ACCOUNTS of chemical research

Article

pubs.acs.org/accounts

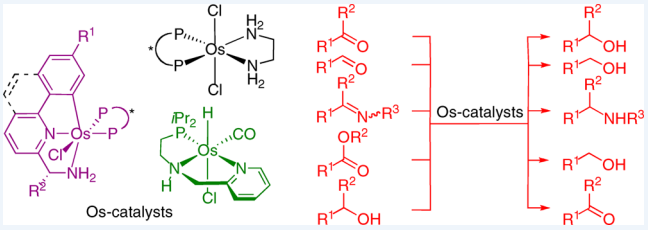
Recent Advances in Osmium-Catalyzed Hydrogenation and Dehydrogenation Reactions

Giorgio Chelucci,*[,†] Salvatore Baldino,[‡] and Walter Baratta*[,‡]

[†]Dipartimento di Agraria, Università di Sassari, Viale Italia 39, I-07100 Sassari, Italy

[‡]Dipartimento di Chimica, Fisica, Ambiente, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy

CONSPECTUS: A current issue in metal-catalyzed reactions is the search for 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 that are able to efficiently promote different organic transformations by careful switching of the reaction parameters, such as temperature, solvent, and cocatalyst. In this context, osmium complexes have shown the ability to catalyze efficiently different types of reactions involving hydrogen, proving at the same time high thermal stability and simple synthesis. In the catalytic reduction of C═X (X = O, N) bonds by both hydrogenation (HY) and transfer hydrogenation (TH) reactions, the most interest has been focused on homogeneous systems based on rhodium, iridium, and in particular ruthenium catalysts, which have proved to catalyze chemo- and stereoselective hydrogenations with remarkable efficiency. By contrast, osmium catalysts have received much less attention because they are considered less active on account of their slower ligand exchange kinetics. Thus, this area remained almost neglected until recent studies refuted these prejudices. The aim of this Account is to highlight the impressive developments achieved over the past few years by our and other groups on the design of new classes of osmium complexes and their applications in homogeneous catalytic reactions involving the hydrogenation of carbon−oxygen and carbon−nitrogen bonds by both HY and TH reactions as well as in alcohol deydrogenation (DHY) reactions. The work described in this Account demonstrates that osmium 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 as well in DHY reactions of alcohols. Thus, for instance, the introduction of ligands with an NH function, possibly in combination with a pyridine ring, led to a new family of $[OsCl_2(PP)(NN)]$ (NN = diamine, 2-aminomethylpyridine; PP = diphosphine) and pincer $[OsCl(CNN)(PP)]$ (HCNN = 6-aryl-2-aminomethylpyridine, 2-aminomethylbenzo[*h*]quinoline) complexes, which are outstanding catalysts for (asymmetric) HY and TH of carbonyl compounds and DHY of alcohols with turnover numbers and turnover frequencies up to 10^5 and 10^6 h^{-1}, respectively. In addition, PNN osmium complexes containing the 2-aminomethylpyridine motif have been found to be among the most active catalysts for HY of esters. These complexes have shown catalytic activities that are comparable and in some cases superior to those reported for analogous ruthenium systems. These results give an idea of the potential of Os complexes for the design of new highly productive and robust catalysts for the synthesis of chiral and nonchiral 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 the improvement of 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 has led to a large number of well-defined chemo- and stereoselective catalysts, while osmium catalysts have been little investigated. Surprisingly, new osmium complexes have recently been prepared and shown to have relevant catalytic performance in HY and dehydrogenation (DHY) processes with activities comparable to or even higher than those of the ruthenium analogues. In comparison to ruthenium, osmium forms a stronger bond toward hydrogen, affording robust catalytically active Os−hydride species. This peculiarity, combined with their simple synthesis and manipulation, may offset the higher cost of Os catalysts compared with their Ru counterparts. In this Account, we describe several impressive results achieved in the past 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 DHY reactions.[3] The Account is organized according to the category of the Os-catalyzed reaction and arranged according to the type of ligand (monodentate, bidentate, etc.) coordinated to the metal.

Received: October 16, 2014
Published: February 4, 2015

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

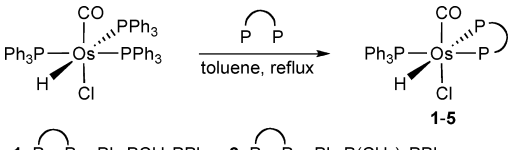
2. TRANSFER HYDROGENATION OF ALDEHYDES AND KETONES

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

2.1. Osmium Complexes with Bidentate Ligands

The Os complexes $[Os(H)(Cl)(CO)(PPh_3)(P\text{^}P)]$ (**1**–**5**) were synthesized as single isomers (Scheme 1) and assessed

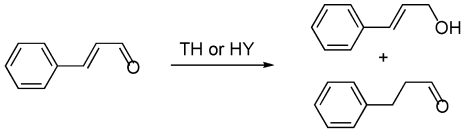
Scheme 1



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

for the selective reduction of *trans*-cinnamaldehyde both by TH and HY.[4] These catalysts showed higher selectivity for the reduction of the C═O bond compared with the C═C bond (Scheme 2). The selectivity for the C═O reduction was found

Scheme 2



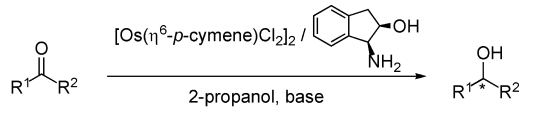
complex	selectivities for cinnamyl alcohol[a]	
	TH (conversion %)[b]	HY (conversion %)[c]
1	63 (10)	61 (25)
2	77 (19)	69 (30)
3	91 (39)	84 (71)
4	74 (20)	65 (28)
5	80 (92)	72 (100)

Reaction conditions: TH = catalyst (0.02 mmol), aldehyde (2 mmol), *i*-PrOH (200 mmol), toluene (30 mL), 110 °C; and HY = complex (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%. [b][amount of product/initial amount of substrate] x 100% after 2 h. [c][amount of product/initial amount of substrate] x 100% after 3 h.

to decrease in the order **3** > **5** > **2** > **4** > **1** and to be greater for TH than HY. Complex **3** exhibited almost 90% selectivity for cinnamyl alcohol in TH.

