence of **5** showed no benzamide formation after 5 h of heating. On the other hand, as shown in entry 6, the precursor complex **3** was also active in the reaction under the same experimental conditions, but it showed a poorer selectivity.

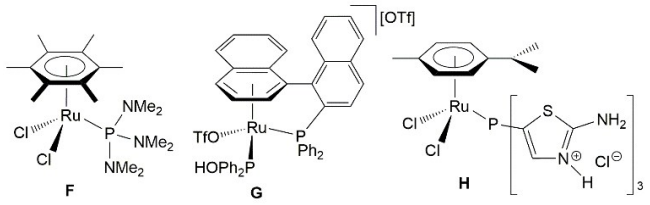
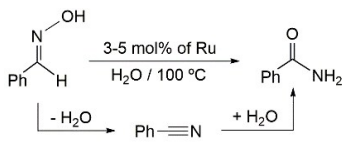


Fig. 4 Structure of the arene-ruthenium(II) complexes **F-H**.

Table 1 Catalytic rearrangement of (*E*)-benzaldoxime using the ruthenium(II) complexes **5** and **6**.[a]



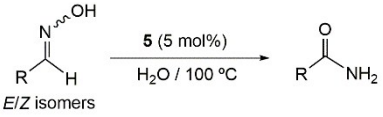
Entry	Catalyst	mol % of Ru	t (h)	Conv. (%)[b]	Yield (%)[b]
1	**5**	5	5	> 99	94
2	**6**	5	24	96	85
3	**5**	3	20	> 99	93
4[c]	**5**	5	16	> 99	90
5[d]	**6**	5	8	98	91
6	**3**	5	5	> 99	76

[a] Reactions were performed under Ar atmosphere starting from 1 mmol of the (*E*)-benzaldoxime (0.33 M in water). [b] Determined by GC (uncorrected GC areas). Differences between GC conversions and yields correspond to the intermediate benzonitrile present in the reaction mixture. [c] Reaction performed at 80 °C. [d] Reaction performed in presence of 5 mol% of $AgSbF_6$.

On the other hand, the lower reactivity of the half-sandwich complex **6** *vs* **5** can be rationalized in terms of its cationic nature, which disfavors the generation of a vacant site on the metal by dissociation of the chloride ligand.[21] In complete accord with this, a marked increase in activity was observed when the rearrangement of (*E*)-benzaldoxime was performed with **6** in the presence of a Ag(I) salt (entry 5 *vs* 2).

The versatility of the most active catalyst *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**) was subsequently explored using an array of other aromatic, heteroaromatic, aliphatic and *α,β*-unsaturated aldoximes.[22] As shown in Table 2, the corresponding amide products were obtained in all the cases in good yields (≥ 91% by GC; ≥ 77% isolated yield after chromatographic purification). For the family of substituted benzaldoximes, influence of the electronic properties of the aryl rings on the activity of **5** was observed, those containing electron-withdrawing groups reacting faster (entries 2-8 *vs* 9-13). On the other hand, as expected on the basis of steric grounds, *ortho*-substituted substrates showed a lower reactivity compared to their *meta*- and *para*-substituted counterparts (entry 3 *vs* 4-5 and entry 9 *vs* 10-11).

Table 2 Catalytic rearrangement of aldoximes using the octahedral Ru(II) complex *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**).[a]

