Recent Advances in Osmium-Catalyzed Hydrogenation and Dehydrogenation Reactions

Recent advances in osmium–catalyzed hydrogenation and dehydrogenation reactions

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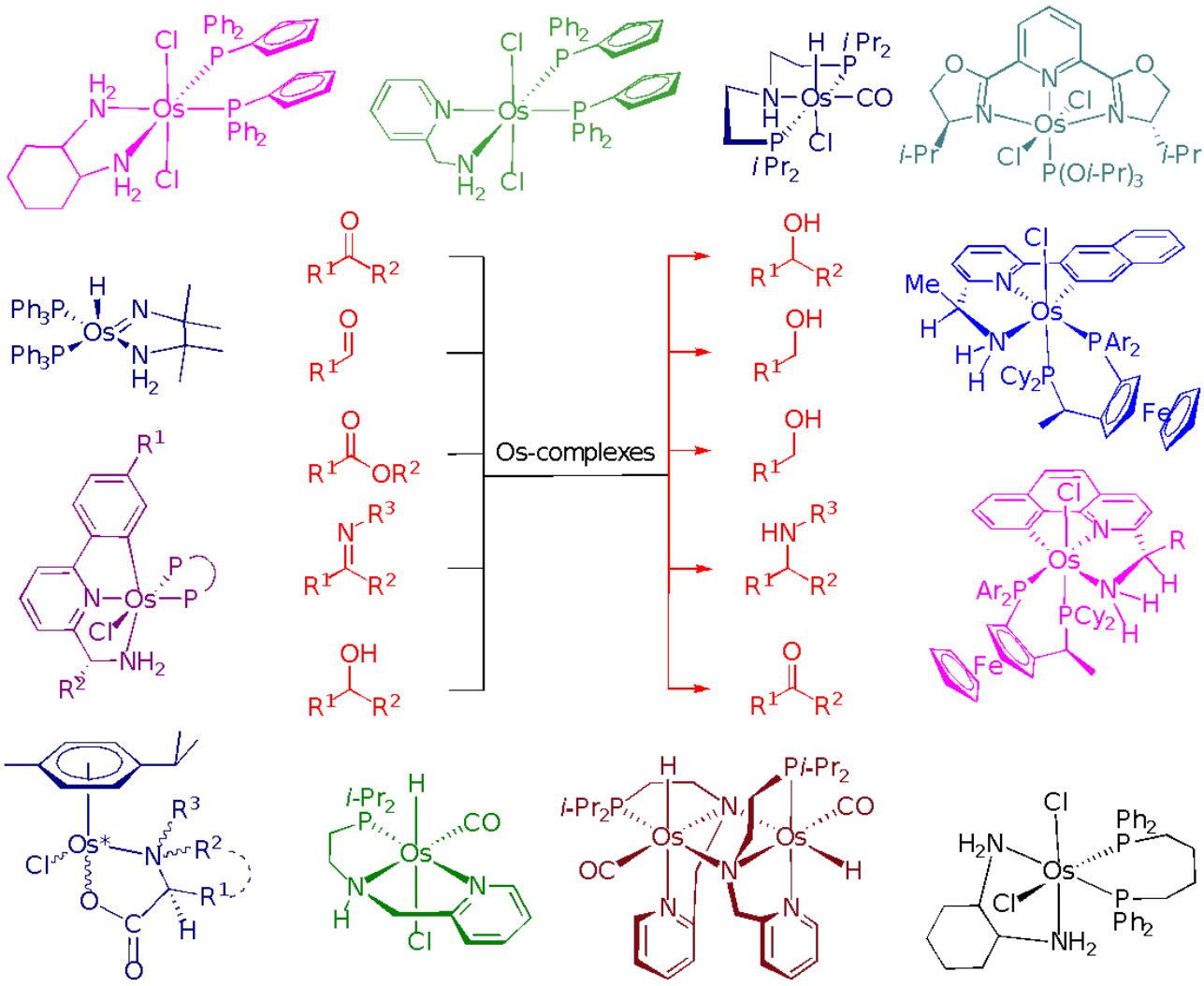
CONSPECTUS: A current issue in metal catalyzed reactions is the search of highly efficient transition-metal complexes affording high productivity and selectivity in a variety of processes. Moreover, there is also a great interest in multitasking catalysts able to efficiently promote different organic transformations by a careful switching of the reaction parameters, as temperature, solvent, co-catalyst, etc. In this contest, osmium complexes are showing to be able to catalyze efficiently different type of hydrogenation reactions, proving at the same time high thermal stability, simple synthesis and manipulation. These advantages may offset the higher cost involved in the case of osmium precursors with respect to their analogues. The aim of this Account is to highlight several impressive developments reached over the last few years by our and other groups on the application of Os-complexes in homogeneous catalytic reactions involving the hydrogenation of carbon–oxygen and carbon–nitrogen bonds by both dihydrogen (HY) and transfer hydrogenation (TH) reactions, as well as in alcohol deydrogenation (DHY) reactions, showing also the current point of view on the mechanism of these catalytic transformations. The work described in this Account demonstrates that Os-complexes are emerging as powerful catalysts for asymmetric and non-asymmetric syntheses, showing a remarkably high catalytic activity in HY and TH reactions of ketones, aldehydes, imines and esters with comparable or superior efficiency to those reported for analogous ruthenium systems. These results give a glimpse of the potential of Os-complexes for leading to the designing of new highly productive and robust catalysts for the synthesis of chiral and non-chiral alcohols and amines, as well as ketones from alcohols. Thus, we hope that this report will promote increased interest in the chemistry of these metal complexes, opening novel opportunities for new catalytic processes as well as for improvement the

existing ones.



1. Introduction

Ruthenium, rhodium and iridium complexes are usually employed as homogeneous catalysts for transfer hydrogenation (TH)[1] and hydrogenation (HY)[2] reactions of C=X (X = O, N) bonds, while osmium catalysts have received much less attention because they are considered less active on account of their slower ligand exchange kinetics. The notable research focused in the last two decades on ruthenium led to a large number of well-defined chemo- and stereo-selective catalysts, while osmium catalysts have been little investigated. Surprisingly, new osmium complexes have been recently prepared and shown to have relevant catalytic performance in hydrogenation and dehydrogenation processes with activity comparable or even higher with respect to the ruthenium analogues. In comparison to ruthenium, osmium leads to a stronger bond toward hydrogen, affording more stable catalytically active Os-hydride species that is a prerequisite for achieving catalysts displaying high productivity. This pecularity, combined with the simple synthesis and manipulation, may offset the

higher cost of Os-catalysts compared to their Ru-counterpats.We now describe several impressive results reached in the last few years by our and other groups on the application of Os-complexes in the hydrogenation of carbon–oxygen and carbon–nitrogen bonds by both HY and TH reactions, as well as in alcohol deydrogenation (DHY) reactions.[3] The Account is organized according to the category of the Os-catalyzed reactions, and arranged according to the type of ligand (monodentate, bidentate, etc.) coordinated to the metal.

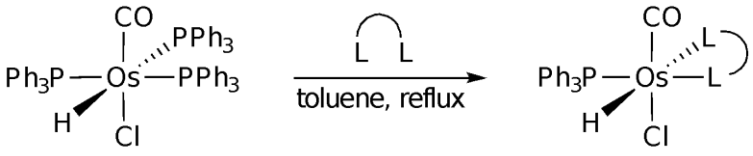
2. HYDROGENATION BY HYDROGEN TRANFER OF ALDEHYDES AND KETONES

Hydrogenation by TH of carbonyl compounds is an important catalytic reduction reaction for preparing the corresponding alcohols without the use of hazardous hydrogen gas or moisture-sensitive hydride reagents.[1] Among a large variety of transition metal complexes acting as highly efficient catalysts in this process a number of osmium complexes have been recently developed showing to be very active and robust catalysts.

2.1. Osmium complexes with bidentate ligands

The Os-complexes $OsHCl(CO)(PPh_3)(L\text{-}L)$ **1**–**5** were synthesized as only *trans* isomers (Scheme 1) and assessed for the selective reduction of *trans*-cinnamaldehyde both by TH and HY.[4] They showed higher selectivity for the reduction of the C=O than C=C bond (Scheme 2). The selectivity for both reductions was found to decrease in the order **3**>**5**>**2**>**4**>**1**, and to be greater for TH than HY. Complex **3** showed to possess almost 90% selectivity to cinnamyl alcohol for TH.

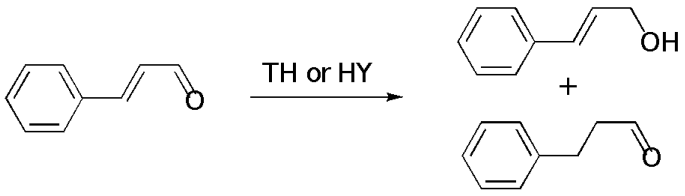
Scheme 1



1-5

1: L L = $Ph_2PCH_2PPh_2$, **2**: L L = $Ph_2P(CH_2)_2PPh_2$,
3: L L = $Ph_2P(CH_2)_3PPh_2$, **4**: L L = *cis*-$Ph_2PCH{=}CHPPh_2$,
5: L L = dppf

Scheme 2



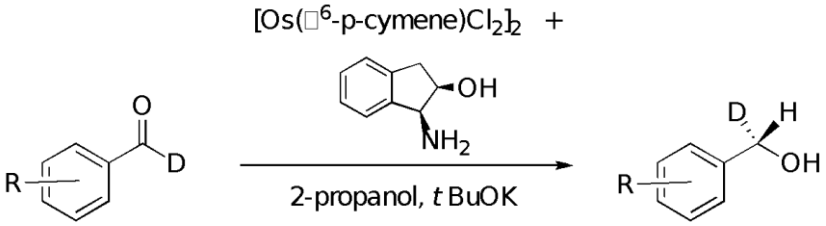
complex	selectivities for cinnamyl alcohol[a]	
	TH	HY
1	63	61
2	77	69
3	91	84
4	74	65
5	80	72

Reaction conditions: TH = catalyst (0.02 mmol), aldehyde (2 mmol), *i*-PrOH (200 mmol), toluene (30 mL), 110 °C; and HY = catalyst (0.02 mmol), aldehyde (2 mmol), H_2 (5 atm), toluene (45 mL), 90 °C. [a][Amount of cinnamyl alcohol/amount of cinnamyl alcohol and hydrocinnamaldehyde] x 100%

Faller and Lavoie screened the catalyst generated *in situ* from [Os(η^6-*p*-cymene)Cl_2]$_2$ and (1*R*,2*S*)-(+)-*cis*-1-amino-2-indanol in the presence of *t*BuOK for the asymmetric transfer hydrogenation (ATH) of ketones (Scheme 3).[5] This catalyst was highly enantioselective, yielding alcohols with high enatiomeric excesses (>90%), which in the case of α-tetralone reaches 97% and 98%, respectively. However, when the osmium catalyst was applied to reactions with higher substrate loadings (over longer time periods), the enatioselectivity was slightly diminished.

Next, the same catalytic system was investigated for ATH of *ortho* and *para*-substituted benzaldehyde-α-*d* derivatives, giving high conversions (>98%) and modest to moderate enantioselectivities (up to 60% ee) (Scheme 4).[6]

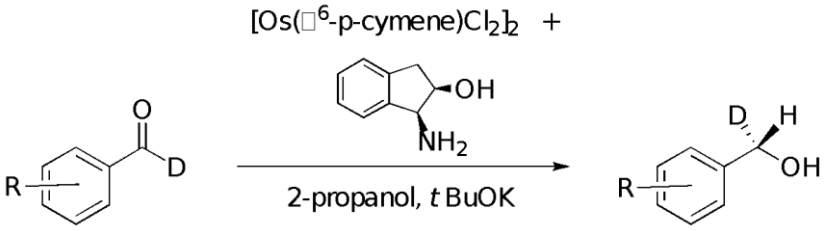
Scheme 3



R	ee (%)	R	ee (rotation)
4-Br	59 (*S*)	2-Me	33 (-)
4-H	60 (*S*)	2-CF_3	25 (-)
4-Me	51 (*S*)		
4-OMe	44 (*S*)		

Reaction conditions: catalyst (3 mol%), 2-propanol, *t* BuOK (0.006 M), -78 to +25 °C

Scheme 4



R	ee (%)	R	ee (rotation)
4-Br	59 (*S*)	2-Me	33 (-)
4-H	60 (*S*)	2-CF_3	25 (-)
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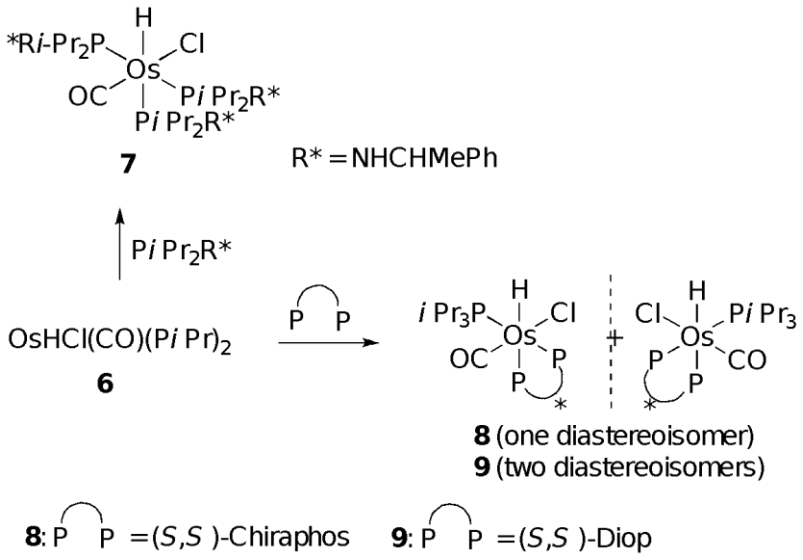
4-OMe	44 (*S*)		

Reaction conditions: catalyst (3 mol%), 2-propanol, *t* BuOK (0.006 M), -78 to +25 °C

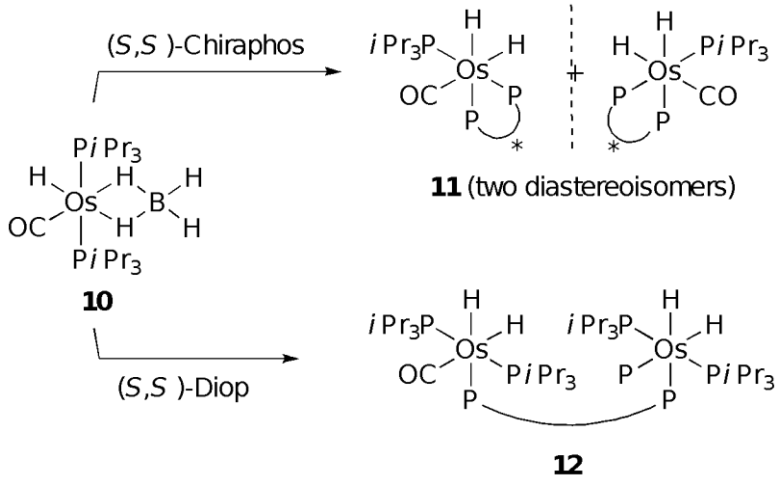
Werner and co-workers synthesized a variety of chloro(hydrido)- and dihydridoosmium(II) complexes with chiral ligands, and a number of them were assessed in the ATH of acethophenone.[7] The five-coordinate compound $OsHCl(CO)(PiPr_3)_2$ (**6**) was reacted with $PiPr_2R^*$ (R* = NHCH(Me)Ph) to give the octahedral complexes *mer*-**7** (Scheme 5). Reaction of **6** with (*S*,*S*)-Chiraphos generated only the diastereoisomer complex **8**, whereas with (*S*,*S*)-Diop led to two diastereoisomeric chelate complexes **9**, whose ratio was dependent on the reaction conditions (3:2 in boiling hexane after 24 h, and 1:1 after 5 days) (Scheme 5). $OsH(\kappa^2\text{-}H_2BH_2)(CO)(PiPr_3)_2$ (**10)** was reacted both with (*S*,*S*)-Chiraphos and (*S*,*S*)-Diop to give the mononuclear octahedral complex **11** as a diastereoisomeric mixture in about 10:1 ratio, or the dinuclear compound **12**, respectively (Scheme 6). Treatment of $OsH_2Cl_2(CO)(PiPr_3)_2$ (**13**) with two equivalents of (*S*,*S*)-Chiraphos afforded **14**, which was converted into **16** via formation of the intermediate **15** (Scheme 7).