Faller and Lavoie screened the catalyst generated in situ from $[Os(\eta^6\text{-}p\text{-cymene})Cl_2]_2$ 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 very good enatiomeric excesses (up to 98%). The same catalytic system was also investigated for ATH of ortho- and para-substituted benzaldehyde-α-*d* derivatives, giving high conversions (>98%)

Scheme 3

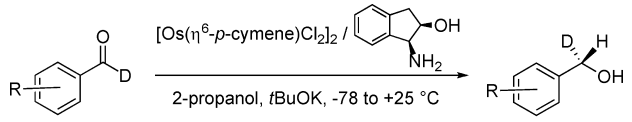


ketone	base	temp (°C)	time (h)	conv (%)	ee (%)
acetophenone	KOH	-24	24	87	91
acetophenone	*t*BuOK	-24	24	86	92
1-(naphthalen-1-yl)ethanone	*t*BuOK	-24	48	80	94
2-(naphthalen-1-yl)ethanone	*t*BuOK	-24	48	77	89
1-tetralone	*t*BuOK	+25	12	84	97
1-indanone	*t*BuOK	-25	48	37	98

Reaction conditions: substrate to metal ratio = 100:1, using 2 mL of 0.1 M base/2-propanol. $[Os(\eta^6\text{-}p\text{-cymene})Cl_2]_2$/ligand mole ratio = 1:4.

and modest to moderate enantioselectivities (up to 60% ee) (Scheme 4).[6]

Scheme 4

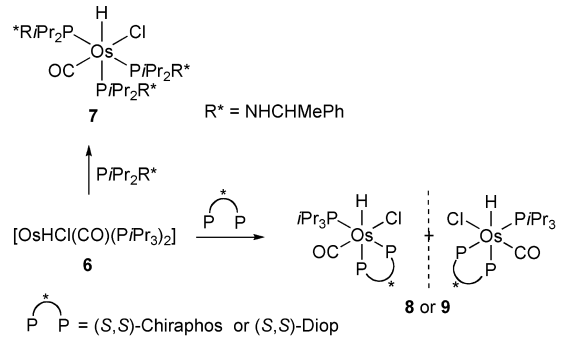


R	ee (%)	R	ee
4-Br	59 (*S*)	2-Me	33 (-)
4-H	60 (*S*)	2-CF_3	25 (-)
4-Me	51 (*S*)		
4-OMe	44 (*S*)		

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

A variety of hydridoosmium(II) complexes were synthesized and assessed for the ATH of acetophenone.[7] The five-coordinate compound $[Os(H)(Cl)(CO)(PiPr_3)_2]$ (**6**) was reacted with $PiPr_2R^*$ (R* = NHCH(Me)Ph) to give the octahedral complex *mer*-**7** (Scheme 5). The reaction of **6** with

Scheme 5



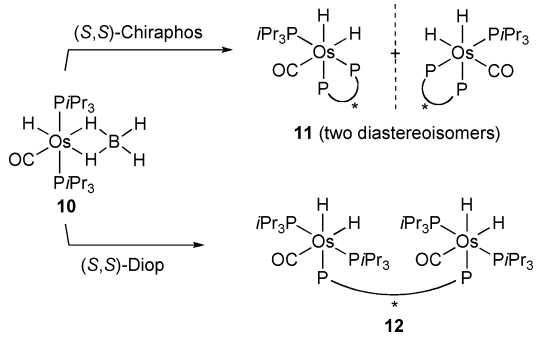
8: only one of the two diastereoisomeric complexes (undetermined) was formed from (*S*,*S*)-Chiraphos
9: two diastereoisomers were formed from (*S*,*S*)-Diop

(2*S*,3*S*)-(−)-bis(diphenylphosphino)butane ((*S*,*S*)-Chiraphos) generated only one of the two diastereoisomeric complexes **8** (undetermined), while the reaction with (4*S*,5*S*)-(+)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)-butane ((*S*,*S*)-Diop) gave two diastereoisomeric chelate complexes **9**, whose ratio was dependent on the reaction

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363–379

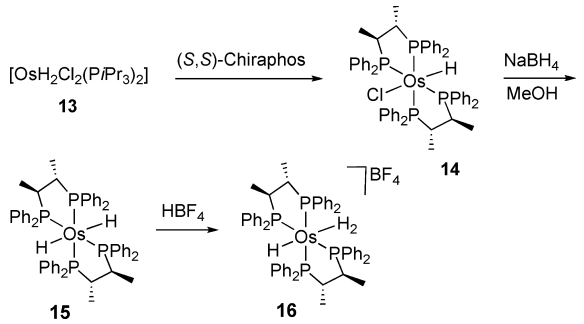
conditions (Scheme 5). $[OsH(\kappa^2\text{-}H_2BH_2)(CO)(PiPr_3)_2]$ (**10**) reacted with (*S*,*S*)-Chiraphos to give the mononuclear octahedral complex **11** as a diastereoisomeric mixture, while the reaction with (*S*,*S*)-Diop quite surprisingly afforded the dinuclear compound **12** (Scheme 6). Treatment of

Scheme 6



$[OsH_2Cl_2(CO)(PiPr_3)_2]$ (**13**) with 2 equiv of (*S*,*S*)-Chiraphos afforded **14**, which was converted into dihydrogen complex **16** via protonation of dihydrido complex **15** (Scheme 7). For the

Scheme 7



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

Table 1. ATH of Acetophenone Catalyzed by Hydridoosmium Complexes 7, 8, 9, and 12

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

Reaction conditions: complex (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 (0.1 M in 2-propanol, 3 mL) was added to the catalyst.

Inspired by Noyori's work on the catalysts $[RuCl_2(PP)(1,2\text{-diamine})]$ (PP = diphosphine),[8] which indicated that the use of ancillary ligands featuring an NH functionality is crucial to achieve highly active HY catalysts, we developed $[OsCl_2(PP)(Ampy)]$-based catalysts, where Ampy is the mixed bidentate nitrogen ligand 2-aminomethylpyridine.[9] Thus, Os complexes **17**−**21** were prepared (Schemes 8 and 9).[9] Treatment of $[OsCl_2(PPh_3)_3]$ with Ampy in mesitylene at 40 °C led to *trans*,*cis*-**17**, which isomerized to *cis*,*cis*-**18** upon being heated at 150 °C (Scheme 8). The reaction of $[OsCl_2(PPh_3)_3]$ with $Ph_2P(CH_2)_4PPh_2$ (dppb) and subsequent treatment with Ampy gave an inseparable mixture of *trans*-**19** and *cis*-**20** in a 1:3 molar ratio, while the reaction with 2-(pyridin-2-yl)ethanamine resulted in the formation of *trans*-**21** (Scheme 9).

The Os compounds **17**−**21** were catalytically active for TH of acetophenone. With the mixture **19**/**20**, TH of acetophenone occurred in 30 s (turnover frequency (TOF) = 5.7×10^5 h^{-1}), showing that its activity is higher than that of the analogous complex *cis*-$[RuCl_2(dppb)(Ampy)]$ (TOF = 3.0×10^5 h^{-1}).[9] With **19**/**20** the reduction of acetophenone was obtained at extremely low catalyst loading. In contrast to the Ru analogues (turnover number (TON) $\leq 10^4$), **19**/**20** was catalytically active even at 0.001 mol % (TON $\approx 1.8 \times 10^5$) with a gradual decrease in the rate as the Os concentration was reduced (TOF = 5.5×10^5 to 3.4×10^5 h^{-1} at 0.02 to 0.001 mol %). This indicated that **19**/**20** is a more robust catalyst than the Ru analogues, making this Os system suitable for the synthesis of alcohols on a preparative scale. The mixture **19**/**20** enabled the fast reduction of several ketones, including *tert*-butyl ketones that are difficult to hydrogenate, and also the chemoselective reduction of 5-hexen-2-one (Scheme 10).