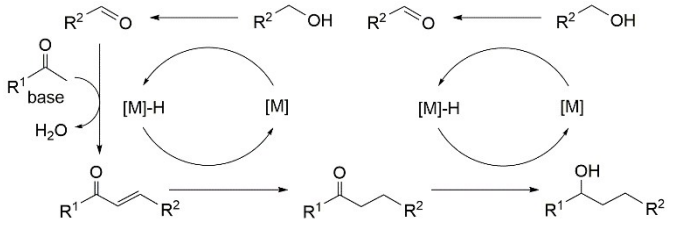


Entry	Aldoxime	t (h)	Conv. (%)[b]	Yield (%)[b]
1	R = Ph	5	> 99	94 (83)
2	R = 4-C_6H_4F	4	> 99	98 (89)
3	R = 2-C_6H_4Cl	5	> 99	96 (83)
4	R = 3-C_6H_4Cl	3	> 99	96 (83)
5	R = 4-C_6H_4Cl	3	> 99	97 (88)
6	R = 4-C_6H_4Br	4	> 99	95 (86)
7	R = C_6F_5	2	> 99	98 (90)
8	R = 4-$C_6H_4NO_2$	2	> 99	96 (86)
9	R = 2-C_6H_4Me	12	> 99	94 (82)
10	R = 3-C_6H_4Me	6	> 99	98 (89)
11	R = 4-C_6H_4Me	7	> 99	93 (84)
12	R = 4-C_6H_4OMe	9	> 99	91 (75)
13	R = 4-C_6H_4SMe	7	> 99	94 (85)
14	R = 2-Pyridyl	24	> 99	91 (77)
15	R = 3-Pyridyl	6	> 99	96 (86)
16	R = *n*-C_6H_{13}	5	> 99	95 (84)
17	R = Cy	5	> 99	92 (79)
18	R = (*E*)-CH=CHPh	8	> 99	93 (80)

[a] Reactions were performed under Ar atmosphere starting from 1 mmol of the corresponding aldoxime (0.33 M in water). [b] Determined by GC (uncorrected GC areas), isolated yields after work-up are given in brackets. Differences between GC conversions and yields correspond to the intermediate nitrile present in the crude reaction mixture.

Remarkably, complex *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**) was able to rearrange pyridine-2-carbaldoxime, a challenging substrate given its tendency to form catalytically inert metal-chelates (entry 14).[19b,g] However, compared to its 3-substituted isomer (entry 15), a longer reaction time was in this case required to obtain the desired picolinamide in high yield.

To further expand the catalytic utility of complex **5** we also explored its behaviour in one C-C bond forming reaction; the *α*-alkylation/reduction of acetophenones with primary alcohols. The *α*-alkylation of methyl-ketones employing alcohols as alkylating agents has been extensively studied in the last years with both homo- and heterogeneous catalysts, and represents a nice example of the borrowing hydrogen methodology (also known as hydrogen autotransfer methodology).[23] The process involves the initial catalytic oxidation of the primary alcohol into the corresponding aldehyde, which subsequently undergoes aldol condensation with the methyl-ketone substrate to generate an enone. Final catalytic reduction of the enone furnishes the saturated *α*-alkylated ketone product (Scheme 3).

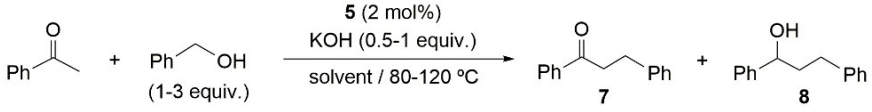


Scheme 3 The *α*-alkylation and the *α*-alkylation/reduction of methyl-ketones with primary alcohols.

Despite its great synthetic potential for the preparation of secondary alcohols, a similar process in which the *α*-alkylated ketone product is reduced in an additional step has been comparatively much less studied (Scheme 3).[13] With regard to the use of ruthenium catalysts, Cho and co-workers reported the selective *α*-alkylation/reduction of both aryl and alkyl methyl-ketones with different primary alcohols employing 5 mol% of [$RuCl_2(PPh_3)_3$] (**2**), 3 equiv. of the alcohol, and KOH as the base (3 equiv.). The reactions, which were performed in 1,4-dioxane at 80 °C for 40 h, delivered the desired saturated alcohols in 43-85% yield.[24] Yus and co-workers also demonstrated that, depending of the stoichiometry employed, either alkylated ketones or the corresponding saturated alcohols can be obtained using 2 mol% of the complex *cis*-[$RuCl_2(DMSO)_4$] (**3**) in combination with PPh_3 (2 mol%) and 1 equiv. of KOH in 1,4-dioxane at 80 °C. The saturated alcohols were isolated in 25-82% yield after 24 h when the primary alcohol was used in a two-fold excess relative to the methyl-ketone.[25,26]

With these precedents in mind, we initially checked the catalytic behaviour of complex *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**) in the *α*-alkylation/reduction of acetophenone with benzyl alcohol in 1,4-dioxane at 80 °C. Thus, as shown in Table 3, when the reaction was carried out with equimolar amounts of the reactants and KOH (1 equiv.) as the base, 24 h of heating were required to achieve a 96% conversion, the reaction affording a mixture of the desired 1,3-diphenylpropan-1-ol **8** and the intermediate *α*-alkylated ketone 1,3-diphenylpropan-1-one **7** in almost 1:1 ratio (entry 1). In addition, *ca.* 7% of 1-phenylethanol resulting from the conventional transfer hydrogenation (TH) of the acetophenone