In the ATH of acetophenone complexes **7**,**8**,**9** and **12** showed good catalytic activity, but low stereoselectivity; while complexes **11**,**14**,**15** and **16** were not active at all (Table 1).

Scheme 5



Scheme 6



Scheme 7

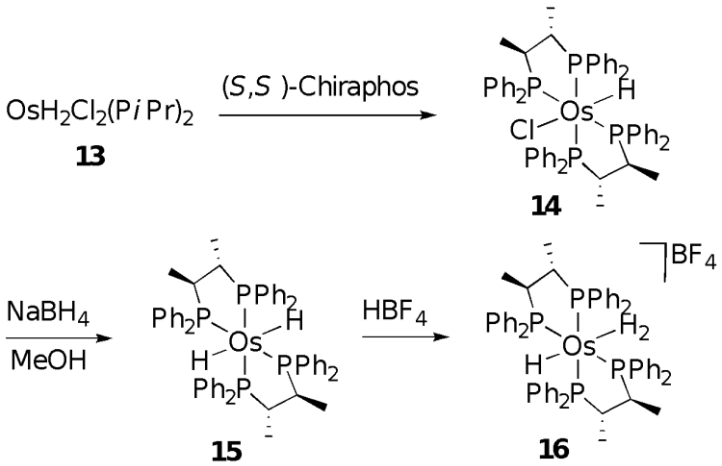


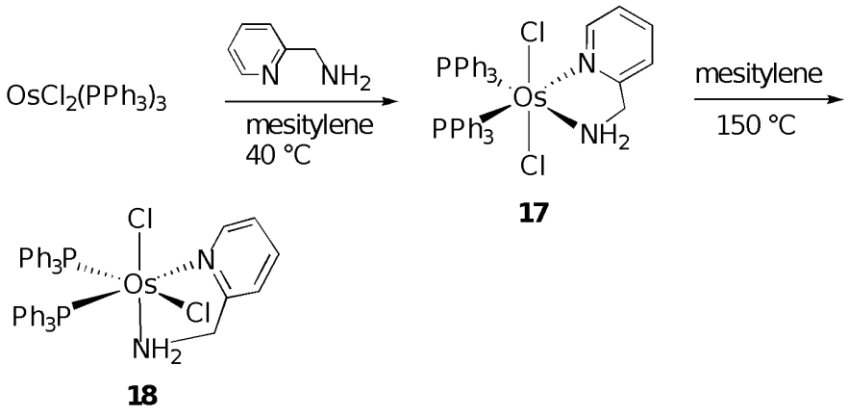
Table 1. ATH of acetophenone catalyzed by the hydrido-osmium complexes **7**,**8**,**9** and **12**.

complex	time (h)	conv. (%)	ee (%)	conf.
7	16	70	3.5	(+)-*R*
8	7 days	85	20	(-)-*S*
8/KOH[a]	22	62	17.4	(+)-*R*
9	18	94	3.5	(-)-*S*
9/KOH[a]	40	35	1.2	(+)-*R*
12	45	63	1.4	(+)-*R*

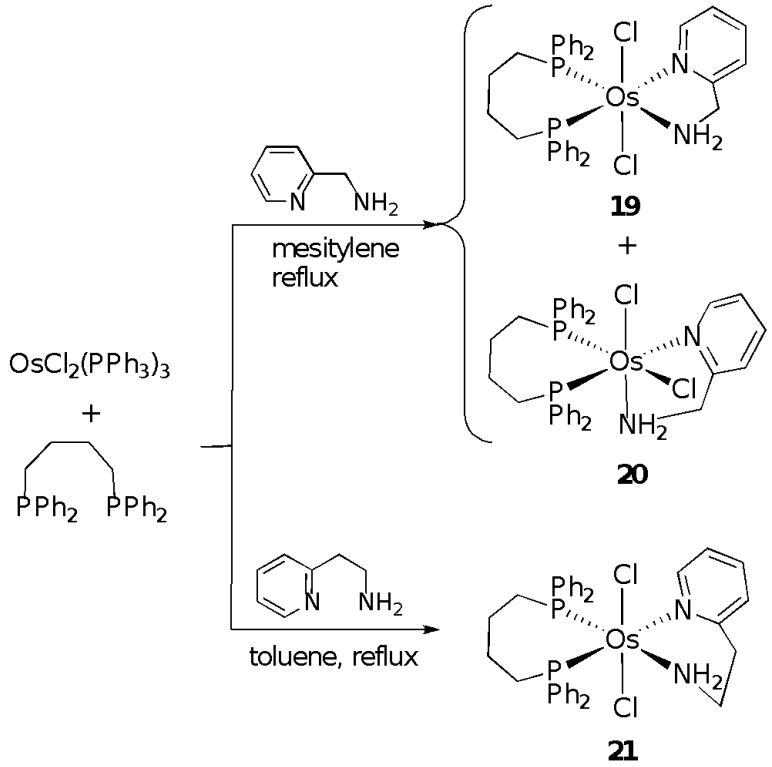
Reaction conditions: catalyst (0.1 mmol), toluene (12.5 mL), 2-propanol (12.5 mL), 85 °C, 1 h, then acetophenone (10 mmol) in 2-propanol (12.5 mL). [a]KOH (3 mL) 0.1 M in 2-propanol was added to the catalyst.

Ispired by the Noyori's work, indicating that the use of ancillary ligands featuring an NH functionality is crucial for achieve excellent results both in terms of activity and enantioselectivity, we decided to replace the diamine in the Noyori's catalyst [$RuCl_2$(PP)(1,2-diamine)] (PP = diphosphane)[8] with the mixed bidentate nitrogen ligand 2-aminomethylpyridine (Ampy). In this contest, we prepared the Os-compounds **17**-**21** (Scheme 8 and 9).[9] Treatment of $OsCl_2(PPh_3)_3$ with Ampy led to *trans,cis*-**17**, which by prolonged heating afforded the complex **25** as a single specie (Scheme 8). Reaction of $OsCl_2(PPh_3)_3$ with $Ph_2P(CH_2)_4PPh_2$ (dppb) and subsequent reaction with Ampy led to a mixture of *trans*-**19** and *cis*-**20** in about an 1:3 molar ratio (Scheme 9). Employment of 2-(pyridin-2-yl)ethanamine, which displays a longer CH_2 chain than Ampy, resulted in the formation of *trans*-**21** (Scheme 9).

Scheme 8

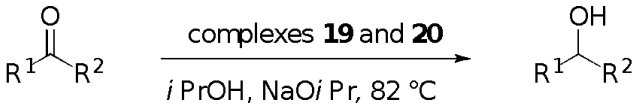


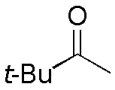
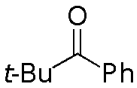
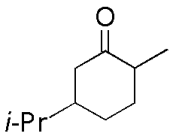
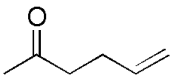
Scheme 9



The Os-compounds **17**-**21** were catalytically active for TH of acetophenone. With the mixture **19** and **20**, TH of acetophenone occurred in 30s with remarkably high reaction rates (TOF of 5.7 x 10^5 h^{-1}) and so showing that its activity is higher than that of the analogue *cis*-[$RuCl_2$(dppb)(Ampy)] (TOF = 3.0 x 10^5 h^{-1}).[9] The mixture **19** and **20** enabled the fast reduction of different ketones (even bulky) and also the chemoselective reduction of 5-hexen-2-one, without reduction or isomerization of the terminal olefinic bond (Scheme 10).

Scheme 10

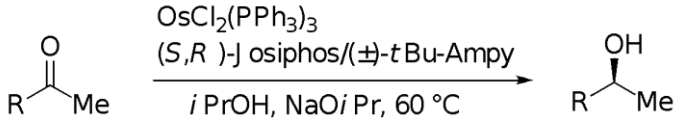


ketone	conversion (%)	time (h)	TOF [h^{-1}]
	93	30	3.2×10^3
	98	30	1.7×10^4
	99	30	2.7×10^4
	96	2	3.2×10^5

Experimental conditions: ketone (0.1 M) with complex **19** and **20** (1:3 mol%)(Os = 0.05 mol%) and NaO*i* Pr (2 mol%) in 2-propanol at 82 °C.

With the catalyst generated *in situ* from $OsCl_2(PPh_3)_3$, (*S*,*R*)-Josiphos and Ampy or racemic 1-methyl(pyridin-2-yl)methanamine ((±)-Me-Ampy)) or 1-*t*-butyl(pyridin-2-yl)methanamine ((±)-*t*-Bu-Ampy)), ATH of acethophenone afforded (*S*)-phenylethanol with both high ee (91-95%) and TOF (up to 1.9×10^4).[9] Attempts to increase the reaction stereoselectivity by sustitution of (*S*,*R*)-Josiphos with the bulkier (*S*,*R*)-Josiphos*, containing the 4-OMe-3,5-$Me_2C_6H_2$ groups instead of Ph ones, brought to similar ee (92-95%) with a slightly reduced catalytic activity (TOF up to 1.3×10^4). With the catalyst generated *in situ* from $OsCl_2(PPh_3)_3$, (*S*,*R*)-Josiphos and (±)-*t*-Bu-Ampy, ATH of the some aryl-methyl ketones afforded the related (*S*)-alcohols with 94–96% ee and TOF up to 1.2×10^4 (Scheme 11), establishing that the $OsCl_2$(PP)(Ampy) system can be efficiently used for the preparation of chiral alcohols.

Scheme 11

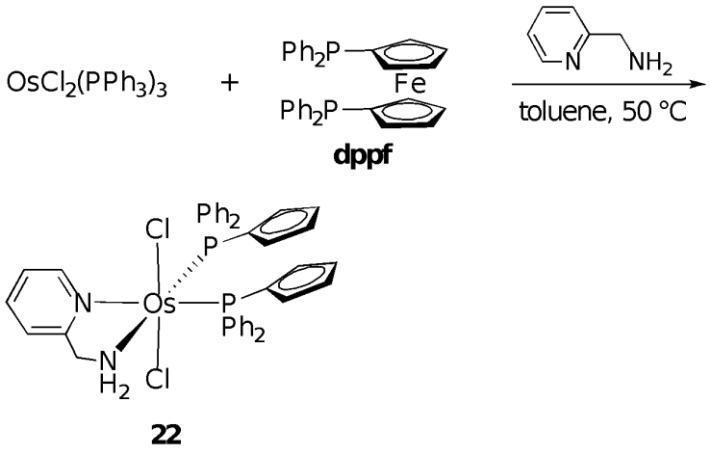


R	yield (%)	time (min)	ee (%)	TOF (h^{-1})
2-ClC_6H_4	99	30	94	1.2×10^4
2-$MeOC_6H_4$	98	60	95	9.1×10^3
2-MeC_6H_4	99	60	96	8.6×10^3

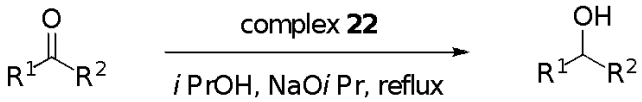
Reaction conditions: ketone (0.1 M), [$OsCl_2(PPh_3)_3$]/ (*S*,*R*)-J osiphos/(±)-*t*-Bu-Ampy (Os 0.05 mol%) and NaO*i* Pr (2 mol%) in 2-propanol at 60 °C.

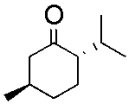
Very recently we prepared the Os-complex *trans*-**22** (Scheme 12) and compared its ability to catalyze a variety of organic transformations involving ketones and alcohols with the related Ru-complex.[10] By using a catalyst loading of 0.1−0.0005 mol% Os−complex **22** catalyzed efficiently the selective TH of aldehydes and ketones to alcohols (TOF up to 3×10^5), showing rates comparable to or even higher than those of the related Ru-complex.

Scheme 12



Scheme 13

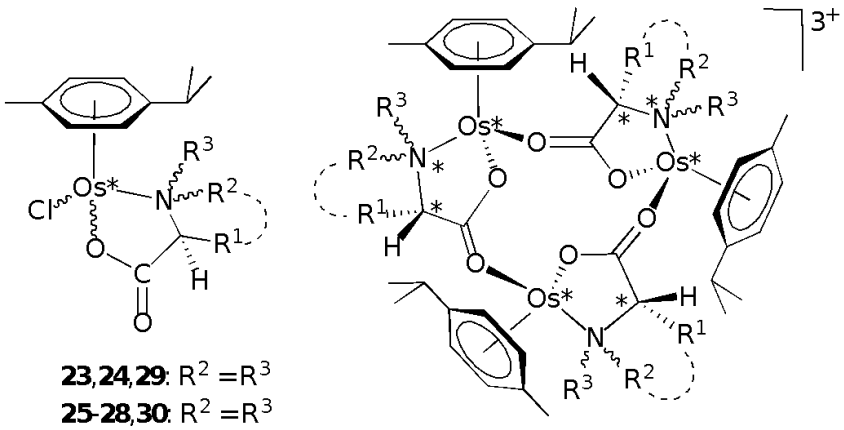


R^1	R^2	conv. (%)	time (min)	TOF (h^{-1})
Ph	H	98	5	3.0×10^5
4-$MeOC_6H_4$	H	98	5	1.8×10^5
n-C_5H_{11}	H	98[a]	30	6.0×10^3
$C_2H_5(CH_3)CH$	H	99	30	1.5×10^5
$Me_2CH{=}CH(CH_2)_2CH(Me)CH_2$	H	98[a]	120	2.6×10^3
$PhCH{=}CH$	H	90[a]	120	8.9×10^4
Ph	Me	98	10	1.9×10^4
4-$MeOC_6H_4$	Me	87[b]	5	1.0×10^4
Ph	*t*-Bu	91[a]	60	4.7×10^3
Ph	Ph	98	60	7.8×10^4
$CH_2{=}CHCH_2CH_2$	Me	98[a]	5	4.3×10^4
		96[a]	10	4.6×10^4

Reaction conditions: carbonyl compound (0.1 M), Os-complex (0.005 mol%) with NaO*i* Pr (2.0 mol %) in 2-propanol at reflux temperature. [a]Os-complex (0.05 mol%). [b]Os-complex (0.1 mol%)

Carmona and co-workers reported the synthesis of the mononuclear osmium arene complexes **23−30** containing L-α-amino carboxylate ligands, which underwent chloride abstraction by $AgBF_4$ in methanol to afford the related cationic trimers **31−36** (Figure 1).[11,12] Trimerization most probably occurred through the chiral-at-metal mononuclear species $[(\eta^6\text{-}p\text{-}MeC_6H_4iPr)Os(Aa)(MeOH)]^+$ and takes place with chiral self-recognition: i.e., only the equal configurations at metal R_{Os},R_{Os},R_{Os} and S_{Os},S_{Os},S_{Os} diastereomers were detected. Both monomers and trimers were active catalysts for TH of acetophenone in the presence of HCOONa, affording in most cases conversions around 90% within few hours, with up to 72% ee (Scheme 14). The reaction rate was strongly dependent on the number of aminic protons present in the amino carboxylate ligand, increasing in the sequence $NR_2<NRH<NH_2$. The catalytic activity of the prolinate trimer **34** with other ketones was also examined, giving up to 82% stereoselctivity (Table 2).