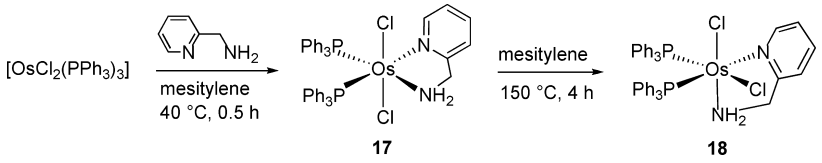
With the catalyst generated in situ from $[OsCl_2(PPh_3)_3]$, (*S*)-1-[(R_p)-2-(diphenylphosphino)ferrocenyl]-ethyldicyclohexylphosphine ((*S*,*R*)-Josiphos), and ligand (Ampy, (±)-1-methyl-1-(pyridin-2-yl)methanamine ((±)-Me-Ampy), or (±)-1-*tert*-butyl-1-(pyridin-2-yl)methanamine ((±)-*t*Bu-Ampy)), ATH of acetophenone afforded (*S*)-phenylethanol with both high ee (91−95%) and TOF (up to 1.9×10^4 h^{-1}).[9] As found for the analogous Ru precursor $[RuCl_2(PPh_3)_3]$,[10] an increase in enantioselectivity was observed when the combination of $[OsCl_2(PPh_3)_3]$ and (*S*,*R*)-Josiphos was used with the racemic mixture of R-Ampy (R = Me, *t*Bu) on account of the diastereoselective formation of the catalyst. With the catalyst generated in situ from $[OsCl_2(PPh_3)_3]$, (*S*,*R*)-Josiphos, and (±)-*t*Bu-Ampy, ATH of aryl methyl ketones afforded the related (*S*)-alcohols with 94−96% ee and TOFs of up to 1.2×10^4 h^{-1} (Scheme 11). These impressive results established that the $[OsCl_2(PP)(Ampy)]$ system can be efficiently used for the preparation of chiral alcohols and opened the way for the design of novel highly efficient Os-based catalysts for TH, HY, DHY, and borrowing hydrogen reactions.

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 that of the related Ru complex.[11] At a loading of only 0.1−0.0005 mol %, complex **22** efficiently catalyzed the chemoselective (C═O vs C═C) TH of aldehydes and ketones to alcohols (TOFs of up to 3×10^5 h^{-1}) (Scheme 13), showing rates comparable to or even higher than those with the related Ru complex. Importantly, Os complex **22** was competitive with the most active CNN pincer Ru system for the TH of aldehydes.[12]

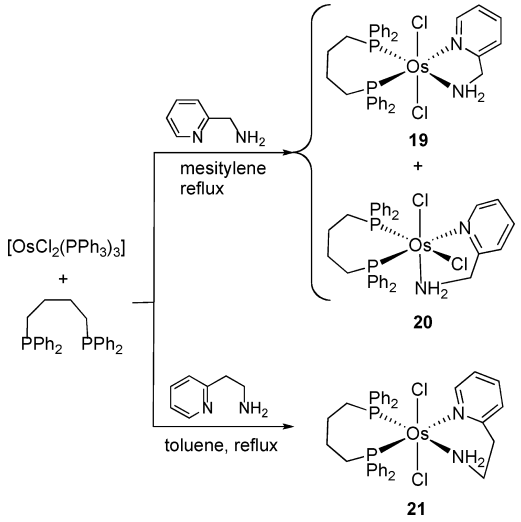
Carmona and co-workers reported the synthesis of the mononuclear osmium arene complexes **23**−**30** containing L-α-aminocarboxylate ligands, which underwent chloride abstraction by $AgBF_4$ in methanol to afford the related cationic trimers **31**−**36** (Figure 1).[13,14] Trimerization most probably occurred through the chiral-at-metal mononuclear species $[(\eta^6\text{-}p\text{-cymene})Os(Aa)(MeOH)]^+$ and took place with chiral self-

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

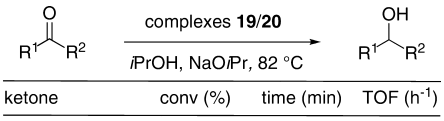
Scheme 8



Scheme 9



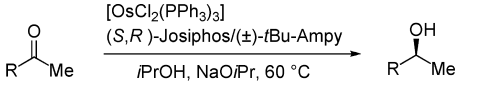
Scheme 10



ketone	conv (%)	time (min)	TOF (h^{-1})
*t*Bu	93	30	8.0×10^3
*t*Bu, Ph	98	30	1.7×10^4
*i*Pr	99	30	2.7×10^4
	96	2	3.2×10^5

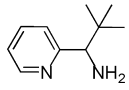
Reaction conditions: ketone (0.1 M), complexes **19**/**20** (1/3)(Os = 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 82 °C.

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*)-Josiphos/(±)-*t*Bu-Ampy (Os 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 60 °C.

(±)-*t*Bu-Ampy: 

recognition, i.e., only the diastereomers with equal configurations at the metal (R_{Os},R_{Os},R_{Os} and S_{Os},S_{Os},S_{Os}) were detected. Both the monomers and trimers were active catalysts for TH of acetophenone with 2-propanol in the presence of HCOONa as the base, affording in most cases conversions of 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 aminocarboxylate ligand, increasing in the sequence NR_2 < NRH < NH_2. The catalytic activity of the prolinate trimer **34** with other ketones was also examined, and this complex was found to give up to 82% stereoselectivity (Table 2).

The results obtained were explained by assuming that Noyori's mechanism applies to their systems displaying NH protons (Scheme 15). The cationic 2-propanol−osmium complex affords the catalytically active hydride species, which transfers a hydride from Os−H and a proton from N−H to the substrate C═O function, affording 1-phenylethanol via a six-membered cycle. Reaction of the coordinatively unsaturated 16-electron complex with 2-propanol gives the Os−H complex, which closes the cycle. Figure 2 depicts an exhaustive description of the proposed six-membered metallacycles involving the N−H and Os−H moieties with the ketone, consistent with the observed enantioselectivities.

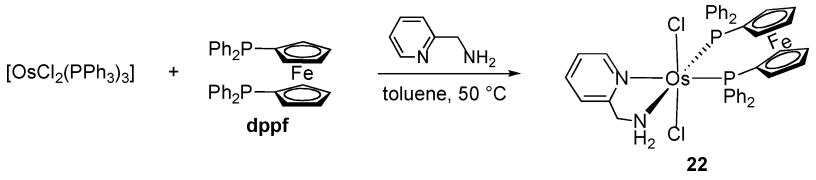
2.2. Osmium Complexes with Tridentate Ligands

Metal complexes containing polydentate ligands are expected to afford robust catalysts that display high productivity resulting from retardation of deactivating side reactions. Since the pincer Ru complexes [RuCl(CNN)(PP)] containing a metal−carbon bond showed outstanding activity and productivity in TH and HY of carbonyl compounds,[15] we prepared the pincer CNN Os complexes **39**−**43**[16] by ortho metalation of (6-phenylpyridin-2-yl)methanamine-based ligands **38a**−**c** (Scheme 16). These complexes were remarkably active catalysts for TH of ketones, affording TOFs of up to 1.3×10^6 h^{-1} (Scheme 17), which were slightly higher than those showed by the Ru analogues. Importantly, the unsaturated ketone hex-5-en-2-one could also be chemoselectively reduced to hex-5-en-2-ol. Chiral derivatives **41**−**43** (0.005 mol %) allowed the ATH of methyl aryl ketones, providing the related alcohols with up to 97% ee (Scheme 17). The reduction of 3-methoxyphenyl methyl ketone with 97% stereoselectivity at a 0.002 mol % loading of **43** indicates that these osmium complexes are outstanding catalysts for the preparation of chiral alcohols, which are usually obtained with 1−0.1 mol % loadings of Ru catalysts.