Table 3 Catalytic α-alkylation/reduction of acetophenone with benzyl alcohol using *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**): Optimization of the reaction conditions.[a]



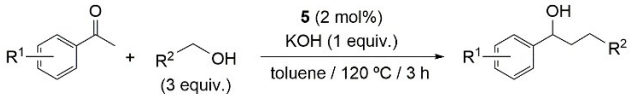
Entry	Equiv. of KOH	Equiv. of BnOH	T (°C)	Solvent	t (h)	Conv. (%)[b]	**7**/**8** yield (%)[b]	**7**/**8** ratio (%)[b]
1	1	1	80	1,4-dioxane	24	96	89[c]	47:42
2	1	2	80	1,4-dioxane	3 (24)	94 (> 99)	88 (94)[d]	65:23 (14:80)
3	1	3	80	1,4-dioxane	3 (24)	92 (> 99)	86 (94)[d]	63:23 (11:83)
4	1	1	120	toluene	24	> 99	> 99	50:50
5	1	2	120	toluene	3	> 99	> 99	22:78
6	1	3	120	toluene	3	> 99	> 99	13:87
7[e]	1	3	120	toluene	3	> 99	> 99	21:79
8[f]	1	3	120	toluene	3	> 99	> 99	32:68
9	0.5	3	120	toluene	3	98	98	36:62

[a] Reactions were performed under Ar atmosphere starting from 1 mmol of acetophenone (1 M solution in the appropriate solvent) and 1-3 mmol of benzyl alcohol. [b] Determined by GC (uncorrected GC areas). [c] 7% of 1-phenylethanol was detected by GC in the reaction mixture. [d] 6% of 1-phenylethanol was detected by GC in the reaction mixture. [e] Reaction performed with 2 mol% of complex **6**. [f] Reaction performed with 2 mol% of complex **3**.

substrate was detected by GC in the crude reaction mixture.[24] An increase in the benzyl alcohol/acetophenone ratio to 2:1 and 3:1 led to a faster consumption of the ketone substrate, but 24 h were still required to generate the saturated aryl-carbinol **8** as the major reaction product (up to 83% GC-yield; entries 2 and 3). At shorter times (3 h), the α-alkylated ketone **7** was in both cases the predominant species in solution. As in the previous case, small amounts of 1-phenylethanol were also formed. To our delight, better results in terms of both activity and selectivity were obtained when the same C-C coupling process was performed in toluene at 120 °C (entries 4-6). Under these conditions, the formation of 1-phenylethanol could be completely suppressed. In particular, employing a benzyl alcohol/acetophenone ratio of 3:1, the total consumption of acetophenone was reached in only 3 h, with the desired alcohol **8** being formed in a remarkable 87% GC-yield (entry 6).[27] At this point, it is pertinent to note that, under identical conditions, the use of complexes [$RuCl\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}(\eta^6$-*p*-cymene)][$PF_6$] (**6**) and *cis*-[$RuCl_2(DMSO)_4$] (**3**) also resulted in the complete conversion of the starting acetophenone substrate after 3 h of heating. However, the selectivity of the process was in all the cases slightly lower (entries 7-8 *vs* 6). An additional experiment performed with complex **5** pointed out the need to use a stoichiometric amount of base to achieve an optimal selectivity towards the desired alcohol (entry 9 *vs* 6). A blank experiment in the absence of **5** was also performed, the reaction leading to a mixture of **7** and **8** in *ca.* 1:1 ratio.

Having established suitable reaction conditions to generate the desired 1,3-diphenylpropan-1-ol **8** in high yield (entry 6 in Table 3), the scope of the process was next explored. The results are summarized in Table 4. As shown in entries 2-6, the reaction could be successfully expanded to a series of substituted acetophenone derivatives, which, regardless of their substitution pattern and electronic nature, readily reacted with benzyl alcohol to generate the corresponding secondary aryl-carbinols in 77-91% GC-yield (63-83% isolated yield after chromatographic work-up). As in the case of acetophenone (entry 1), minor amounts of the intermediate α-alkylated ketone were detected in all these reactions by GC.