Figure 1

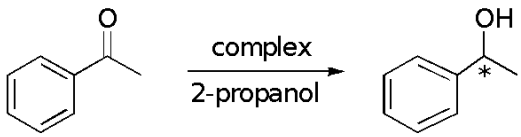


23,**24**,**29**: $R^2 = R^3$
25-28,**30**: $R^2 = R^3$

31-36

23,**31** (Ala): R^1 =Me, R^2 =H, R^3 =H
24,**32** (Phe): R^1 =Bn, R^2 =H, R^3 =H
25 (MePhe): R^1 =Bn, R^2 =H, R^3 =Me
26,**33** (Aze): R^1-R^2 =-$(CH_2)_2$-, R^3 =H
27,**34** (Pro): R^1-R^2 =-$(CH_2)_3$-, R^3 =H
28,**35** (Pip): R^1-R^2 =-$(CH_2)_4$-, R^3 =H
29 (Me_2Phe): R^1 =Bn, R^2 =Me, R^3 =Me
30,**36** (MePro): R^1-R^2 =-$(CH_2)_3$-, R^3 =Me

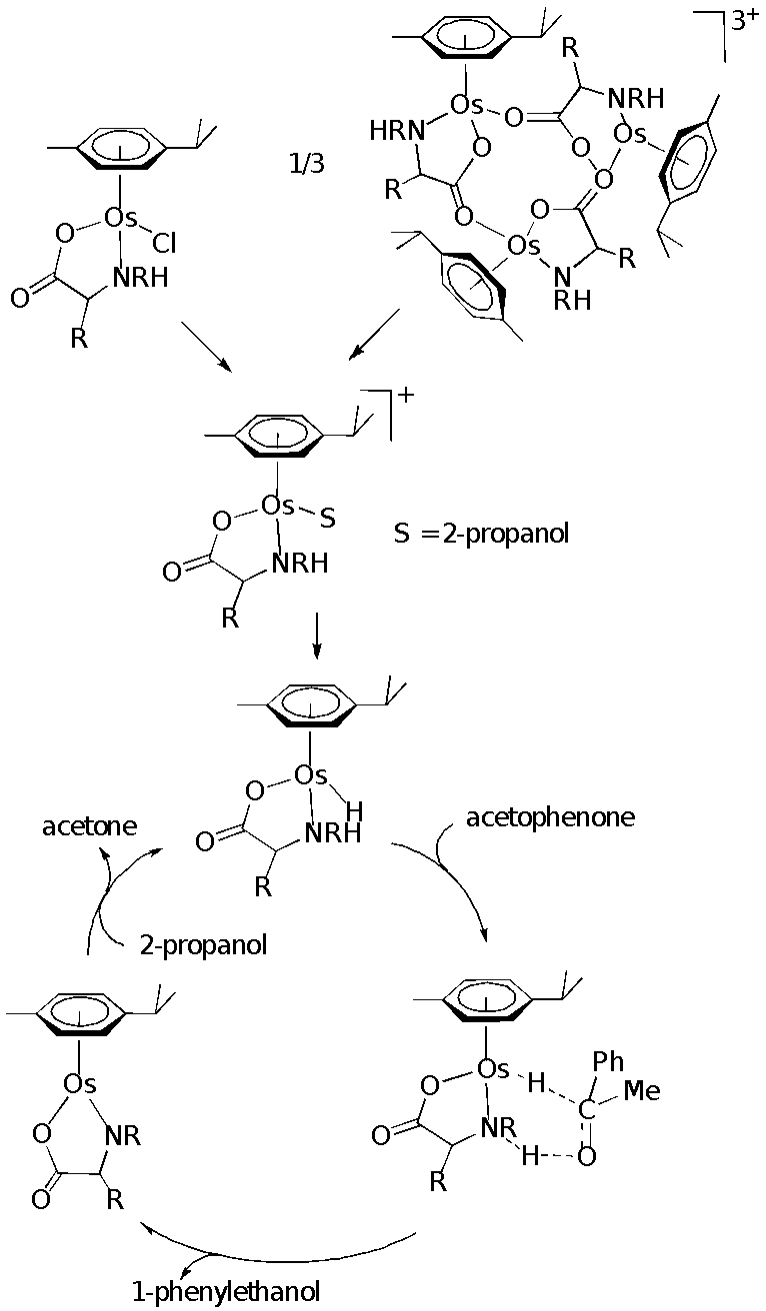
Scheme 14



complex	conf. at N	time (h)	conv. (%)	ee (%)
23		1	87	8 (*R*)
24		1.4	98	28 (*R*)
25	*R*	2.25	36	32 (*S*)
26	*S*	5	92	46 (*R*)
27	*S*	1	86	66 (*R*)
		2	97	60 (*R*)
28	*R*	2	97	48 (*S*)
29		24	41	0
30	*S*	24	36	6 (*R*)
31		2.5	84	10 (*R*)
33	*S*	1.25	35	50 (*R*)
34	*S*	1	70	72 (*R*)
		6	99	70 (*R*)
35	*R*	1.75	70	52 (*S*)
36	*S*	24	18	4 (*R*)

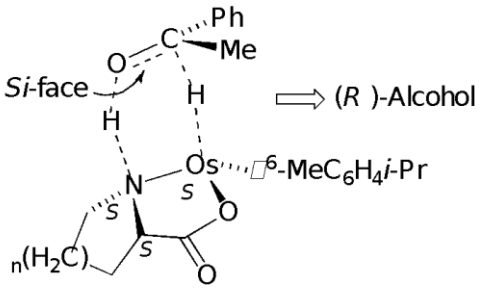
Reaction conditions: all reactions were carried out at 83 °C; catalyst 0.04 mmol in 6.6 mL of 2-propanol; molar ratio catalyst/HCOONa/acetophenone = 3/6/200; molar ratio catalyst/HCOONa/acetophenone for trinuclear complexes = 3/4/200.

Scheme 15

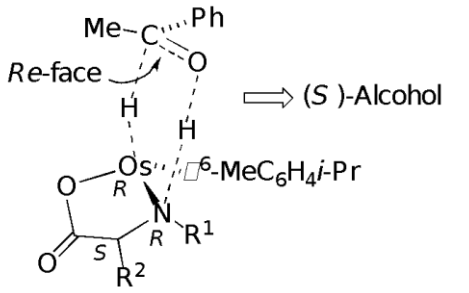


The results obtained were accounted by assuming that the Noyori's mechanism, depicted in Scheme 15, applies to their systems, but only to amino carboxylates with NH protons. Figure 2 shows a detailed view of the proposed six membered metallacycle intermediate in which an NH containing metallic hydride is involved. These proposed transition states accounts for the sign of the obtained enantioselectivities.

Figure 2

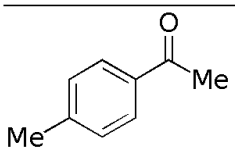
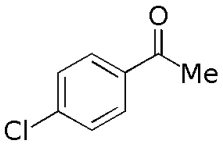
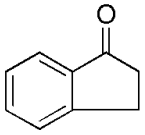
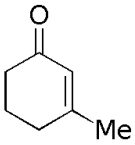


n = 0, azetidine-2-carboxylate (**26**, **33**)
n = 1, prolinate (**27**, **34**)



R^1 = Me, R^2 = Bn, *N*-methylphenylalaniate (**25**)
R^1- R^2 = $(CH_2)_4$, piperidine-2-carboxylate (**28**, **35**)

Table 2. ATH catalyzed by the trimer $[(\eta^6\text{-}p\text{-}MeC_6H_4iPr)Os(Pro)\}_3][BF_4]_3$ (**34**)

ketone	time (h)	conv. (%)	ee (%)	conf.
	1.5	62	60	*R*
	1.5	86	44	*R*
	1.5 8	31 80	82 76	*R* *R*
	2	8	42	*R*

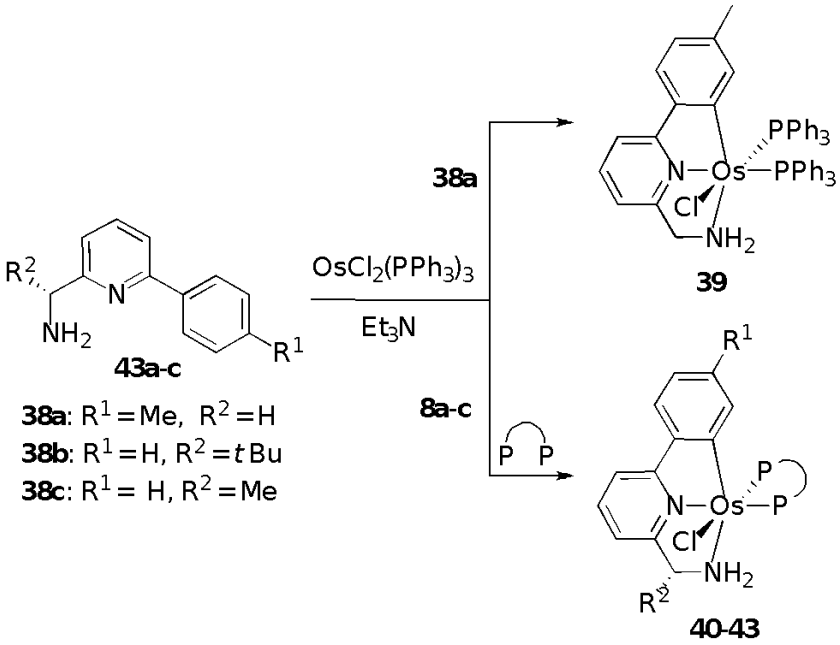
Reaction conditions: catalyst 0.04 mmol in 6.6 mL of 2-propanol, molar ratio catalyst/HCOONa/ketone = 3/4/200, 83 °C.

2.2. Osmium complexes with tridentate ligands

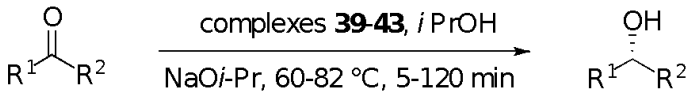
Since pincer complexes [MCl(CN)(PP)] appeared very attractive for practical applications, because the

presence of a metal–carbon bond gives to these compounds a high degree of thermal stability that prevents their easy deactivation and leads to highly productive catalysts, we prepared the pincer CNN Os-complexes **39**–**43**[13] by ortho-metalation of (6-phenylpyridin-2-yl)methanamine based ligands **38a**–**c**[14] (Scheme 16). These pincer complexes showed to be remarkably active catalysts for TH reduction of different types of ketones affording TOF up to 2 x 10^5 h^{-1} with a catalyst loading as low as 0.005 mol% (Scheme 17). ATH of methyl aryl ketones also proved possible with the chiral derivatives **39**–**43** (0.005 mol%) at 60 °C, affording enantioselectivities up to 97% ee. Importantly, the unsaturated ketone hex-5-en-2-one could also be chemoselectively reduced to hex-5-en-2-ol.

Scheme 16



Scheme 17

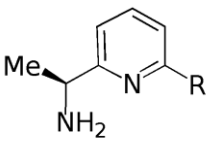


complex	R^1	R^2	temp (°C)	conv (%)	time (min)	TOF (h^{-1})	ee (%)
39	Me	Ph	82	96	10	1.8×10^5	
40	Me	Ph	82	98	5	1.3×10^5	
40	Me	2-ClC_6H_4	82	99	5	9.0×10^5	
40	-$(CH_2)_4$-		82	95	10	6.0×10^5	
40	Me	$CH_2CH_2CH{=}CH_2$	82	96	10	1.7×10^5	74
41	Me	Ph	60	94	120	1.2×10^5	83
42	Me	Ph	60	95	30	1.7×10^5	93
43	Me	Ph	60	97	30	1.7×10^5	91
43	Me	2-MeIC_6H_4	60	92	60	4.0×10^5	90
43	Me	2-ClC_6H_4	60	96	30	1.3×10^5	97
43	Me	2-$MeOC_6H_4$	60	95	30	1.9×10^5	97
43	Me	3-$MeOC_6H_4$	60	94	10	2.0×10^5	97

Reaction onditions: ketone (0.1 M), complex (0.005 mol%), NaO*i* Pr (2 mol%) in *i* PrOH.

We also used ligands (*S*)-**38c** and (*S*)-**44a**–**f**[15] (Figure 3) in combination with $OsCl_2(PPh_3)_3$ and (*R*,*S*)-Josiphos* to produce a variety of in situ generated pincer Os-complexes,[16] which efficiently catalyzed TH of acetophenone. The best ligand resulted to be (*S*)-**44f** that afforded (*R*)-1-phenylethanol in 96% conversion with 87% ee and TOF = 1.5×10^5 h^{-1}. On the basis of these data, the complexes **45** and **46** were prepared from (*R*,*S*)-Josiphos and (*R*,*S*)-Josiphos* in combination with (*S*)-**49f** (Scheme 18). Complex **46**, which was a better catalyst than **45** for TH of acetopheneone, was also assessed for TH of alkyl (hetero)aryl ketones giving up to 99% ee and TOF = 10^5–10^6 h^{-1} (Scheme 19).