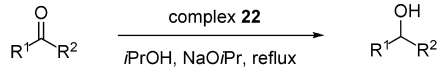
We also used the ligands (*S*)-**38c** and (*S*)-**44a**−**f** (Figure 3) in combination with $[OsCl_2(PPh_3)_3]$ and (*R*)-1-{(S_p)-2-[bis(4-methoxy-3,5-dimethylphenyl)phosphino]ferrocenyl}-ethyldicyclohexylphosphine ((*R*,*S*)-Josiphos*) to produce a variety of in situ-generated pincer Os complexes that efficiently catalyzed the TH of acetophenone.[17] The best-performing ligand was (*S*)-**44f**, which afforded (*R*)-1-phenylethanol with 87% ee (96% conversion) and TOF = 1.5×10^5 h^{-1}. On this basis, complexes **45** and **46** were prepared from (*R*,*S*)-Josiphos

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Scheme 12

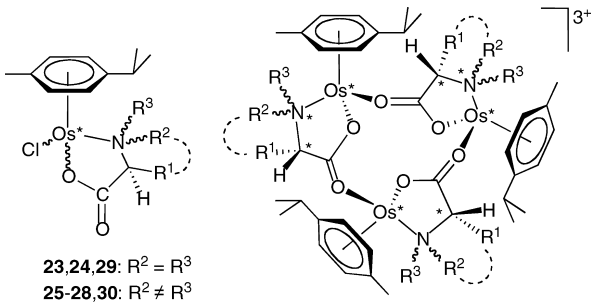


Scheme 13



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
$Me_2C{=}CH(CH_2)_2CH(Me)CH_2$	H	98[a]	120	2.6×10^3
PhCH=CH	H	90[a]	120	8.9×10^4
Ph	Me	98	10	1.9×10^5
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%)



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

31-**36**

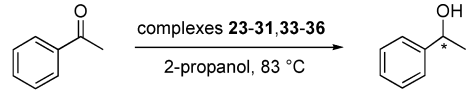
23,**31** (Ala): R^1 = Me, R^2 = H, R^3 = H
24,**32** (Phe): R^1 = Bn, R^2 = H, R^3 = H
25 (MePhe): R^1 = Bn, R^2 = H, R^3 = Me
26,**33** (Aze): R^1-R^2 = -$(CH_2)_2$-, R^3 = H
27,**34** (Pro): R^1-R^2 = -$(CH_2)_3$-, R^3 = H
28,**35** (Pip): R^1-R^2 = -$(CH_2)_4$-, R^3 = H
29 (Me_2Phe): R^1 = Bn, R^2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

Figure 1. Structures of osmium−aminocarboxylate complexes **23**−**36**.

and (*R*,*S*)-Josiphos*, respectively, in combination with (*S*)-**44f** (Scheme 18). Complex **46**, which displayed better performance than **45** in the TH of acetophenone, was also assessed for TH of several alkyl (hetero)aryl ketones and gave up to 99% ee and TOF = 10^5−10^6 h^{-1} (Scheme 19).

We next decided to examine the coordination chemistry and catalytic potential of Os complexes obtained by replacing these CNN ligands with the related ones based on the more rigid structure of the benzo[*h*]quinoline framework. Thus, we prepared the thermally stable pincer Os complex **47** by

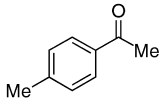
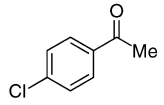
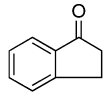
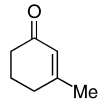
Scheme 14



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; complex (0.04 mmol) in 6.6 mL of 2-propanol; molar ratio complex/HCOONa/acetophenone = 3/6/200; molar ratio complex/HCOONa/acetophenone for trinuclear complexes = 3/4/200.

Table 2. ATH Catalyzed by the Trimer [{(η^6-*p*-Cymene)Os(Pro)}$_3$][BF_4]$_3$ (34)

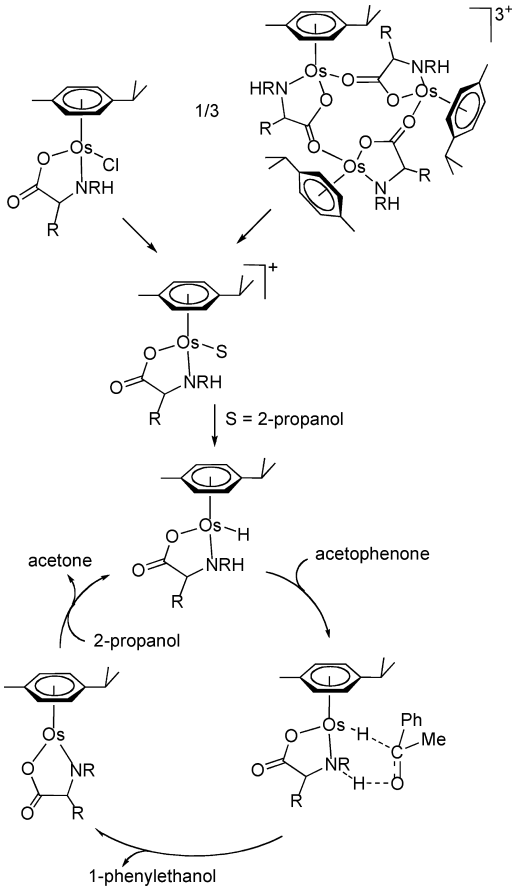
ketone	time (h)	conv (%)	ee (%)	conf
	1.5	62	60	*R*
	1.5	86	44	*R*
	1.5	31	82	*R*
	8	80	76	*R*
	2	8	42	*R*

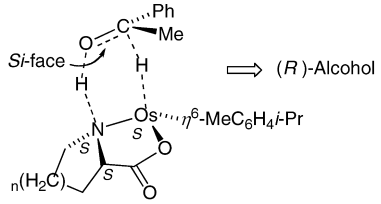
Reaction conditions: complex (0.04 mmol), 2-propanol (6.6 mL), molar ratio complex/HCOONa/ketone = 3/4/200, 83 °C.

treatment of [$OsCl_2(PPh_3)_3$] with dppb followed by further reaction with 2-aminomethylbenzo[*h*]quinoline (Scheme 20).[18] Complex **47** was a highly efficient catalyst for the TH of several ketones. With 0.005 mol % **47**, TOFs of up to 1.8×10^6 h^{-1}

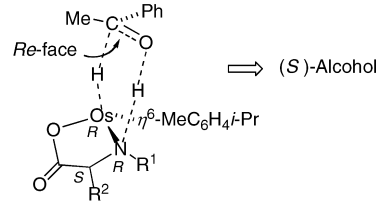
DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Scheme 15





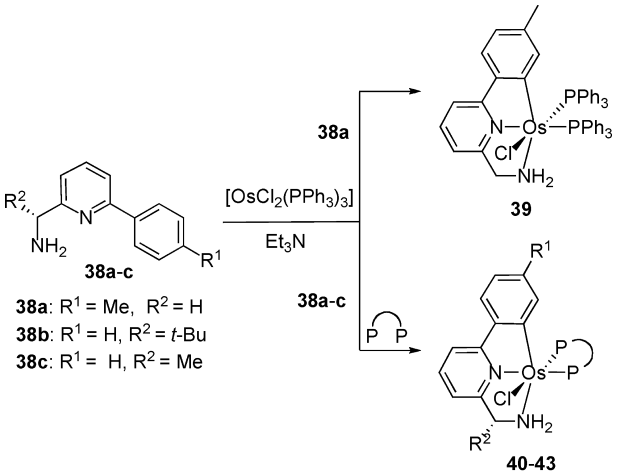
n = 0, azetidine-2-carboxylate (**26**, **33**)
n = 1, prolinate (**27**, **34**)



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

Figure 2. Proposed six-membered metallacycles.