Table 4 Catalytic α-alkylation/reduction of acetophenones with primary alcohols using *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH{=}NOH\}_2$] (**5**).[a]



Entry	R^1	R^2	Conv. (%)[b]	Yield (%)[b]
1[c]	H	Ph	> 99	87 (75)
2[c]	2-Me	Ph	> 99	86 (72)
3[c]	2-OMe	Ph	> 99	89 (73)
4[c]	3-Cl	Ph	> 99	88 (74)
5[c]	2-Br	Ph	> 99	91 (83)
6[c]	4-Br	Ph	> 99	77 (63)
7[d]	H	CH_2Bn	> 99	76 (64)
8[e]	H	CH_2CH_2Bn	> 99	73 (60)
9[f]	H	^{n}Pr	98	72 (60)
10[g]	H	^{i}Bu	98	70 (56)
11[c]	H	n-C_5H_{11}	> 99	79 (68)

[a] Reactions were performed under Ar atmosphere starting from 1 mmol of the corresponding acetophenone (1 M in toluene) and 3 mmol of the corresponding primary alcohol. [b] Determined by GC (uncorrected GC areas), isolated yields after work-up are given in brackets. [c] Differences between GC conversions and yields correspond to the α-alkylated ketone present in the crude reaction mixture. [d] 16% of 1-phenylethanol and 7% of 1,5-diphenylpentan-1-one were detected by GC in the crude reaction mixture. [e] 19% of 1-phenylethanol and 8% of 1,6-diphenylhexan-1-one were detected by GC in the crude reaction mixture. [f] 20% of 1-phenylethanol and 6% of 1-phenylhexan-1-one were detected by GC in the crude reaction mixture. [g] 10% of 1-phenylethanol and 18% of 5-methyl-1-phenylhexan-1-one were detected by GC in the crude reaction mixture.

On the other hand, in addition to benzyl alcohol, other primary alcohols could also be employed for the α-alkylation/reduction of acetophenone (entries 7-11). However, in these cases the yields were slightly lower and, in addition to the corresponding α-alkylated ketones, formation of 1-phenylethanol

was also observed. Regardless of this, the desired secondary alcohols were the major reaction products and could be isolated in pure form in 56-68% yield.

Conclusions

In summary, in this work we have described the preparation and spectroscopic characterization of the first examples of ruthenium complexes containing a phosphino-oxime ligand, namely *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}_2$] (**5**) and [$RuCl\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}(\eta^6$-*p*-cymene)][$PF_6$] (**6**). In addition, the stereochemistry of the former has been unequivocally established by means of single-crystal X-ray diffraction techniques. On the other hand, the utility of these species in homogeneous catalysis has also been demonstrated. In particular, the octahedral complex **5** proved to be an efficient and broad scope catalyst for the rearrangement of aldoximes to primary amides, and for the synthesis of secondary aryl-carbinols by α-alkylation/reduction of acetophenone derivatives with primary alcohols. The results reported herein, along with our previous work with related palladium(II) systems,[2] support further studies on the coordination chemistry and catalytic applications of phosphino-oxime ligands, a field almost unexplored to date.

Experimental

General methods

All the manipulations were performed under argon atmosphere using vacuum-line and standard Schlenk or sealed-tube techniques. Organic solvents were dried by standard methods and distilled under argon before use.[28] All reagents were obtained from commercial suppliers and used as received, with the exception of compounds [$RuCl_2(PPh_3)_3$] (**2**),[29] *cis*-[$RuCl_2(DMSO)_4$] (**3**),[30] [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (**4**)[31] and most of the aldoximes employed in the catalytic experiments,[19] which were prepared by following the method reported in the literature. GC measurements were performed with a Hewlett-Packard HP6890 equipment using a Supelco Beta-Dex™ 120 column (30 m length; 250 μm diameter). Elemental analyses and Far-IR measurements were provided by the Analytical Service of the Instituto de Investigaciones Químicas (IIQ-CSIC) of Seville. Infrared spectra were recorded on a Perkin-Elmer 1720-XFT spectrometer. NMR spectra were recorded on Bruker DPX-300 or AV400 instruments. The chemical shift values (δ) are given in parts per million and are referred to the residual peak of the deuterated solvent employed (^{1}H and ^{13}C), or to an external 85% aqueous H_3PO_4 solution (^{31}P). DEPT experiments have been carried out for all the compounds reported in this paper.