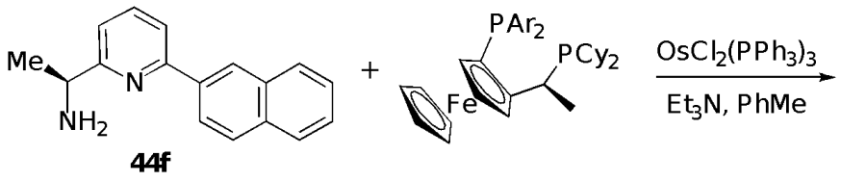
Figure 3

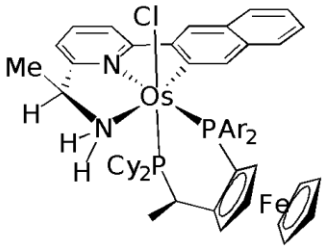


38c, **44a-f**

38c: R = Ph; **49a**: R = 4-$MeOC_6H_4$
44b: R = 4-$MeOC_6H_4$; **44c**: R = 3,5-$Me_2C_6H_4$
44d: R = 3,5-$(F_3C)_2C_6H_4$
44e: R = 1-naphthyl; **44f**: R = 2-naphthyl

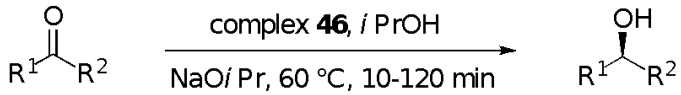
Scheme 18





45: Ar = Ph
46: Ar = 4-MeO-3,5-$Me_2C_6H_2$

Scheme 19



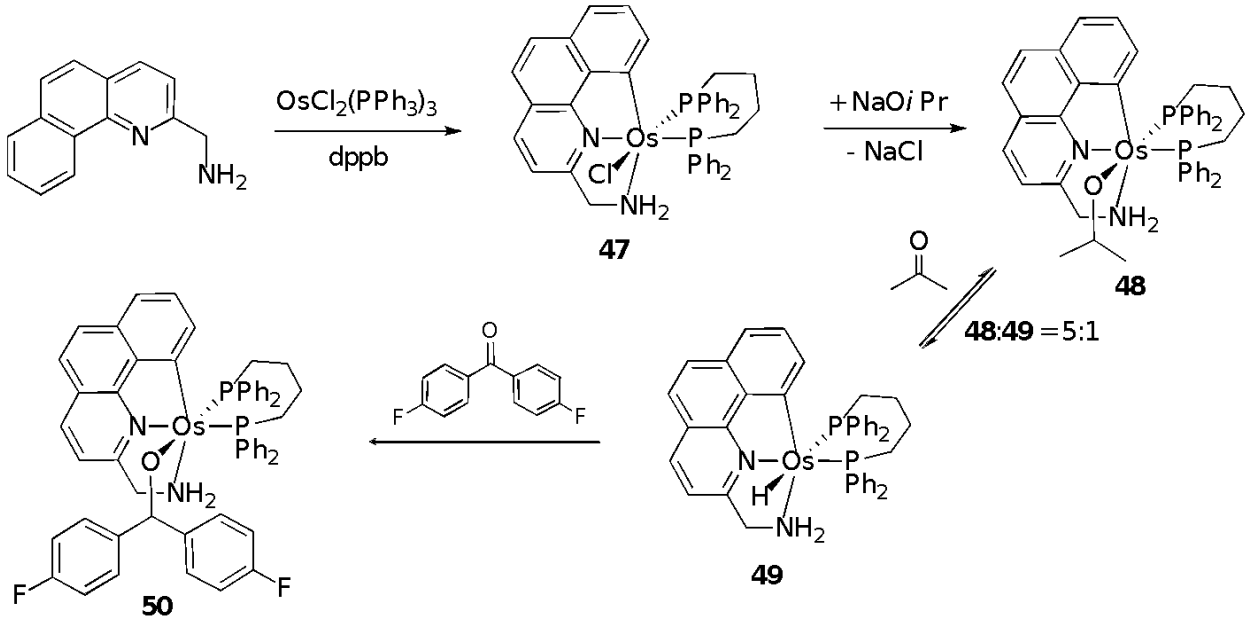
R^1	R^2	conv (%)	time (min)	TOF (h^{-1})	ee (%)
Me	Ph	97	30	3.2×10^5	91
Et	Ph	93	120	7.7×10^4	99
Me[a]	1-naphthyl	98	30	4.7×10^4	96
Me	2-naphthyl	97	30	1.6×10^5	93
Me	2-MeC_6H_4	93	60	2.5×10^4	96
Me[b]	3-ClC_6H_4	97	30	1.3×10^5	99
Me	3-$F_3CC_6H_4$	99	30	2.6×10^5	96
Me	3-$MeOC_6H$	97	60	9.0×10^4	94
Me[b,c]	3,5-$(MeO)_2C_6H_3$	97	30	2.1×10^5	95
Me[a,d]	3,5-$(F_3C)_2C_6H_3$	99	60	1.9×10^4	98
Me	2-pyridyl	99	60	3.9×10^4	86
Me[d]	3-pyridyl	99	30	6.6×10^4	92
Me[a,d]	4-pyridyl	99	10	1.2×10^5	97

Reaction conditions: ketone (0.1 M), complex (0.005 mol%), NaO *i* Pr (2 mol%) in *i*PrOH, 60 °C. [a]Reaction carried out at 82 °C. [b]Substrate/complex/NaO*i* Pr = 10000/1/200. [b]Reaction carried out at 82 °C. [c]Substrate/complex/NaO*i* Pr = 50000/1/1000. [d]In situ reaction.

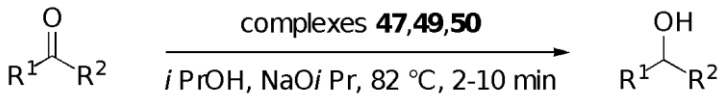
On account of the excellent catalytic performances of the Os–diphosphane derivatives containing 6-aryl-2-aminomethylpyridine based ligands, we next decided to examine the coordination chemistry and the catalytic potential of Os-complexes obtained by replacing these CNN ligands with the related ones based of the more rigid structure of the benzo[h]quinoline framework. Thus, we prepared the thermally

stable pincer Os-complex **47** by treatment of $OsCl_2(PPh_3)_3$ with dppb, followed by further reaction with 2-aminomethylbenzo[h]quinoline (Scheme 20).[17] Complex **47** was a highly efficient catalyst for the TH of several ketones. By using 0.005 mol% of **47** turnover frequency values up to 1.8 x 10^6 h^{-1} were achieved, showing that the osmium has much the same catalytic activity of the analogous ruthenium complex under these catalytic conditions (Scheme 21).[17] Since metal hydride and alkoxide complexes are supposed to be key species involved in catalytic TH and HY processes occuring in basic alcohol media,[18,19] complex **48** was reacted with NaO*i*Pr to afford an equilibrium mixture of alkoxide **48** and the hydride **49** in 5:1 molar ratio (Scheme 20).[17] The hydride **49**, easily isolable by evaporation of the alcohol media and elimination of acetone, was treated with bis(4-fluorophenyl)methanone to afford the alkoxide **50**. Complexes **49** and **50** showed high activity in TH, but with lower rate than **47**, due to their higher moisture and oxygen sensitivity (Scheme 21). ATH was also achieved by preparing *in situ* chiral pincer complexes from 2-aminomethylbenzo[h]quinoline, $OsCl_2(PPh_3)_3$ and (*S*,*R*)-Josiphos or (*S*,*R*)-Josiphos*, which afforded 80% and 90% ee, respectively, with a rate (TOF = 2.1 x 10^5 h^{-1} at 60 °C) higher compared to the related Ru-complexes[17] (Scheme 22).

Scheme 20



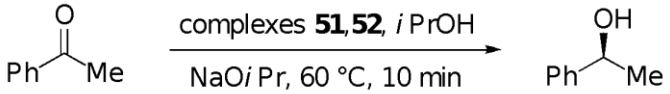
Scheme 21



complex	R^1	R^2	conv (%)	time (min)	TOF (h^{-1})
47	Me	Ph	96	5	1.3×10^6
47	Me	2-$MeOC_6H_4$	99	2	1.8×10^6
47	Me	$CH_2CH_2CH{=}CH_2$	97	10	3.0×10^5
47	-$CH_2(CH_2)_3CH_2$-		98	5	7.0×10^5
49	Me	Ph	97	5	6.1×10^5
50	Me	Ph	99	5	8.1×10^5

Reaction conditions: ketone (0.1 M), complex (0.005 mol%), NaO*i* Pr (2 mol%) in *i*-PrOH at 82 °C.

Scheme 22

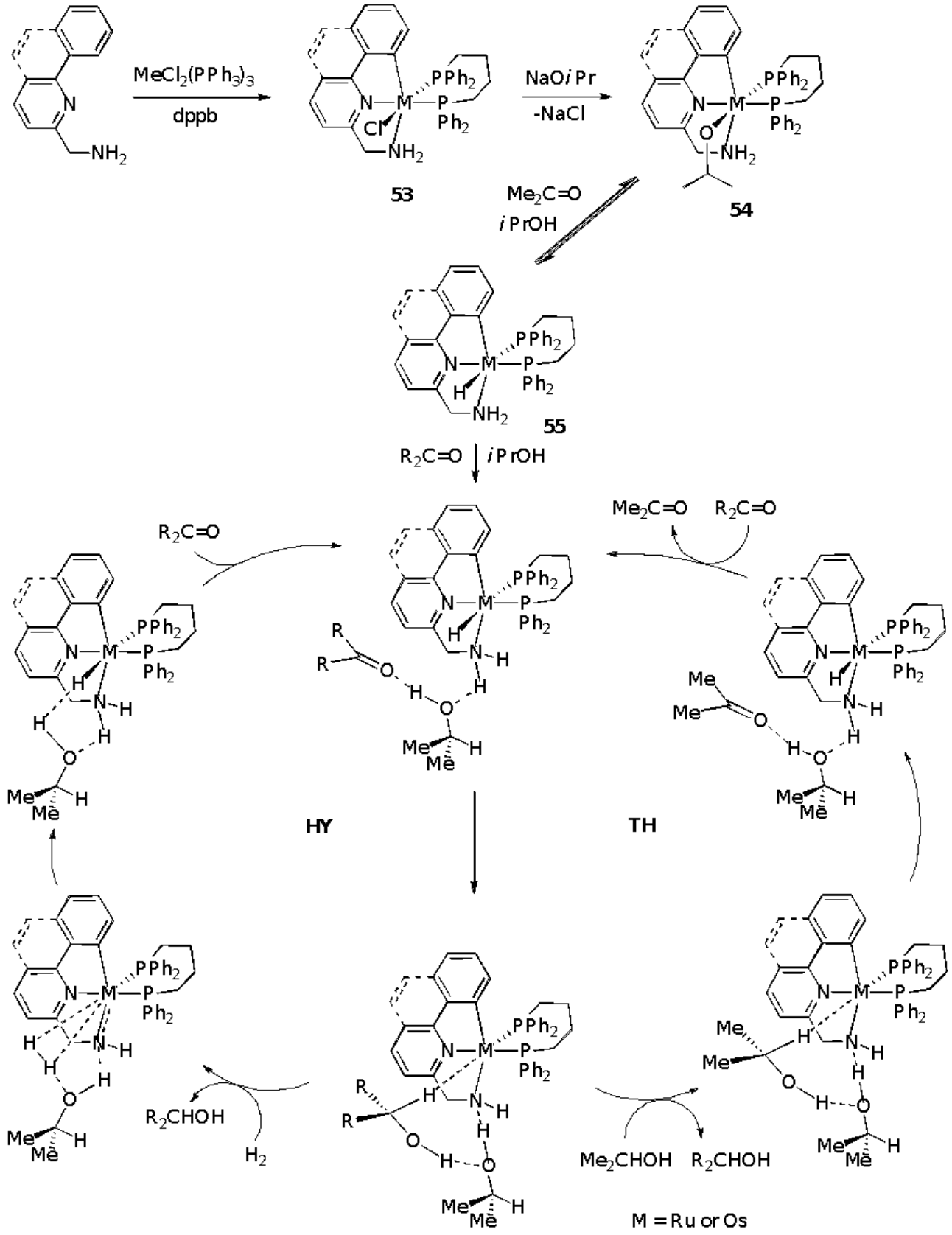


complex **56**: 96% conv, 80% ee.
complex **57**: 96% conv, 90% ee.

51: $OsCl_2(PPh_3)_3$], (*S*,*R*)-J osiphos and 2-aminomethylbenzo[h]quinoline; [Os]/PP/ligand = 1:1.5:2
52: $OsCl_2(PPh_3)_3$], (*S*,*R*)-J osiphos* and 2-aminomethylbenzo[h]quinoline; [Os]/PP/ligand =1:1.5:2

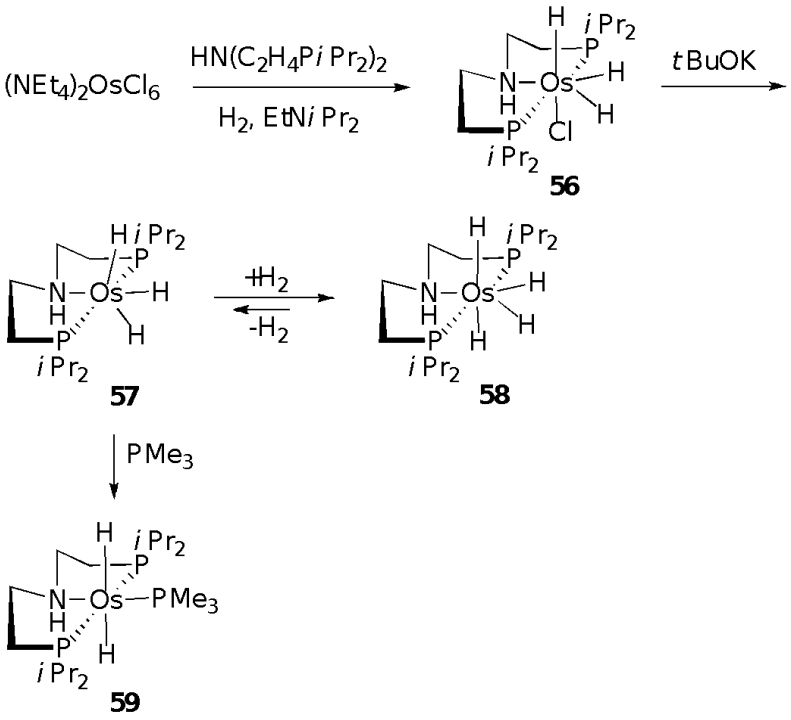
It is worth pointing out that osmium complexes based on (6-phenylpyridin-2-yl)- and (benzo[h]quinolin-2-yl)methanamine ligand frameworks show much the same behavior of the analogous ruthenium complexes for which mechanistic studies have been very recently carried out by us.[20] According to these investigations, the osmium chloride **53** reacts with Na*i*OPr, affording the isopropoxide **54** that rapidly equilibrates with the hydride **55** (Scheme 23). Reaction with the substrate in the presence of 2-propanol leads to the reduction to alcohol product and formation of an osmium amide alcohol adduct which by reaction with 2-propanol affords the alcohol product and the 2-propanol amide adduct that regenerates the hydride closing the cycle. The presence of the NH_2 function is crucial for enhancing the rate of the reaction allowing hydrogen bonding with the alcohol media and facilitating the overall proton transfer. Although the alkoxide and hydride are the only species detected in solution, the amide alcohol adduct plays a crucial role in catalysis.

Scheme 23

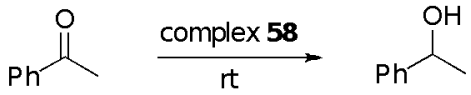

MeCl2(PPh3)3
dppb
NaOiPr
-NaCl
53
54
Me2C=O
iPrOH
55
R2C=O
iPrOH
HY
TH
R2CHOH
H2
Me2CHOH
R2CHOH
M = Ru or Os

The synthesis, structure, and properties of another series of PNP pincer Os-complexes **56**–**59** were reported by the Gusev group (Scheme 24).[21] A series of TH experiments catalyzed by **58** and conducted at room temperature in 2-propanol, ethanol or methanol was carried out and the results, summarized in Scheme 25, indicated that in methanol the reaction was slow, but a significant acceleration was observed in the presence of *t*BuOK in both 2-propanol and ethanol.