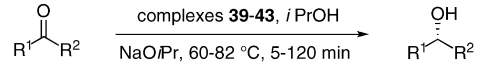
Scheme 16



38a: R^1 = Me, R^2 = H
38b: R^1 = H, R^2 = *t*-Bu
38c: R^1 = H, R^2 = Me

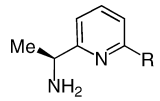
40: P P = dppb, R^1 = Me, R^2 = H
41: P P = dppb, R^1 = H, R^2 = *t*-Bu
42: P P = (*S*,*R*)-Josiphos, R^1 = Me, R^2 = H
43: P P = (*S*,*R*)-Josiphos, R^1 = H, R^2 = Me

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	1.3×10^6	
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	4.0×10^5	
41	Me	Ph	60	94	120	1.2×10^5	74
42	Me	Ph	60	95	30	1.7×10^5	83
43	Me	Ph	60	97	30	1.7×10^5	93
43	Me	2-$MeIC_6H_4$	60	92	60	4.0×10^5	91
43	Me	2-ClC_6H_4	60	96	30	1.3×10^5	90
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
43	Me	3-$MeOC_6H_4$	70	94	120	4.0×10^5	97

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



44a-f

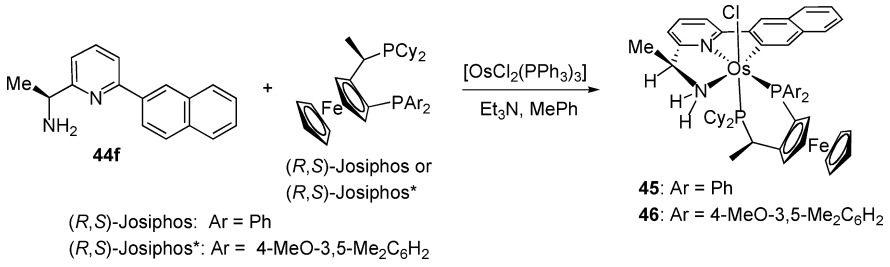
44a: R = 4-$MeOC_6H_4$; **44b**: R = 4-$F_3CC_6H_4$;
44c: R = 3,5-$Me_2C_6H_3$; **44d**: R = 3,5-$(F_3C)_2C_6H_3$
44e: R = 1-naphthyl; **44f**: R = 2-naphthyl

Figure 3. Structures of ligands (*S*)-**44a**−**f**.

were achieved (Scheme 21), showing that the osmium complex has much the same catalytic activity as the analogous Ru complex under these catalytic conditions.[18] With **47**, complete reduction of acetophenone was achieved at a remarkably low catalyst loading (0.001 mol %) in 30 min. Since metal hydride and alkoxide complexes were supposed to be key species involved in catalytic TH and HY processes occurring in basic alcohol media,[19,20] complex **47** was reacted with NaO*i*Pr to afford an equilibrium mixture of alkoxide complex **48** and hydride complex **49** (Scheme 20).[18] The latter complex, which was easily isolable by evaporation of the alcohol and elimination of acetone, was treated with bis(4-fluorophenyl)methanone to afford alkoxide **50**. Complexes **49** and **50** showed high activity in TH but at lower rates than with **47**, possibly because of their moisture and oxygen sensitivity (Scheme 21). ATH of acetophenone was also achieved using the in situ-formed chiral pincer complexes **51** and **52** (obtained from $[OsCl_2(PPh_3)_3]$, 2-aminomethylbenzo[*h*]quinoline, and (*S*,*R*)-Josiphos or (*S*,*R*)-Josiphos*, respectively), which afforded (*S*)-phenylethanol with

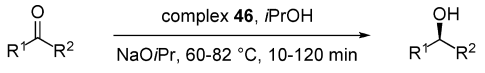
DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Scheme 18



(*R*,*S*)-Josiphos: Ar = Ph
(*R*,*S*)-Josiphos*: Ar = 4-MeO-3,5-$Me_2C_6H_2$

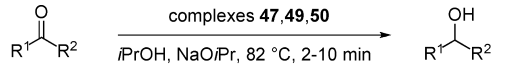
Scheme 19



R^1	R^2	conv (%)	time (min)	TOF (h^{-1})	ee (%)
Me	Ph	97	30	3.2 x 10^5	91
Et	Ph	93	30	1.4 x 10^5	99
Me[b]	1-naphthyl	98	30	5.9 x 10^4	96
Me	2-naphthyl	97	10	3.4 x 10^5	99
Me	2-MeC_6H_4	93	60	5.9 x 10^4	94
Me[a]	3-ClC_6H_4	97	5	4.8 x 10^5	99
Me	3-$F_3CC_6H_4$	99	20	1.8 x 10^5	94
Me	3-$MeOC_6H$	97	30	2.0 x 10^5	99
Me[a,c]	3,5-$(MeO)_2C_6H_3$	97	10	9.0 x 10^5	97
Me[b,d]	3,5-$(F_3C)_2C_6H_3$	99	30	5.1 x 10^4	98
Me	2-pyridyl	99	30	1.2 x 10^5	91
Me[d]	3-pyridyl	99	30	7.6 x 10^4	90
Me[b,d]	4-pyridyl	99	10	8.3 x 10^4	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. [c]Substrate/complex/NaO*i*Pr = 50000/1/1000. [d]In situ reaction.

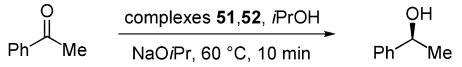
Scheme 21



complex	R^1	R^2	conv (%)	time (min)	TOF (h^{-1})
47	Me	Ph	96	5	1.3 x 10^6
47[a]		Ph	94	30	4.3 x 10
47	Me	2-$MeOC_6H_4$	99	2	1.8 x 10^6
47	Me	$CH_2CH_2CH{=}CH_2$	97	10	3.0 x 10^5
47	-$CH_2(CH_2)_3CH_2$-		98	5	7.0 x 10^5
49	Me	Ph	97	5	6.1 x 10^5
50	Me	Ph	99	5	8.1 x 10^5

Reaction conditions: ketone (0.1 M), complex (0.005 mol%), NaO*i*Pr (2 mol%) in *i*PrOH at 82 °C. [a]Complex (0.001 mol%).