Synthesis of *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}_2$] (5) from *cis*-[$RuCl_2(DMSO)_4$] (3)

A suspension of *cis*-[$RuCl_2(DMSO)_4$] (**3**) (0.100 g, 0.210 mmol) and 2-$Ph_2PC_6H_4CH=NOH$ (**1**) (0.152 g, 0.500 mmol) in 30 mL of THF was heated under reflux for 6 h. The resulting brown solution was then evaporated to dryness, and the solid residue thus generated dissolved in CH_2Cl_2 (*ca.* 10 mL). Addition of diethyl ether (*ca.* 50 mL) precipitated a yellow solid, which was washed with diethyl ether (2 x 20 mL) and vacuum-dried. Yield: 0.143 g (87%). IR (KBr): ν = 3290 (br, O-H), 1623 (m, C=N) cm^{-1}. ^{31}P{^{1}H} NMR (CD_2Cl_2): δ = 51.9 (s) ppm. ^{1}H NMR (CD_2Cl_2): δ = 6.57 (br, 4H, CH_{arom}), 6.92-7.59 (m, 24H, CH_{arom}), 8.52 (br, 2H, CH=N), 11.27 (br, 2H, OH) ppm. ^{13}C{^{1}H} NMR (CD_2Cl_2): δ = 126.6 (m, part AA´of an AA´XX´ spin system, C_{arom}), 127.3 (m, 3 CH_{arom}), 129.8 (d, J_{PC} = 11.2 Hz, CH_{arom}), 130.0 (s, CH_{arom}), 131.1 (s, part AA´of an AA´XX´ spin system, CH_{arom}), 132.1 (s, part AA´of an AA´XX´ spin system, C_{arom}), 132.5 (s, CH_{arom}), 132.7 (s, part AA´of an AA´XX´ spin system, C_{arom}), 133.3 (m, part AA´of an AA´XX´ spin system, CH_{arom}), 134.1 (m, part AA´of an AA´XX´ spin system, CH_{arom}), 134.5 (m, part AA´of an AA´XX´ spin system, CH_{arom}), 135.6 (m, part AA´of an AA´XX´ spin system, C_{arom}), 154.5 (s, C=N) ppm. Elemental analysis calcd. (%) for $RuC_{38}H_{32}Cl_2N_2O_2P_2$: C 58.32, H 4.12, N 3.58; found: C 58.45, H 4.07, N 3.67.

Synthesis of *cis,cis,trans*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}_2$] (5) from [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (4)

A solution of [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (**4**) (0.122 g, 0.200 mmol) and 2-$Ph_2PC_6H_4CH=NOH$ (**1**) (0.366 g, 1.200 mmol) in 30 mL of toluene was heated under reflux overnight. The resulting brown solution was then concentrated under vacuum to *ca.* 10 mL and stored in a freezer at -10 °C for 24 h. The cooling led to the precipitation of *cis*-[$RuCl_2\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}_2$] (**5**) as a yellow solid, which was separated, washed with diethyl ether (2 x 20 mL) and vacuum-dried. Yield: 0.234 g (75%).

Synthesis of [$RuCl\{\kappa^2$-(*P,N*)-2-$Ph_2PC_6H_4CH=NOH\}(\eta^6$-*p*-cymene)][$PF_6$] (6)

A solution of [{RuCl(μ-Cl)(η^6-*p*-cymene)}$_2$] (**4**) (0.122 g, 0.200 mmol) and 2-$Ph_2PC_6H_4CH=NOH$ (**1**) (0.125 g, 0.410 mmol) in 30 mL of CH_2Cl_2 was stirred at room temperature for 1 h. The resulting orange solution was then evaporated to dryness, and the solid residue thus formed dissolved in MeOH (20 mL) and treated overnight with $NaPF_6$ (0.084 g, 0.500 mmol). The solvent was then removed under vacuum, the crude product extracted with CH_2Cl_2 (*ca.* 50 mL), and the extract filtered. Concentration of the filtrate to *ca.* 5 mL, followed by the addition of diethyl ether (*ca.* 50 mL), precipitated a yellow solid, which was washed with diethyl ether (2 x 20 mL) and vacuum-dried. Yield: 0.230 g (80%). IR (KBr): ν = 3206 (br, O-H), 1616 (m, C=N) cm^{-1}. ^{31}P{^{1}H} NMR (acetone-d_6): δ = -144.1 (sept, $^1J_{PF}$ = 701.7 Hz, PF_6^-), 38.9 (s, PPh_2) ppm. ^{1}H NMR (acetone-d_6): δ = 0.70 (d, 3H, $^3J_{HH}$ = 6.6 Hz, CH*Me*$_2$), 0.97 (d, 3H, $^3J_{HH}$ = 7.5 Hz, CH*Me*$_2$), 2.15 (s, Me), 2.55 (m, 1H, C*H*Me$_2$), 5.70 (d, 1H, $^3J_{HH}$ = 5.4 Hz, CH of cymene), 6.00 (d, 1H, $^3J_{HH}$ = 6.6 Hz, CH of cymene), 6.05 (d, 1H, $^3J_{HH}$ = 5.4 Hz, CH of cymene), 6.20 (d, 1H, $^3J_{HH}$ = 6.6 Hz, CH of cymene), 7.29 (m, 1H, CH_{arom}), 7.54-