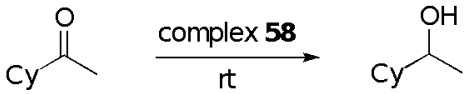
Scheme 24



Scheme 25



[cat] loading, mol%	TOF[a,b]	solvent
[Os] 0.016%	1900	*i* PrOH
[Os] 0.16%	420	EtOH
[Os] 0.4%	95	MeOH
[Os] 0.01%	5700	*i* PrOH, 0.05 mol% *t* BuOK
[Os] 0.04%	1800	EtOH, 0.4 mol% *t* BuOK

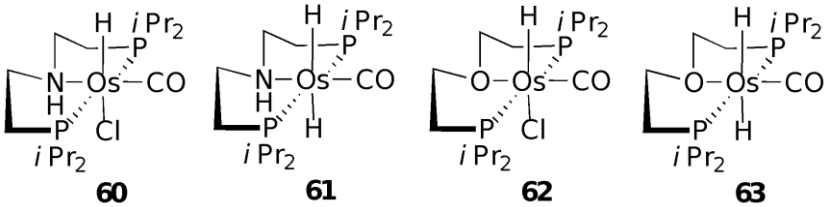


[cat] loading, mol%	TOF[a,b]	solvent
[Os] 0.013%	4600	*i* PrOH
[Os] 0.07%	430	EtOH
[Os] 0.33%	130	MeOH
[Os] 0.0016%	19000	*i* PrOH, 0.05 mol% *t* BuOK
[Os] 0.0016%	32700	EtOH, 0.5 mol% *t* BuOK

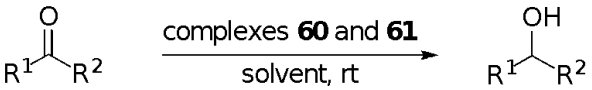
[a]TOF (h^{-1}) at 50% conv., [b]50% conversion was reached within 1-2 h

Related PNP pincer complexes of osmium **60**-**63** were also reported by the same research group (Figure 4).[22] Complex **61** showed to be an excellent TH catalyst in 2-propanol without base, while the chloride **60** was similarly active under basic conditions (Scheme 26). Both catalysts worked well using large substrate-to-catalyst ratios of 10^4–10^5 and gave very high turnover frequencies at room temperature.

Figure 4



Scheme 26

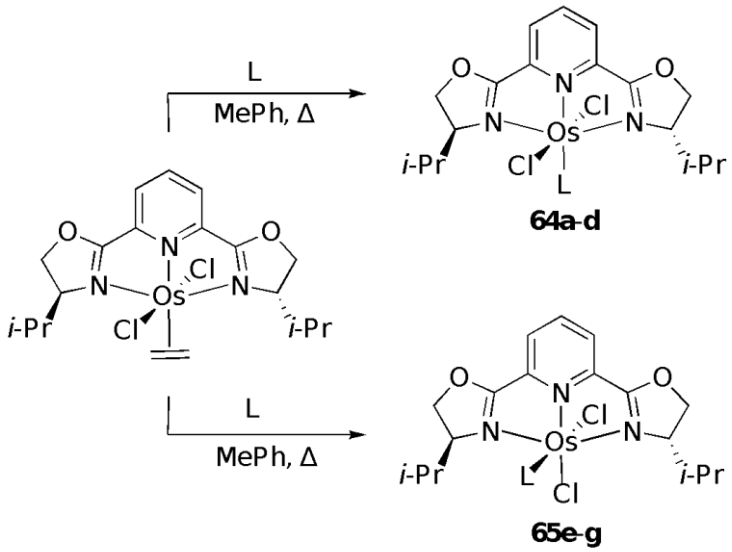


complex	R^1	R^2	ROH	[base][a]	time (h)[b]	TOF[c]
60	Ph	Me	*i* Pr	1.0	1.0	1.4×10^4
61	Ph	Me	*i* Pr		0.5	1.3×10^4
61	Ph	Me	*i* Pr	1.0	2.0	1.6×10^4
60	Ph	Me	Et	0.3	2.5	1.0×10^2
61	Ph	Me	Et		1.8	3.0×10^2
61[d]	Ph	Me	Et		2.0	2.6×10^2
61	Ph	Me	Et	1.0	0.8	4.7×10^2
61	$-(CH_2)_5-$		*i* Pr		1.7	1.9×10^2
61	$-(CH_2)_5-$		*i* Pr	1.0	1.3	6.3×10^2
61	$-(CH_2)_5-$		Et		0.8	5.5×10^2
61	$-(CH_2)_5-$		Et	1.0	0.8	9.6×10^2

[a]*t* BuOK (mol%). [b]Time to reach 50% conversion at rt. [c]Turnover frequencies at 50% conversion. [d]Cyclohexylamine was added (ratio 1:1).

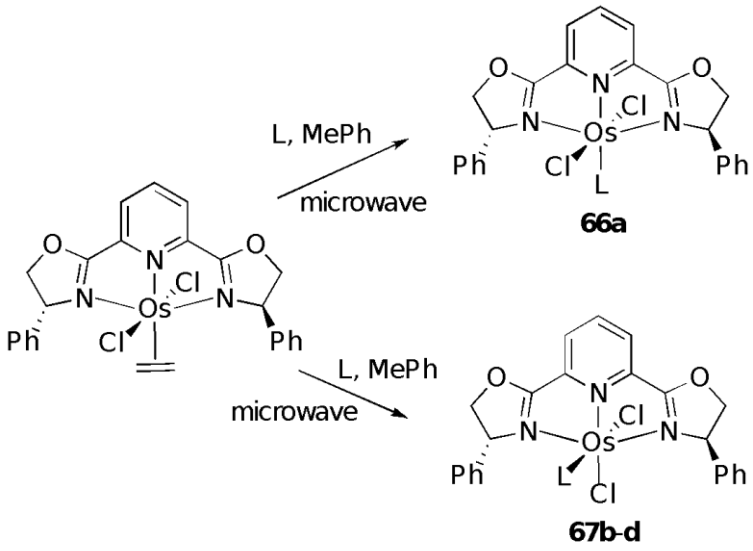
Gamasa and co-workers have very recently reported the synthesis and catalytic application of osmium(II)-pybox complexes **64**–**67** bearing phosphine and phosphite ligands (Scheme 27 and 28).[23] Comparing the catalytic activity of both (*S*,*S*)-*i*Pr-pybox and (*R*,*R*)-Ph-pybox complexes in ATH under under standard reaction conditions [acetophenone (5 mmol), 2-propanol (75 mL), catalyst (0.2 mol%), NaOH (ketone/catalyst/NaOH = 500:1:24 at 82 °C] it resulted that the former displayed higher efficiency, in sharp contrast with the results obtained with analogous ruthenium Ph-pybox complexes that were the most active catalysts.[24] Importantly, the efficiency of the catalyst resulted to depend not only on the chiral ligand but also on the auxiliary ligand (phosphine or phosphite) coordinated to the metal. Next, after optimizated reaction conditions the (*S*,*S*)-*i*Pr-pybox) complexes **64a–d** were examined in the reduction of a number of aryl alkyl ketones. The results reported in Scheme 20 show that the complexes *trans*-**64c** and **64d** were highly efficient catalysts affording nearly quantitative conversion and 90–94% ee. Importantly, these results showed for the first time that Os–complexes based on aprotic nitrogen ligands efficiently catalyze ATH of ketones.

Scheme 27



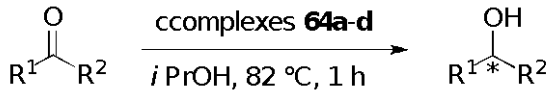
a: L = $P(OMe)_3$, **b**: L = $P(OEt)_3$, **c**: L = $P(O\textit{i}\text{-}Pr)_3$, **d**: L = $P(OPh)_3$ **e**: L = PPh_3, **f**: L = $P\textit{i}\,Pr_3$, **g**: L = PCy_3

Scheme 28



a: L = $P(OMe)_3$, **b**: L = PPh_3, **c**: L = $P\textit{i}\,Pr_3$, **d**: L = PCy_3

Scheme 29

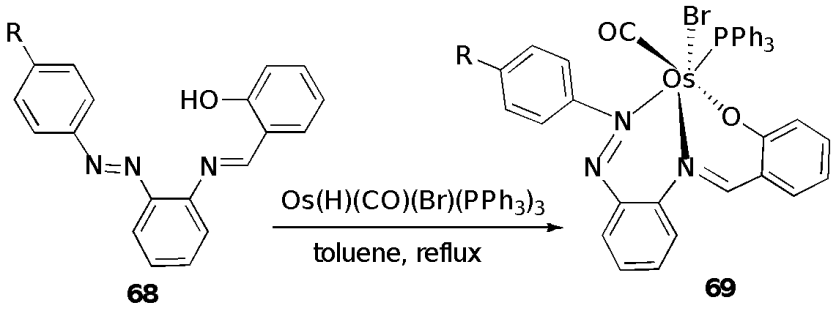


catalyst	R^1	R^2	conv. (%)	ee (%)(conf.)
64a	Ph	Me	98	94 (*R*)
64d	Ph	Me	98	92 (*R*)
64b	Ph	Et	98	92 (*R*)
64c	Ph	Et	99	92 (*R*)
64d	Ph	Et	98	94 (*R*)
64a	2-$MeOC_6H_4$	Me	99	74 (*S*)
64b	2-$MeOC_6H_4$	Me	99	74 (*S*)
69a	2-BrC_6H_4	Me	98	57 (*S*)
64b	2-BrC_6H_4	Me	99	55 (*S*)
64a	3-$MeOC_6H_4$	Me	97	79 (*R*)
64c	3-$MeOC_6H_4$	Me	97	79 (*R*)
64d	3-$MeOC_6H_4$	Me	97	80 (*R*)
64a	3-BrC_6H_4	Me	99	92 (*R*)
64b	3-BrC_6H_4	Me	99	91 (*R*)
64a	4-$MeOC_6H_4$	Me	98	93 (*R*)
64c	4-$MeOC_6H_4$	Me	98	94 (*R*)
64a	4-BrC_6H_4	Me	97	72 (*R*)
64b	4-BrC_6H_4	Me	97	73 (*R*)
64a	4-$MeOC_6H_4$	Et	97	97 (*R*)
64b	4-BrC_6H_4	Et	96	96 (*R*)
64c	4-BrC_6H_4	Et	96	96 (*R*)
64a	2-naphthyl	Me	99	54 (*S*)
64c	2-naphthyl	Me	99	55 (*S*)

Reaction conditions: ketone (5 mmol), 2-propanol (75 mL), catalyst (0.6 mol %), KO*t* Bu (ketone/catalyst/KO*t* Bu = 500:3:60). at 82 °C for 1 h.

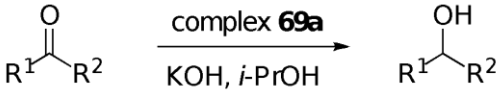
Os-complexes **69** were prepared by reaction of $Os(H)(CO)(Br)(PPh_3)_3$ with 1-{[2-(arylazo)phenyl]iminomethyl}-2-phenol (**68**, HL) (Scheme 30).[25] In TH of alkyl-aryl ketones **69a** resulted catalytically active, while the related Ru-complex showed no activity (Scheme 31).[26]

Scheme 30



compound		R
68a	HL^1	H
68b	HL^2	CH_3
68c	HL^3	Cl
69a	$[(L^1)Os(CO)(Br)(PPh_3)]$	H
69b	$[(L^2)Os(CO)(Br)(PPh_3)]$	CH_3
69c	$[(L^3)Os(CO)(Br)(PPh_3)]$	Cl

Scheme 31



R^1	R^2	time (h)	yield (%)
Ph	Ph	1	80
Ph	Me	1	75
$-CH_2(CH_2)_3CH_2-$		1.5	50
$4\text{-}MeC_6H_4$	Me	1.5	50

Reaction conditions: ketone (2.8 mmol),complex (0.0013 mmol) and KOH (0.0625 mmol) were heated to reflux in *i*-PrOH (10 mL).

3. HYDROGENATION BY MOLECULAR HYDROGEN OF ALDEHYDES AND KETONES

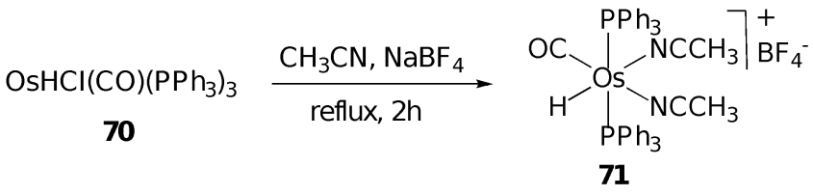
The catalytic asymmetric hydrogenation (AHY) of the polar C=O bond with hydrogen has been extensively investigated in the last decade and represents a core reaction for the synthesis of valuable chiral alcohols.[2]

3.1. Osmium complexes with monodentate ligands

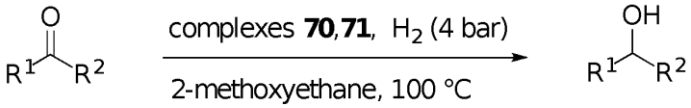
The cationic complex **71** and its neutral precursor **70** (Scheme 32) showed to be efficient catalysts for the hydrogenation of benzaldehyde and cyclohexanone (Scheme 33), with the former showing a catalytic activity lower than both **70** and its analogous Ru-complex.[27] Complexes **70** and **71** were also assesses in the hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline and cyclohexene to cyclohexane. The results showed that **71** was a more efficient catalyst for the hydrogenation of C=C and C=N bonds than for C=O bonds in selected substrates. This enhanced selectivity was rationalized in terms of a greater ability of this charged osmium complex to coordinate the C=C and C=N functional groups of the substrates to the appropriate extent to promote subsequent hydrogen transfer.

Kinetic and mechanistic studies of the HY cyclohexanone were carried out by using the cationic complex 7**1**.[28] All experimental data were consistent with a mechanism involving the oxidative addition of hydrogen as the rate determining step of the catalytic cycle (Scheme 34).