Scheme 22



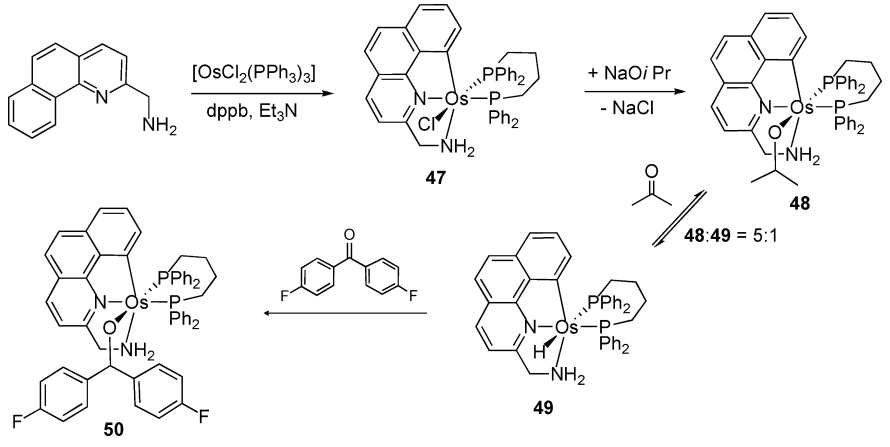
Complex **51**: 96% conv, 80% ee.
Complex **52**: 96% conv, 90% ee.

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

80% and 90% ee, respectively at a high rate (TOF = 2.1 × 10^5 h^{-1})[18] (Scheme 22).

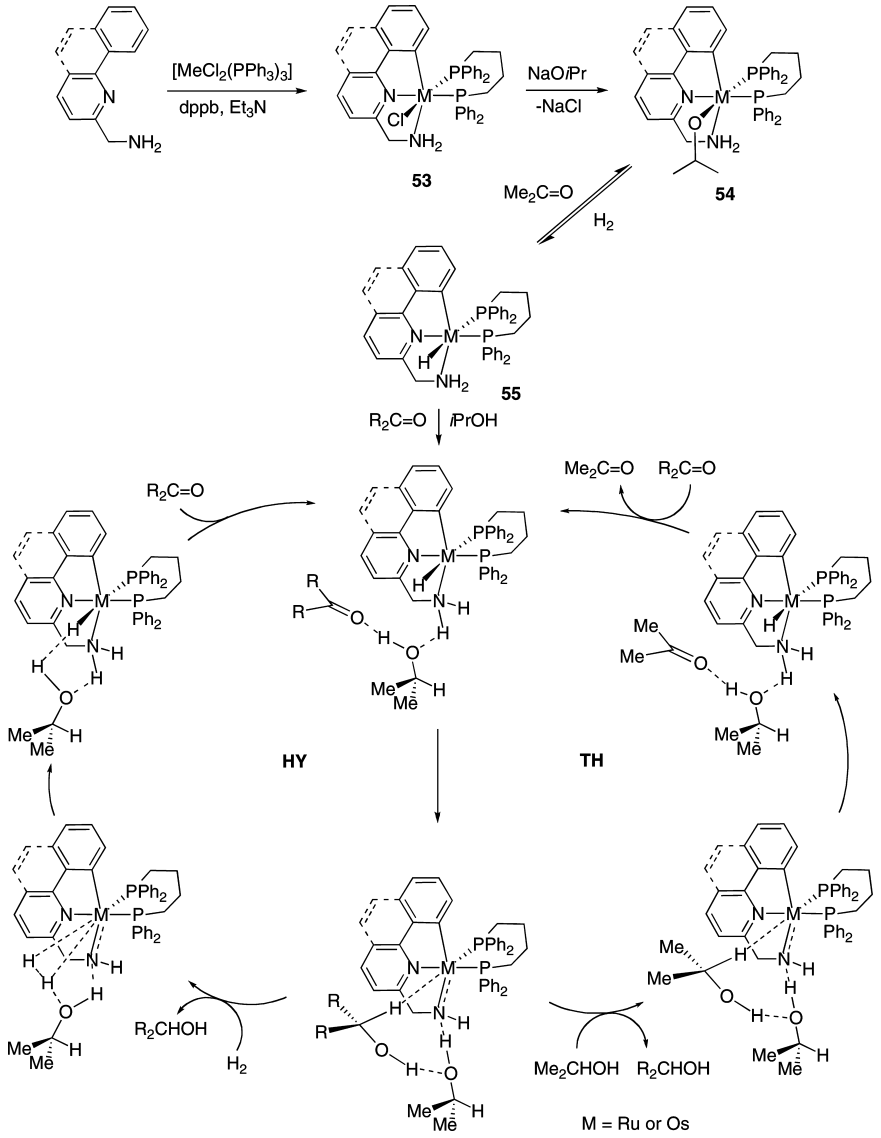
It is worth pointing out that Os complexes based on (6-phenylpyridin-2-yl)- and (benzo[*h*]quinolin-2-yl)methanamine ligands show much the same behavior as the analogous Ru complexes, for which mechanistic studies were very recently carried out by us.[21] According to these investigations, Os–chloride complex **53** reacts with Na*i*OPr to afford isopropoxide complex **54**, which rapidly equilibrates with hydride complex **55** (Scheme 23). Reaction with the substrate in the presence of 2-propanol leads to reduction to the alcohol product and the formation of an Os–amide alcohol adduct; reaction of the latter with 2-propanol affords the alcohol product and the 2-propanol amide adduct, which in turn regenerates the hydride and closes the cycle. The presence of the NH_2 function is crucial for enhancing the rate of the reaction, allowing hydrogen bonding with the alcohol medium and facilitating the overall proton

Scheme 20

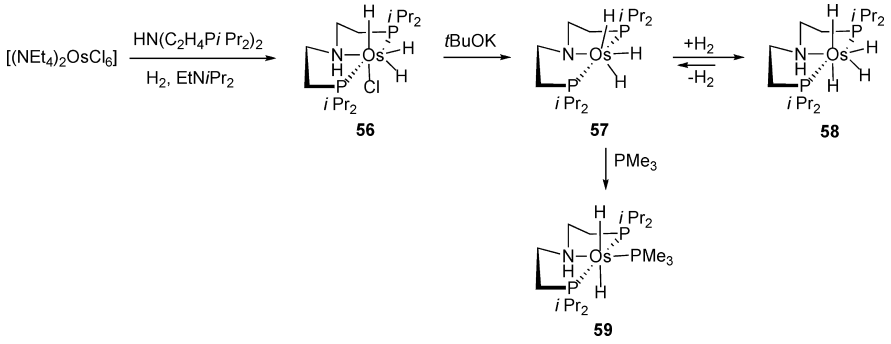


DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363–379

Scheme 23



Scheme 24



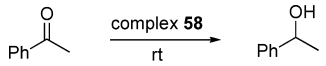
transfer. Although the alkoxide and hydride are the only species detected in solution, the amide alcohol adduct plays a crucial role in catalysis.

The synthesis, structure, and properties of the PNP pincer Os complexes **56**−**59** were reported by Gusev and co-workers (Scheme 24).[22] TH experiments with catalyst **58** conducted at room temperature in 2-propanol, ethanol, or methanol 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 25).

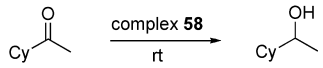
The same group also described the related PXP (X = N, O) pincer Os complexes **60**−**63** (Figure 4).[23] Complex **61** proved to be an excellent TH catalyst in 2-propanol without base, while the chloride complex **60** was similarly active under basic

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

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% conv was reached within 1-2 h

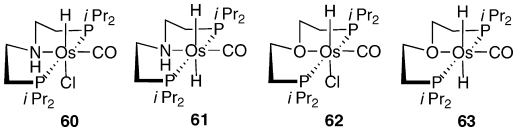
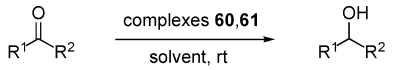


Figure 4. Structures of Os−PXP (X = N, O) pincer complexes **60**−**63**.

conditions (Scheme 26). Both catalysts worked well when used with large substrate-to-catalyst ratios (10^4−10^5), affording high TOFs at room temperature.