7.88 (m, 11H, CH_{arom}), 8.12 (m, 2H, CH_{arom}), 8.90 (dd, 1H, $^4J_{PH}$ = 13.5 Hz, $^4J_{HH}$ = 2.1 Hz, CH=N), 12.54 (d, 1H, $^4J_{HH}$ = 2.1 Hz, OH) ppm. $^{13}C\{^1H\}$ NMR (acetone-d_6): δ = 17.3 (s, Me), 20.0 (s, CHMe_2), 21.9 (s, CHMe_2), 30.1 (s, CHMe$_2$), 89.5 (d, $^2J_{PC}$ = 2.8 Hz, CH of cymene), 91.3 (d, $^2J_{PC}$ = 2.5 Hz, CH of cymene), 93.7 (d, $^2J_{PC}$ = 7.2 Hz, CH of cymene), 96.5 (d, $^2J_{PC}$ = 6.1 Hz, CH of cymene), 102.8 (s, C of cymene), 110.9 (s, C of cymene), 125.5 (d, $^1J_{PC}$ = 47.3 Hz, C_{arom}), 128.8 (d, J_{PC} = 12.1 Hz, CH_{arom}), 129.3 (d, J_{PC} = 10.2 Hz, CH_{arom}), 129.4 (s, C_{arom}), 131.3 (d, J_{PC} = 2.8 Hz, CH_{arom}), 131.8 (d, J_{PC} = 2.8 Hz, CH_{arom}), 132.9 (d, J_{PC} = 10.5 Hz, CH_{arom}), 132.4 (s, CH_{arom}), 133.8 (d, J_{PC} = 7.1 Hz, CH_{arom}), 134.2 (d, $^1J_{PC}$ = 48.5 Hz, C_{arom}), 135.4 (d, J_{PC} = 9.7 Hz, CH_{arom}), 136.3 (d, J_{PC} = 8.8 Hz, CH_{arom}), 136.4 (d, J_{PC} = 9.7 Hz, CH_{arom}), 172.0 (d, $^3J_{PC}$ = 8.2 Hz, C=N) ppm. Elemental analysis calcd. (%) for $RuC_{29}H_{30}F_6P_2ClNO$: C 48.31, H 4.19, N 1.94; found: C 48.44, H 4.10, N 2.07.

General procedure for the catalytic rearrangement of aldoximes using complex 5

The corresponding aldoxime (1 mmol), water (3 mL) and complex **5** (0.039 g, 0.05 mmol) were introduced into a Teflon-capped sealed tube, and the reaction mixture stirred at 100 °C for the indicated time (see Table 2). The course of the reaction was monitored regularly taking samples of *ca.* 20 μL, which, after extraction with CH_2Cl_2 (3 mL), were analyzed by GC. To isolate the amide products, whose identity was assessed by comparison of their NMR spectroscopic data with those reported in the literature, the solvent was eliminated under reduced pressure and the crude reaction mixture purified by column chromatography over silica gel using CH_2Cl_2 as eluent.