Scheme 32



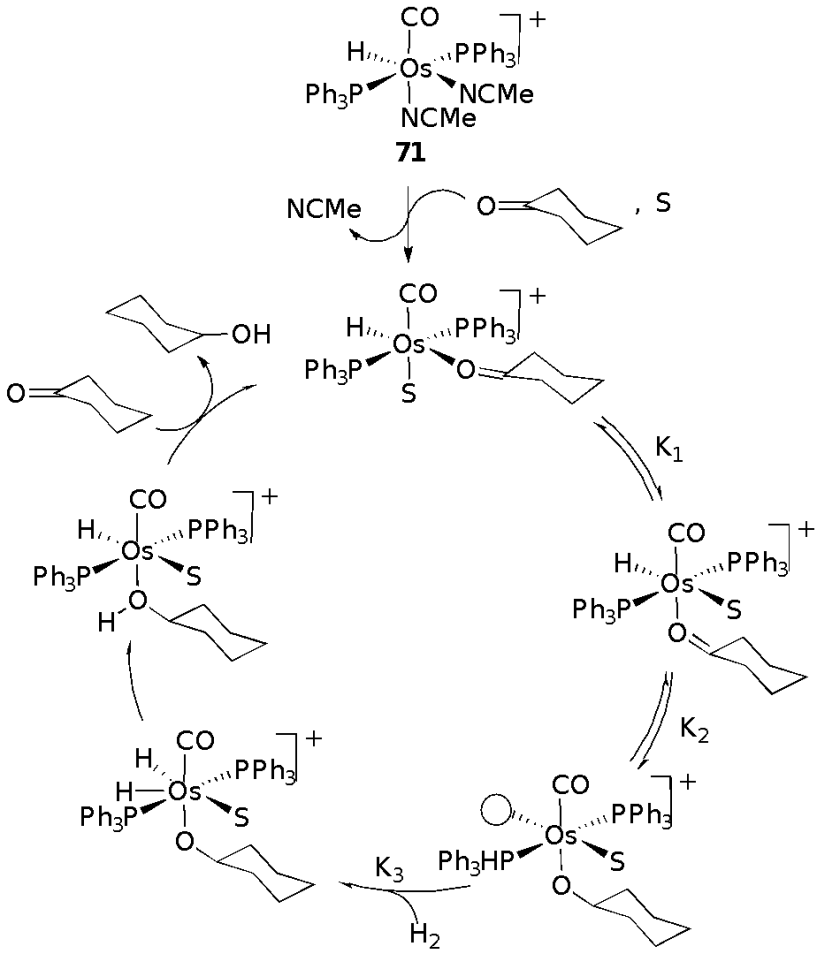
Scheme 33



catalyst[a]	R^1	R^2	TN[b]
70	Ph	H	74
71	Ph	H	42
70	$-(CH_2)_5-$		76
71	$-(CH_2)_5-$		28

[a]catalyst = 0.1 mol%
[b]Turnover number in I h.

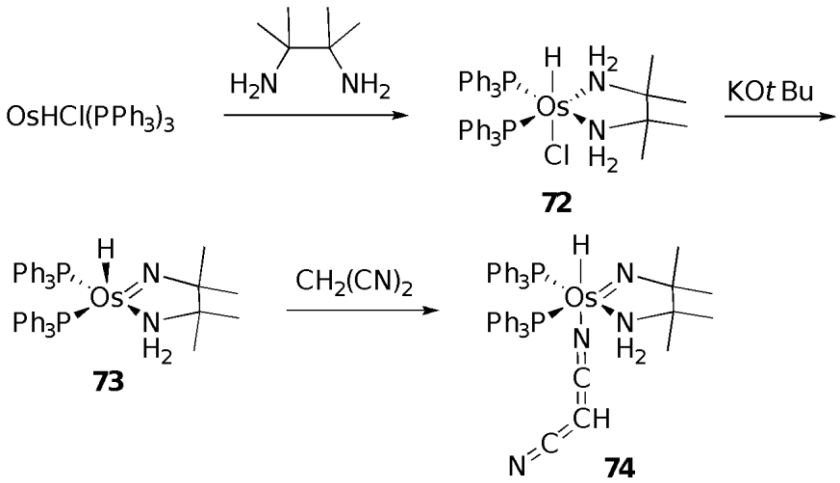
Scheme 34. Proposed catalytic cycle for $[OsH(CO)(NCMe)_2(PPh_3)_2]BF_4$-catalyzed cyclohexanone hydrogenation.



3.2. Osmium complexes with bidentate ligands

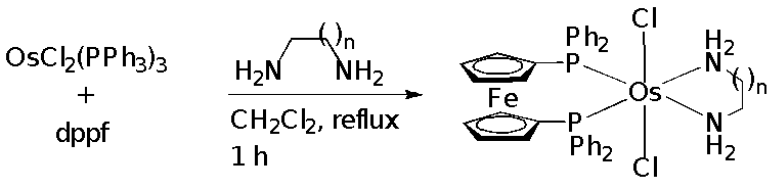
The five coordinate complex **73** was prepared by reacting **72** with KO*t*Bu, in turn formed from $OsHCl(PPh_3)_3$ and 2,3-diamino-2,3-dimethylbutane (Scheme 35).[29] With **73** hydrogenation of acetophenone reached 98% conversion in 20 min. under 5 atm of H_2 at 20 °C. Under the same reaction conditions the related Ru-complex showed a different kinetic behavior. Also the hydrido chloro complex **72**, was able to hydrogenate neat acetophenone by activation with KO*t*Bu.

Scheme 35

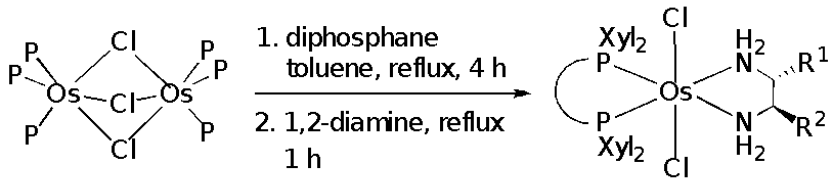


We described the osmium complexes *trans*-**75** and **76**, analogous to those developed by Noyori with ruthenium,[8] by reaction of $OsCl_2(PPh_3)_3$ with dppf followed by diamines (Scheme 36).[30] Conversely, the chiral complexes *trans*-**79**–**82** were obtained by reaction of $[Os_2Cl_4(P(m\text{-tolyl})_3)_5]$ with the bulky diphosphine (**77**,**78**) and 1,2-diamine ligands (Scheme 36). Compounds **75** and **76** displayed exceptionally high catalytic activity in the hydrogenation of methyl-aryl, dialkyl, diaryl ketones and aldehydes, achieving TOF values up to 3.0×10^5 h^{-1} (Scheme 37). With the chiral compounds **79**,**80**,**81** different ketones, including alkyl-aryl, *tert*-butyl and cyclic ketones were successfully hydrogenated with stereotioselectivity up to 99% ee with S/C ratios = 10000–100000 and TOF = 4.1×10^4 h^{-1} (Scheme 38). This indicates that these osmium complexes are valid complement to the Noyori ruthenium catalysts that show poor activity for the bulky *tert*-butyl ketones.

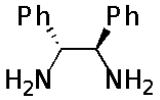
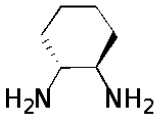
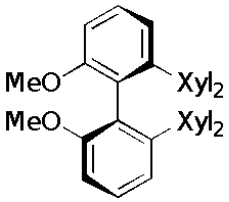
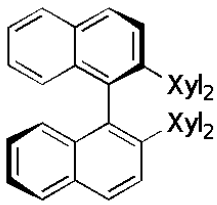
Scheme 36



75 (n = 1), **76** (n = 2)

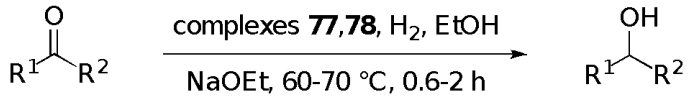


P = P(*m*-tolyl)$_3$

	 (*R*,*R*)-dpen	 (*R*,*R*)-dach
 **77**	**79**	**80**
 **78**	**81**	**82**

Xyl = 3,5-$Me_2C_6H_3$

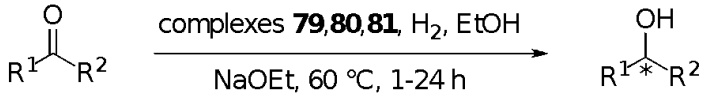
Scheme 37



complex	R^1	R^2	S/C	temp (°C)	conv (%)	time (min)	TOF (h^{-1})
75	Me	Ph	1.0×10^4	70	96	10	1.7×10^5
75	Me	Ph	2.0×10^5	70	90	2 h	2.3×10^5
76	Me	Ph	5.0×10^4	70	>99	30	3.0×10^5
75	Me	*n*-C_8H_{17}	5.0×10^4	60	99	60	8.0×10^4
75	-$(CH_2)_5$-		5.0×10^4	60	>99	60	9.0×10^4
75	Ph	Ph	1.0×10^4	60	>99	30	3.0×10^4
75	H	Ph	1.0×10^4	60	>99	10	9.0×10^4
75[a]	H	*n*-C_5H_{11}	1.0×10^4	60	>99	10	5.7×10^4

Reaction conditions: H_2 (5 atm), ketone or aldehyde (0.5 M), NaOEt (1 mol%), EtOH at 60-70 °C. [a]NaOEt = 0.5 mol%.

Scheme 38

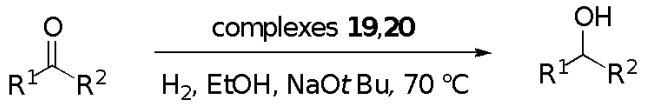


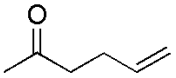
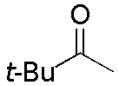
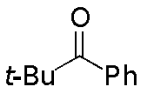
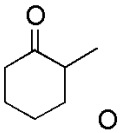
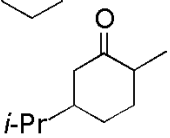
complex	R^1	R^2	conv (%)	time (h)	TOF (h^{-1})	ee (%)
79	Me	Ph	96	0.5	2.0×10^4	90 (*S*)
79[a]	Me	Ph	90	15	1.0×10^4	90 (*S*)
81	Me	Ph	>99	0.5	2.5×10^4	97 (*S*)
82	Me	Ph	99	0.5	4.1×10^4	90 (*S*)
81	Me	3-BrC_6H_4	>99	1	1.0×10^4	94 (*S*)
81	Me	3,5-$(MeO)_2C_6H_3$	>99	0.5	2.0×10^4	99 (*S*)
81	CF_3	Ph	>99	1	1.2×10^4	87 (*R*)
81	Et	Ph	>99	0.5	1.9×10^4	99 (*S*)
81	*i*Pr	Ph	99	3	5.0×10^3	99 (*S*)
81	*t*Bu	Ph	85	24	1.0×10^3	90 (*S*)
81	Me	*t*Bu	92	15	1.2×10^3	71 (*R*)

Reaction conditions: H_2 (5 atm), ketones (0.5 M), substrate/catalyst (10.000), NaOEt (1 mol%), EtOH at 60 °C. [a]Substrate/catalyst (100.000), NaOEt (2 mol %) at 50 °C.

We found that the mixture of the $OsCl_2$(dppb)(Ampy) complexes *trans*-**19** and *cis*-**20** (1:3 ratio) (Scheme 9), was highly active in HY of ketones at low H_2 pressure, in addition to TH.[9] Among the differente screenned alcohols ethanol was found to give the best performance in the presence of KO*t*Bu; thus, a ethanolic mixure of **19** and **20 (**0.05 mol%) reduced acetophenone in 10 min (TOF = 1.5 x 10^4 h^{-1}) (Scheme 39). At a lower osmium loading (0.01 and 0.005 mol%), the reduction also occurred completely with almost the same rate, indicating that these complexes are robust catalysts for hydrogention reactions. This system also catalyzed efficiently the hydrogenation of bulky substrates, including *tert*-butyl ketones that are substrates difficult to reduce (Scheme 39).

Scheme 39

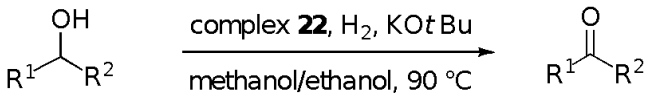


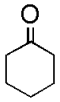
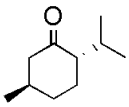
complex (mol%)[a]	ketone	conv (%)	time (h)	TOF (h^{-1})
0.05 0.01 0.005		>99 >99 >99	10 min 1 4	1.5 x 10^5 1.4 x 10^4 1.3 x 10^4
0.01		>99	1	1.4 x 10^4
0.01		>99	3	1.1 x 10^4
0.01		97	2	1.1 x 10^4
0.01		99	3	7.0 x 10^4
0.01		>99	2	1.3 x 10^4

Reaction conditions: ketone (0.5 M), KO*t* Bu (2 mol%), ethanol, H_2 (5 atm) at 70 °C. [a]Mixture **19**/**20** = 1:3

We also determined that the complex *trans*-**22** (Scheme 12) was also catalytically active in the HY of aldehydes and ketones at low hydrogen pressure (5 atm) and in the presence KO*t*Bu showing TOF up to 1.0 x 10^4 h^{-1} in a methanol/ethanol mixture (Scheme 40).[9] Comparative results between Os-catalyst **22** and the related Ru-catalyst (reference) suggested that osmium is a valid complement to ruthenium for both HY and TH reactions, taking into account that osmium is more robust and so allowing to operate a higher temperature.

Scheme 40



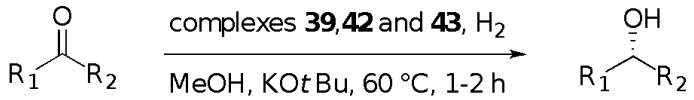
R^1	R^2	conv (%)	time (min)	TOF (h^{-1})
Ph	H	97	10	1.0×10^3
4-$MeOC_6H_4$	H	97	10	4.7×10^3
$PhCH_2$	H	91	8 h	1.0×10^3
PhCH=CH	H	90	30	4.6×10^3
Ph[a]	Me	98	10	9.0×10^3
4-$MeOC_6H_4$	Me	95	30	3.7×10^3
Ph	4-ClC_6H_4	97	30	4.6×10^3
		99	15	6.8×10^3
		90	2 h	3.7×10^3

Reaction conditions: carbonylic compound (0.5 M), KO*t* Bu (2 mol %) in methanol/ethanol (3/1, v/v) with the Os-catalyst (0.1 mol %) under 5 atm of H_2 at 90 °C.

3.3. Osmium complexes with tridentate ligands

We found that the pincer osmium complexes **39**,**42** and **43** (Scheme 16), exceptionally active in TH reactions, were also efficient catalysts for the HY of ketones in methanol with KO*t*Bu. [13] Thus various ketones were quantitatively converted into the corresponding alcohols within 1-2 h in the presence of 0.005 mol% of the catalyst (TOF up to 5.2×10^4 h^{-1}) (Scheme 44). The AHY of methyl aryl ketones also proved possible with the chiral derivatives **42** and **43** (0.005 mol%), affording enantioselectivities of up to 98% ee (Scheme 41).

Scheme 41

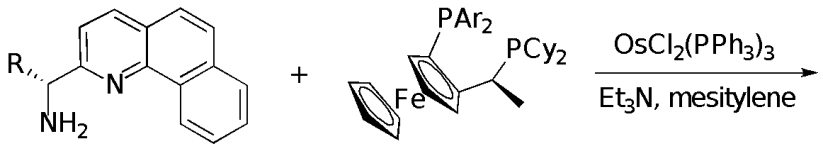


complex	R^1	R^2	conv (%)	time (h)	TOF (h^{-1})	ee (%)
39	Me	Ph	99	1	2.5×10^4	
39	Me	3-$MeOC_6H_4$	99	1	2.6×10^4	
39	-$CH_2(CH_2)_3CH_2$-		99	0.5	3.3×10^4	
39	Me	*n*-C_5H_{11}	99	1	2.9×10^4	
42	Me	Ph	98	0.5	5.2×10^4	80
43	Me	Ph	99	2	1.2×10^4	86
43	Me	2-$MeOC_6H_4$	99	2	2.2×10^4	93
43	Me	3-$MeOC_6H_4$	99	2	2.0×10^4	98
43	Me	3-ClC_6H_4	99	1	2.8×10^4	98
43[a]	Me	3-ClC_6H_4	98	2	3.0×10^4	98

Reaction conditions: H_2 (5 atm), ketones (0.5 M), complex (0.005 mol %), KO*t*Bu (5 mol%), MeOH. [a]0.001 mol% Os.