Scheme 26

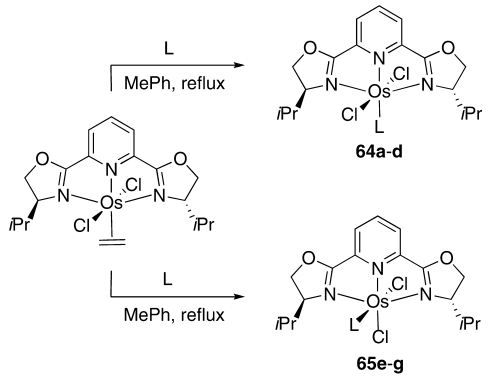


complex	R^1	R^2	ROH	base[a]	time (h)[b]	TOF[c]
60	Ph	Me	*i*Pr	1.0	1.0	1.4×10^4
61	Ph	Me	*i*Pr		0.5	1.3×10^4
61	Ph	Me	*i*Pr	1.0	2.0	1.6×10^4
60	Ph	Me	Et	0.3	2.5	1.0×10^2
61	Ph	Me	Et		1.8	3.0×10^2
61[d]	Ph	Me	Et		2.0	2.6×10^2
61	Ph	Me	Et	1.0	0.8	4.7×10^2
61	-$(CH_2)_5$-		*i*Pr		1.7	1.9×10^2
61	-$(CH_2)_5$-		*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	0.1	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).

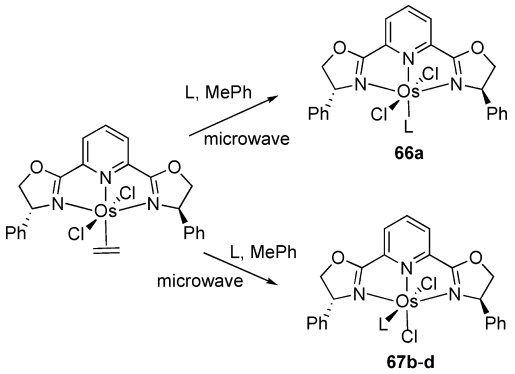
Gamasa and co-workers very recently reported the synthesis and catalytic application of osmium(II)−pybox complexes **64**−**67** bearing phosphine and phosphite ligands (Schemes 27 and 28).[24] In the ATH of acetophenone, Os complexes with (*S*,*S*)-*i*Pr-pybox were more active than those with (*R*,*R*)-Ph-pybox, in the opposite way to the analogous Ru complexes.[25] After optimization of the reaction conditions, the (*S*,*S*)-*i*Pr-pybox complexes **64a**−**d** were examined in the reduction of a number of aryl alkyl ketones. Complexes *trans*-**64c** and *trans*-**64d** were highly efficient catalysts, affording nearly quantitative conversion with 90−94% ee (Scheme 29). It should be noted that

Scheme 27



a: L = $P(OMe)_3$, **b**: L = $P(OEt)_3$, **c**: L = $P(O\text{-}iPr)_3$, **d**: L = $P(OPh)_3$, **e**: L = PPh_3, **f**: L = $PiPr_3$, **g**: L = PCy_3

Scheme 28



a: L = $P(OMe)_3$, **b**: L = PPh_3, **c**: L = $PiPr_3$, **d**: L = PCy_3

these results showed for the first time that Os complexes based on aprotic nitrogen ligands can efficiently catalyze the ATH of ketones.

Os complexes **69a**−**c** were prepared by the reaction of $[Os(H)(Br)(CO)(PPh_3)_3]$ with 1-{[2-(arylazo)phenyl]-iminomethyl}-2-phenols **68a**−**c** (Scheme 30).[26] Complex **69a** was examined in TH of representative aliphatic and aromatic ketones and afforded moderate to high yields of the corresponding alcohols; conversely, the related Ru complex showed no activity (Scheme 31).[27]

3. HYDROGENATION OF ALDEHYDES AND KETONES WITH MOLECULAR HYDROGEN

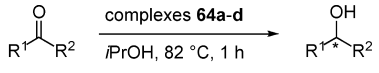
Catalytic HY of the polar C═O bond with hydrogen catalyzed by ruthenium complexes has been extensively investigated in the past decade and represents a core reaction for the synthesis of alcohols.[2] By contrast, Os catalysts have been sparingly employed in HY because they are considered to have low activity. In 2008 we reported the first example of asymmetric hydrogenation (AHY) of ketones catalyzed by Os complexes, which displayed exceptionally high activity similar to that of the Ru analogues. This work led to a renewed interest in osmium-catalyzed processes involving the cleavage of H−H and C−H bonds.

3.1. Osmium Complexes with Monodentate Ligands

The cationic complex **71** and its neutral precursor **70** (Scheme 32) were efficient catalysts for the hydrogenation of benzaldehyde and cyclohexanone, with complex **70** showing a

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

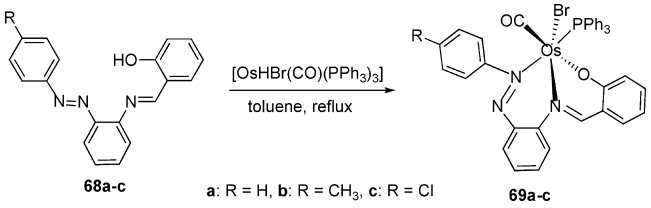
Scheme 29



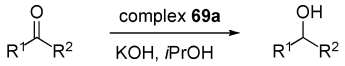
catalyst	R^1	R^2	conv (%)	ee (%)(conf)
64a	Ph	Me	98	94 (*R*)
64d	Ph	Me	98	92 (*R*)
64b	Ph	Et	98	92 (*R*)
64c	Ph	Et	99	92 (*R*)
64d	Ph	Et	98	94 (*R*)
64a	2-$MeOC_6H_4$	Me	99	74 (*S*)
64b	2-$MeOC_6H_4$	Me	99	74 (*S*)
69a	2-BrC_6H_4	Me	98	57 (*S*)
64b	2-BrC_6H_4	Me	99	55 (*S*)
64a	3-$MeOC_6H_4$	Me	97	79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

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

Scheme 30



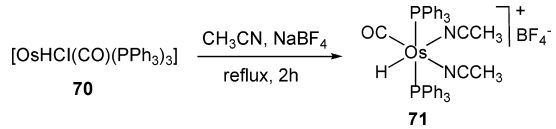
Scheme 31



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-MeC_6H_4	Me	1.5	50

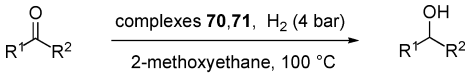
Reaction conditions: ketone (2.8 mmol), complex (0.0013 mmol) and KOH (0.0625 mmol) were heated to reflux in *i*PrOH (10 mL).