General procedure for the catalytic α-alkylation/reduction of acetophenones with primary alcohols using complex 5

The corresponding acetophenone (1 mmol), the appropriate alcohol (3 mmol), KOH (0.056 g, 1 mmol) and complex **5** (0.016 g, 0.02 mmol) were introduced into a Teflon-capped sealed tube under an argon atmosphere. Toluene (1 mL) was then added at room temperature, and the resulting suspension heated at 120 °C for the indicated time (see Table 4). After this time, a sample of *ca.* 20 µL was taken and, after dilution with CH_2Cl_2 (3 mL), analyzed by GC to determine the composition of the reaction mixture. To isolate the alcohol products, whose identity was assessed by comparison of their NMR spectroscopic data with those reported in the literature, the reaction mixture was diluted with Et_2O (5 mL) and extracted with water (5 mL). The aqueous phase was extracted twice with Et_2O (2 x 5 mL) and the combined organic phases washed with brine (5 mL). After removal of the volatiles under vacuum, the oily residue was purified by column chromatography (silica gel) using Et_2O/hexane (1:20) as eluent.

X-Ray crystal structure determination of complex 5

Crystals of complex **5** suitable for X-ray diffraction analysis were obtained by slow diffusion of diethyl ether into a saturated solution of the complex in THF. The most relevant crystal and refinement data are collected in Table 5. Data collection was performed with an Oxford Diffraction Xcalibur Nova single crystal diffractometer using Cu-Kα radiation (λ = 1.5418 Å). Images were collected at a fixed crystal-to-detector distance of 63 mm, using the oscillation method with 1.3° oscillation and 23.77-38.88 s variable exposure time per image. Data collection strategy was calculated with the program CrysAlis Pro CCD.[32] Data reduction and cell refinement was performed with the program CrysAlis Pro RED.[32] An empirical absorption correction was applied using the SCALE3 ABSPACK algorithm as implemented in the program CrysAlis Pro RED.[32]

Table 5 Crystal data and structure refinement for compound **5**

Empirical formula	$C_{38}H_{32}Cl_2N_2O_2P_2Ru \cdot C_4H_8O$
Formula weight	854.67
Temperature/K	293(2)
Wavelength/Å	1.54184
Crystal system	Triclinic
Space group	*P*-1
Crystal size/mm	0.10 x 0.03 x 0.03
a/Å	10.6726(5)
b/Å	11.5721(8)
c/Å	17.6589(9)
α (°)	83.597(5)
β (°)	78.172(4)
γ (°)	63.038(6)
Z	2
Volume/Å^3	1905.6(2)
Calculated density/g cm^{-3}	1.489
μ/mm^{-1}	5.751
F(000)	876
ϑ range/°	4.29-69.34
Index ranges	$-6 \le h \le 12$ $-13 \le k \le 14$ $-21 \le l \le 21$
Completeness to ϑ_{max}	97.9%
No. of reflns. collected	15022
No. of unique reflns.	6968 (R_{int} = 0.049)
No. of parameters/restraints	485/18
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1.027
R_1 [$I > 2\sigma(I)$]^a	0.0373
wR_2 [$I > 2\sigma(I)$]^a	0.0923
R_1 (all data)	0.0445
R_2 (all data)	0.0980
Largest diff. peak and hole/e Å^{-3}	0.443, -0.674

^{a} $R_1 = \sum(||F_o|-|F_c||)/\sum|F_o|$; $wR_2 = \{\sum[w(F_o^2-F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$

The software package WINGX was used for space group determination, structure solution, and refinement.[33] The structure was solved by direct methods using SIR92,[34] and refined by full-matrix least-squares on F^2 using SHELXL2014.[35] During the final stages of the refinements, all the positional parameters and the anisotropic temperature factors of all non-H atoms were refined. H atoms were geometrically located and their coordinates were refined riding on their parent atoms, with the exception of H1o, H2o, H7 and H27 which were found from the difference Fourier maps and included in a refinement with isotropic temperature parameters. One THF molecule of solvation per molecule of the complex was found in the asymmetric unit. The maximum residual electron density is located near to heavy atoms. The function minimized

was $\{\Sigma[\omega(F_o^2 - F_c^2)^2]/\Sigma[\omega(F_o^2)^2]\}^{1/2}$ where $\omega = 1/[\sigma^2(F_o^2) + (0.0465P)^2 + 0.9823P]$ with $\sigma(F_o^2)$ from counting statistics and $P = [\text{Max}(F_o^2,0) + 2F_c^2]/3$. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography.[36] Geometrical calculations were made with PARST.[37] The crystallographic plots were made with ORTEP-3.[33]

Acknowledgements

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The first ruthenium complexes containing a phosphino-oxime ligand have been synthesized, and their catalytic utility for the rearrangement of aldoximes to primary amides, as well as for the α-alkylation/reduction of acetophenones with primary alcohols, demonstrated.