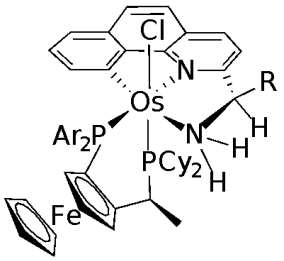
We prepared chiral orthometalated Os-complex **84** by treatment of $OsCl_2(PPh_3)_3$ with (*S*,*R*)-Josiphos, followed by 2-aminomethylbenzo[*h*]quinoline (**83a)** (Scheme 42).[31] Moreover, according to our previous studies on Ru- and Os-complexes showing that (*S*,*R*)-Josiphos correctly matched with chiral 1-substituted-1-(pyridin-2-yl)methanamines and CNN ligands of *R* configuration,[xx] prepared the complex **85** as a single stereoisomer by reaction of $OsCl_2(PPh_3)_3$ with (*S*,*R*)-Josiphos* and (*R*)- **90b** (Scheme 42).[31] The Os-complexes **47** (Scheme 20) and **84** and **85** were found to be active in the hydrogenation of C=O bonds with H_2 at low pressure (Scheme 43). Os-complex **47** catalyzed the quantitative HY of various ketones at 70 °C in 30 min (5 atm H_2) with a low amount of base (KO*t*Bu/Os = 5), affording a TOF up to 3.2×10^4 h^{-1}. On the other hand, the chiral complexes **84** and **85** showed to hydrogenate acetophenone at 70 °C with 86 and 92% ee, respectively, and at good rate (TOF up to 2.0×10^4 h^{-1}) in a MeOH/EtOH mixture and with a KO*t*Bu/Os ratio of 200 (Scheme 46). Interestingly, a similar performance was reached with the *in situ* prepared system $OsCl_2(PPh_3)_2$/(*S*,*R*)-Josiphos*/**83b** , affording (*S*)-1-phenylethanol with 90% ee. With this *in situ* generated catalyst the reduction of other ketones was very successful (up to 99% ee) (Scheme 43).

Scheme 42



83a,b

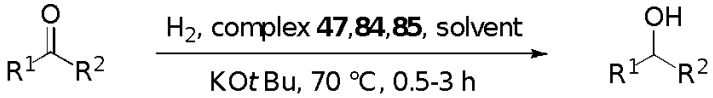
a: R = H, **b**: R = Me



84: Ar = Ph, R = H

85: Ar = 4-MeO-3.5-$Me_2C_6H_2$, R = Me

Scheme 43



complex	R^1	R^2	conv (%)	time (h)	TOF (h^{-1})	ee (%)
47[a]	Me	Ph	99	30	3.2×10^4	
47[a]	Et	Ph	99	30	2.7×10^4	
47[a]		*n*-C_8H_{17}	99	30	2.8×10^4	
47[a]	-$CH_2(CH_2)_3CH_2$-		99	30	2.8×10^4	
47[a]	-CH(Me)$(CH_2)_3CH_2$-		99	3 h	5.4×10^4	
84[b]	Me	Ph	99	30	2.0×10^4	86 *S*
85[b]	Me	Ph	97	60	1.4×10^4	92 *S*
in situ[c]	Me	Ph	99	30	2.4×10^4	90 *S*
in situ[c]	Me	3-$MeOC_6H_4$	99	30	2.2×10^4	91 *S*
in situ[c]	Me	2-naphthyl	99	30	1.6×10^4	94 *S*
in situ[c]	Et	Ph	99	60	1.3×10^4	99 *S*

Reaction conditions: [a]Ketone (0.5 M) in MeOH, under H_2 (5 atm), substrate/Os/KO*t*-Bu = 10000:1:5 at 70 °C. [b]Ketones (0.5 M) in MeOH/EtOH (7:3), under H_2 (5 atm), at 70 °C, substrate/complex/KO*t*-Bu = 10000:1:200. [c]Ketones (0.5 M) in MeOH/EtOH (7:3), under H_2 (5 atm), at 70 °C, $OsCl_2(PPh_3)_3$/(*S*,*R*)-Josiphos*/**83b** = 1:1.5:2.

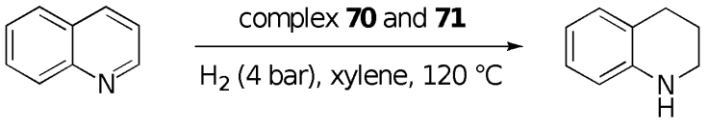
The proposed mechanism for the catalytic hydrogenation with Os-pincer complexes in basic alcohol

media is depicted on Scheme 23. According to the studies on the analogous Ru-pincer complexes, the Os-chloride **53** reacts with alkali alkoxide, leading to a osmium alkoxide **54** that converts into the hydride **55**.[20] The reaction with the ketone substrate leads to the alcohol product with formation of an osmium amide alcohol adduct, which reacts with H_2 affording the hydride osmium and closing the cycle. While in the catalytic TH the hydride is generated from the osmium isopropoxide, in the HY the metal hydride is formed by heterolytic H_2 splitting. As in the TH, in the HY the NH_2 group has a key role for enhancing the rate of the reaction allowing hydrogen bonding with the alcohol media and facilitanting the overall proton transfer. In addition, the nature of the alcohol also plays a crucial role methanol and ethanol showing better performance with respect to 2-propanol.

5. HYDROGENATION OF IMINES

The complex **71** and its precursor **70** (Scheme 35) were used for the quinoline hydrogenation to 1,2,3,4-tetrahydroquinoline (Scheme 44).[27,28] The cationic complex **71** was a more efficient catalyst then **70** (Scheme 44), showing also to be an efficient and regioselective catalyst for the hydrogenation of the nitrogen-containing ring of quinoline (Q), isoquinoline (iQ), 5,6- and 7,8-benzoquinoline (BQ), and acridine (A) (Table 3).[32] The high activity and stability of the Os-complex allowed to carry out kinetic and mechanistic studies for the hydrogenation of Q, iQ and A. These studies demonstrated that the addition of hydrogen (the second molecule of H_2, in the case of Q and iQ) was the rate-determining step of each of these hydrogenation reactions.

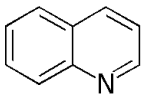
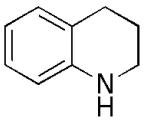
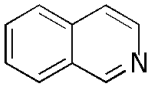
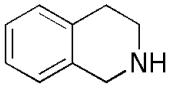
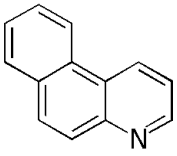
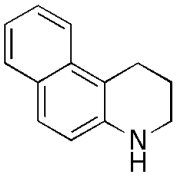
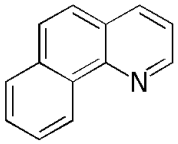
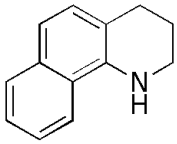
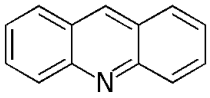
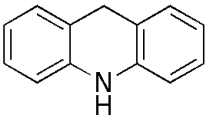
Scheme 44



catalyst[a]	TN[b]
70	2
71	42

[a]catalyst = 0.1 mol%
[b]Turnover number in 1 h

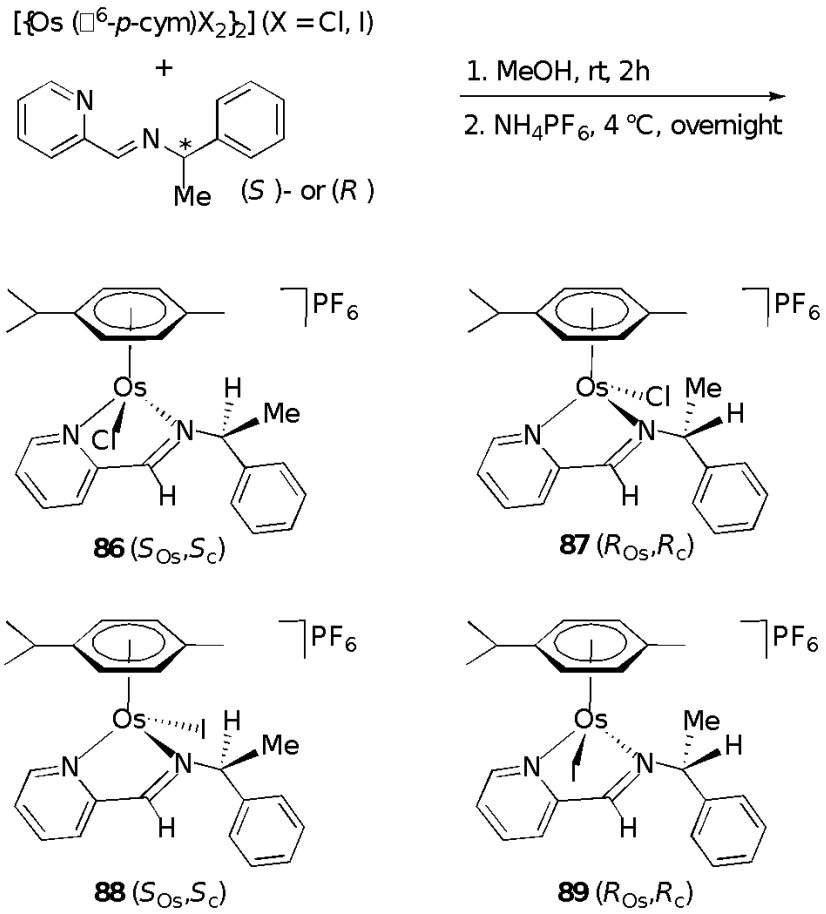
Table 3. Hydrogenation of nitrogen-containing rings by complex **71**.

substrate	product	TN[a]
		23
		20
		2
		<1
		46

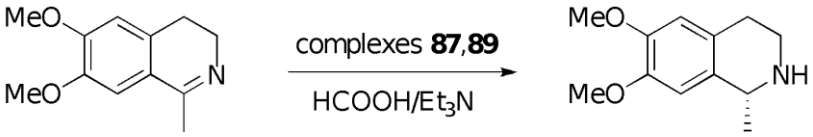
Reaction conditions: [Os] = 1.7×10^{-3} M, [substrate] = 0.17 M, $P(H_2)$ = 4 atm, T = 125 °C, xylene.
[a]TN = turnover number (1 h).

The four Os(II)-arene complexes **86**–**89** were synthesized by reaction of of $[Os(\eta^6\text{-}p\text{-cymene})X_2]_2$ (X = Cl, I) and the chiral ligands ((*S*)- or (*R*)-1-phenyl-*N*-(pyridin-2-ylmethylene)ethanamine (Scheme 45).[33] These complexes were obtained as a mixture of two diastereomers differing only in the metal configuration (R_{Os} or S_{Os}) and isolated as single isomer by crystallization. The catalytic activity of **87** and **89** was evaluated for the reduction of 6,7-dimethoxy-1-methyl- 3,4-dihydroisoquinoline, affording reasonable conversions (20–76%), but low ee (22–23 %) (Scheme 46).

Scheme 45



Scheme 46



catalyst	temp. (°C)	Time (h)	Conv. (%)	ee (%)
87	45	22	40	22
89	60	18	76	22
89	28	23	20	23

Reaction conditions: catalyst (0.1 mol%), $HCOOH/Et_3N$ (5.2)

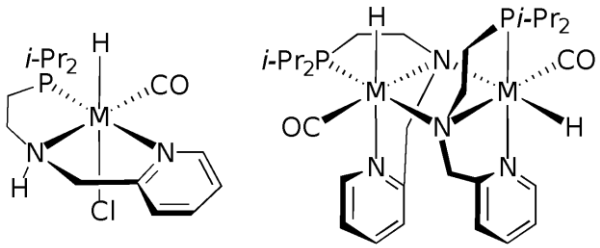
6 . HYDROGENTION OF ESTERS

The hydrido carbonyl chloride Os-complex **90** was treated with KO*t*Bu to afford the unusual dimer **91** (Figure 5).[34] The catalytic activity of these complexes under H_2 (50 bar) was first tested in the HY of methyl benzoate. The Os-dimer **91** was an efficient catalyst, but with a slower rate compared to the corresponding Ru-complex **93** (Figure 5). The chloride **90** and the corresponding Ru-complex **92** (Figure 1) were also similarly active, but only in the presence of KO*t*Bu. The complex **91** was further

investigated in the HY of a series of esters (Scheme 47) and alkenoates (Scheme 48). This complex was equally active for the HY of ethyl, *i*-butyl, methyl benzoates and ε-caprolactone, but failed with isopropyl 2-bromobenzoate and methyloxalate. Activity and selectivity was also tested with substrates containing C=C bonds. The results showed significant differences for Os- and Ru-catalysts. Hydrogenation of methyl 2-nonenoate was not selective with **91** and **9**2, affording methyl nonanoate and nonanol, respectively. Os-dimer **91** successfully catalyzed reduction of methyl 3-nonenoate to 3-nonenol, whereas the related Ru-dimer **93** proved inactive in this reaction. Methyl oleate was hydrogenated with **91** with retention of the C=C bond to give (Z)-octadec-9-enol, whole with **93** afforded a mixture of octadecanol and (*E*)- and (*Z*)-octadec-9-enols.

The authors indicated that both the Noyori-type outer-sphere and the classical innersphere hydrogenation mechanisms were possible with the NNHP*i*Pr complexes (Scheme 49). The superior activity of **91** versus $RuH_2(CO)(PNHPiPr)$ for hydrogenation of methylbenzoate suggested an important role of hemilability of the NNHP*i*Pr-coordinated catalysts.

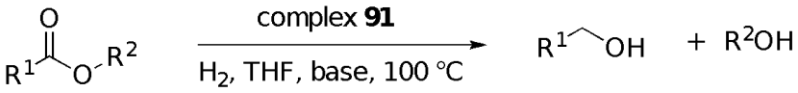
Figure 5



90 (M = Os)
92 (M = Ru)

91 (M = Os)
93 (M = Ru)

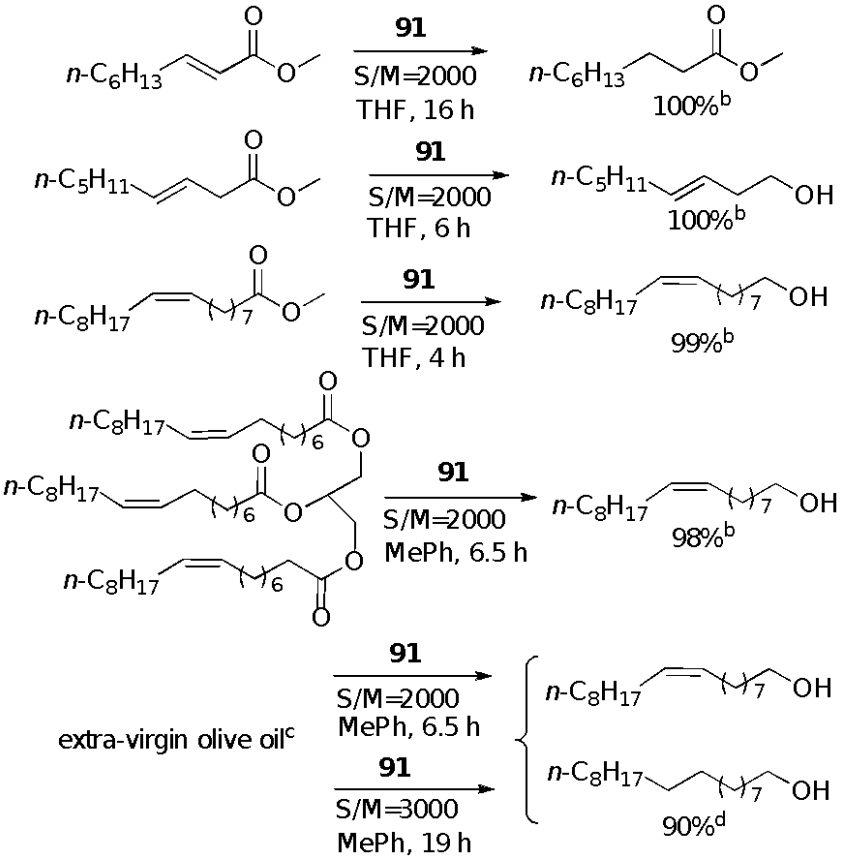
Scheme 47



R^1	R^2	time (h)	conv (%)
Ph	Et	1.6	99
Ph	*i* Pr	1.5	93
2-BrC_6H_5	*i* Pr	17	0
n-C_6H_4	Me	2	100
Me	Et	3	100
-$(CH_2)_5$-		1.4	99
MeCH(OH)	Me	9	72
MeOC(O)	Me	23	0

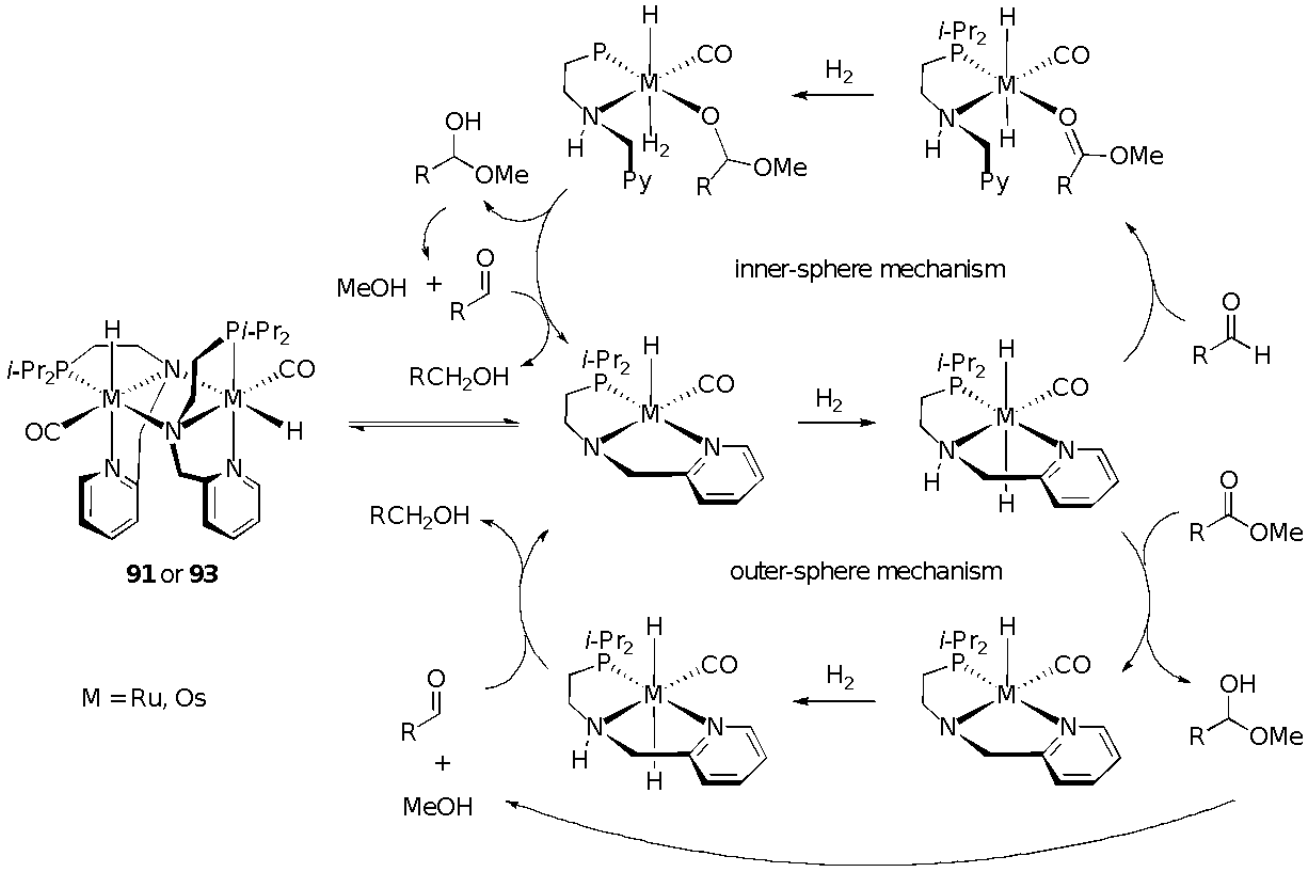
Reaction conditions: substrate (20 mmol), molar ratio substrate/metal = 2000, H_2 (50 bar), THF (7 mL) at 100 °C.

Scheme 48



Hydrogenation of alkenoates at 100 °C and H_2 (50 bar), S/M = molar ratio of alkenoate groups to metal. [a]With tBuOK (0.5 mol%). [b]Conversion. [c]A mixture of triglycerides of oleic (ca. 85%), linoleic (ca. 2–3%), and palmitic acids as the main components. [d]Total yield of isolated alcohol mixture,containing approximately 85% of oleyl alcohol.

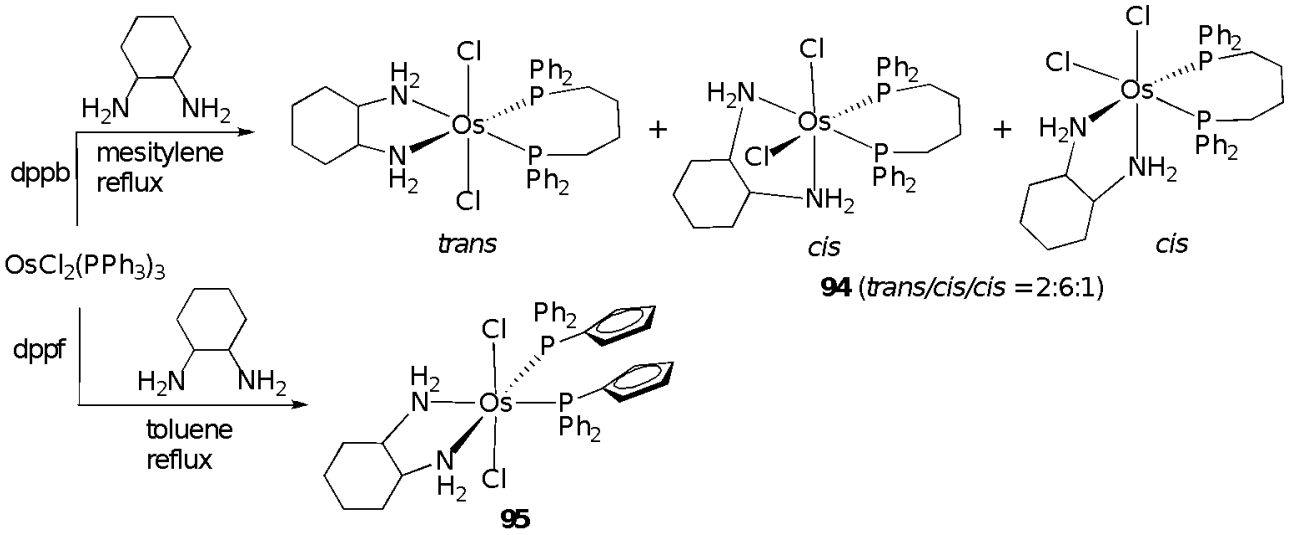
Scheme 49. Inner- and outer-sphere mechanism for ester hydrogenation catalyzed by complex **91** or **93**.



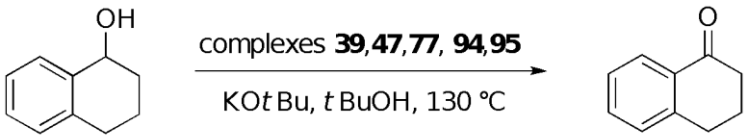
7. DEHYDROGENATION OF ALCOHOLS TO KETONES

We have recently reported the first example of the use of Os-complexes in the dehydrogenation (DHY) of alcohols to ketones.[35] Complex **94** was prepared as mixture *trans/cis/cis*=2:6:1 by reaction of $OsCl_2(PPh_3)_3$ with dppb and (±)-*trans*-1,2-di-aminocyclohexane (*trans*-dach) in mesitylene at reflux, while complex **95** was obtained as a single *trans*-isomer treating $OsCl_2(PPh_3)_3$ with dppf and *trans*-dach (Scheme 50). The bidentate amino derivatives **94**,**95** and **77** (Scheme 39), and the pincer Os-complexes **39** (Scheme 16) and **47** (Scheme 20) were assessed in the dehydrogenation of 1,2,3,4-tetrahydro-1-naphthol (α-tetralol). Complexes **94**,**95** and **77** catalyzed efficiently the dehydrogenation of α-tetralol affording almost complete conversion (93–98%), whereas the pincer complexes **39** and **47** displayed low activity, leading to incomplete formation of α-tetralone (Scheme 51). The best activity was obtained with complex **77** that gave 98% conversion in 6 h. This complex was also an efficient catalyst for the dehydrogenation of a number of alcohol (Table 4) and sterols (Scheme 52).

Scheme 50



Scheme 51



complex	time (h)	conversion (%)
39	24	44
47	24	36
77	6	98
94	22	93
95	24	96

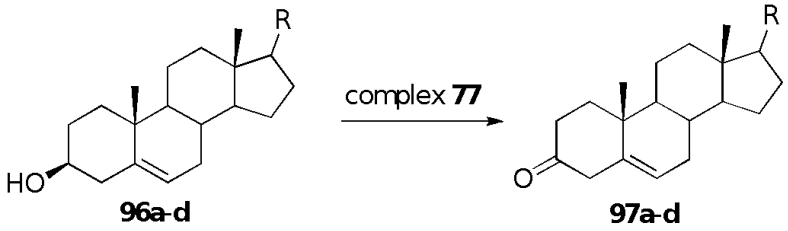
Reaction conditions: catalyst (0.4 mol %), KO*t* Bu (2 mol%), *t* BuOH,130 °C.

Table 4. Dehydrogenation of alcohols with complex **77**.

alcohol	conv (%)	time (h)	TOF (h^{-1})
1,2,3,4-tetrahydronaphthalen-1-ol	98	6	80
2,3-dihydro-1*H*-inden-1-ol	98	6	50
9*H*-fluoren-9-ol	88[a]	20	20
1-phenylethanol	96	20	40
1-(4-methoxyphenyl)ethanol	68	20	-
1-(2-methylcyclohex-1-enyl)ethanol	82	20	30
1-(2,4,4-trimethylcyclohex-1-enyl)ethanol	97	20	70
cyclohex-2-enol	91[b]	2	220
heptan-2-ol	91[c]	0	15
heptan-3-ol	40	30	-
diphenylmethanol	41	30	-

Reaction conditions: complex (0.4 mol%), KO*t* Bu (2 mol%) in *t*-BuOH at 130 °C. [a]Substrate/catalyst/KOtBu = 125:1:5. [b]Isomerization to cyclohexanone. [c]Substrate/catalyst/KOtBu = 50:1:5.

Scheme 52



96a-d **97a-d**

R = **a**: CH(Me)$(CH_2)_3$*i* Pr, **b**: CH(Me)CH=CHCH(Et)*i* Pr, **c**: =O, **d**: COMe

alcohol	conv (%)	time (h)	TOF (h^{-1})
96a	98	20	15
96b	98	20	8
96c	86	20	6
96d	95	20	25

Reaction conditions: complex (0.8 mol%), KOtBu (4 mol%) in tBuOH/toluene (2:1, v/v) at 145 °C.

More recently, we found that the Ampy Os-complex **22** (Scheme 13) showed good efficiency in DHY of some alcohols.[10] Thus, for instance, by using complex **22** the sterol **96a** underwent 98% conversion in 1 h, while the anologue diamine derivate **95** afforded 96% conversion after 20 h.[35]

8. CONCLUSIONS

The work described in this account demonstrates that Os-complexes have recently showed a remarkably high catalytic activity in the hydrogenation and transfer hydrogenation reactions of ketones, aldehydes, esters and imines, allowing the synthesis of chiral and non-chiral alcohols and amines in high yields and very short reaction times. Moreover, the high productivity and thermal stability, simple synthesis and manipulation proved by Os-complexes may offset the higher cost compared to their Ru-analogues. Importantly, Os-complexes are able to catalyze both TH and HY reactions, as well as dehydrogenation of alcohols, with comparable or superior efficiency to those reported for analogous ruthenium systems. These results give a glimpse of the potential of Os-complexes for leading to the designing of new highly productive and robust catalysts for the synthesis of chiral and non-chiral alcohols and amines, as well as ketones from alcohols. Thus, we hope that this report will promote increased interest in the chemistry of these metal complexes, opening novel opportunities for new catalytic processes as well as for improvement the existing ones.

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Notes

The authors declare no competing financial interest.

Biographies

Giorgio Chelucci received his laurea degree in chemistry from Sassari University (Sardegna) in 1978. After 5 years of postlaurea work he became a Researcher in the Department of Chemistry at the University of Sassari. His research, documented by about 150 peer-reviewed papers, 5 book chapters and 3 patents, centers on the design, synthesis, and application in catalysis of chiral ligands with particular interest toward those based on the pyridine framework and on metal-catalyzed catalytic reactions.

Salvatore Baldino received his laurea degree in chemistry from Sassari University in xxxx and his Ph.D. from the Sassari University under the supervision of Dr. Giorgio Chelucci in xxxx. Currently, he is conducting postdoctoral research with Prof. Walter Baratta at the University of Udine. His research focuses on the synthesis and application in metal-catalyzed reactions of chiral and non-chiral lgands.

Walter Baratta was graduated in chemistry from the University of Pisa in 1989. During his Ph.D he spent one year in the group of Prof. P. Pregosin at the Technical Institute of Zürich (CH). In 1994 he carried out postdoctoral studies in the laboratory of Prof. W. Herrmann at the Technical Institute of München (D) (Alexander von Humboldt fellowship). After returning to Italy he became Research Associate in 1996 at the University of Udine and in 2005 was appointed Associate Professor. His research interests are mainly focused on the development of efficient homogeneous ruthenium and osmium catalysts for transfer hydrogenation and hydrogenation of carbonyl compounds.

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