Scheme 32



catalytic activity higher than those of **71** and their analogous Ru complexes (Scheme 33).[28] Complexes **70** and **71** were also assessed in the hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline and cyclohexene to cyclohexane. The

Scheme 33



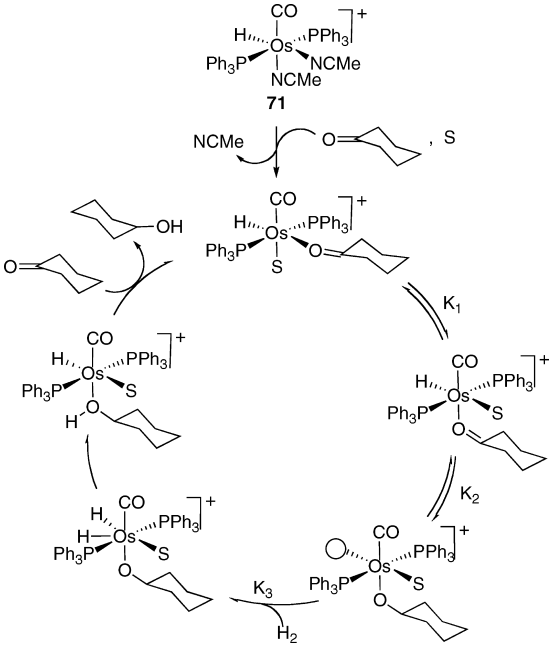
complex[a]	R^1	R^2	TON[b]
70	Ph	H	74
71	Ph	H	42
70	-$(CH_2)_5$-		76
71	-$(CH_2)_5$-		28

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

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 the subsequent hydrogenation.

Kinetic and mechanistic studies of the HY of cyclohexanone were carried out using cationic complex **71**.[29] All of the experimental data were consistent with a mechanism involving oxidative addition of hydrogen as the rate-determining step of the catalytic cycle (Scheme 34).

Scheme 34. Proposed Catalytic Cycle for $[OsH(CO)(NCMe)_2(PPh_3)_2]BF_4$-Catalyzed Hydrogenation of Cyclohexanone



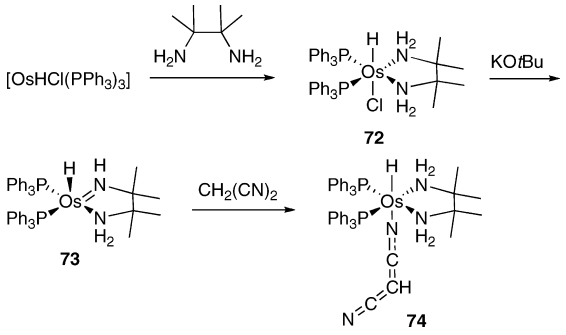
3.2. Osmium Complexes with Bidentate Ligands

The five-coordinate complex **73** was prepared by reacting KO*t*Bu with **72**, which was obtained from $[Os(H)(Cl)(PPh_3)_3]$ and 2,3-diamino-2,3-dimethylbutane (Scheme 35).[30] Hydrogenation of acetophenone with **73** reached 98% conversion in 20 min under 5 atm H_2 at 20 °C without base. By contrast, the hydrido chloro complex **72** required the addition of KO*t*Bu to catalyze ketone HY.

We described the synthesis of osmium complexes *trans*-**75** and *trans*-**76**, similar to complexes developed by Noyori with

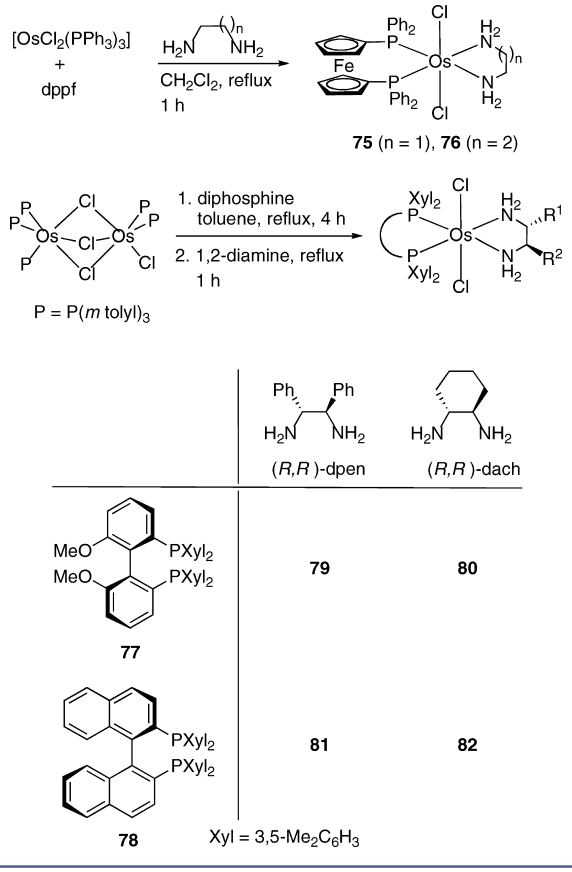
DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Scheme 35



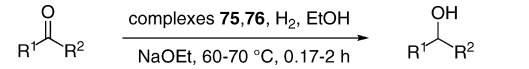
ruthenium,[8] by the reaction of $[OsCl_2(PPh_3)_3]$ with dppf followed by diamines (Scheme 36).[31] Moreover, the chiral

Scheme 36



complexes *trans*-**79**–**82** were obtained by the reaction of $[Os_2Cl_4\{P(m\text{-tolyl})_3\}_5]$ with bulky diphosphine (**77**, **78**) and 1,2-diamine ligands (Scheme 36). Compounds **75** and **76** displayed exceptionally high catalytic activity in the hydrogenation of aldehydes and methyl aryl, dialkyl, and diaryl ketones with remarkably high substrate/catalyst (S/C) ratios (10000–200000) and TOFs (up to 3.0×10^5 h^{-1}) (Scheme 37). With the chiral compounds **79**, **81**, and **82**, alkyl aryl, cyclic, and bulky *tert*-butyl ketones were hydrogenated with up to 99% ee, high S/C ratios (10000–100000) and TOF (4.1×10^4 h^{-1}) (Scheme 38). This indicates that these osmium–diamine complexes are valid complements to the Noyori Ru catalysts, which show poor activity for the HY of *tert*-butyl ketones.

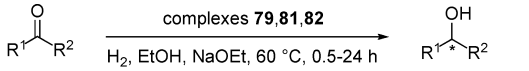
Scheme 37



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	97	60	9.0×10^4
75	Ph	Ph	1.0×10^4	60	>99	30	3.0×10^4
75[a]	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/complex = 10000, NaOEt (1 mol%), EtOH at 60 °C. [a]Substrate/complex = 100000, NaOEt (2 mol%) at 50 °C.

We found that in addition to TH, the $[OsCl_2(\text{diphosphine})(\text{Ampy})]$ complexes **19**/**20** and **22** (Schemes 9 and 12, respectively) were highly active in HY of ketones at low H_2 pressure.[9] Thus, with **19**/**20** (0.05 mol %), acetophenone was promptly hydrogenated in ethanol within 10 min (TOF = 1.5×10^4 h^{-1}) (Scheme 39). Remarkably, the reduction also occurred completely at almost the same rate with lower osmium loadings (0.01 and 0.005 mol %). This system also efficiently catalyzed the hydrogenation of bulky substrates, including sterically demanding substrates such as menthone and *tert*-butyl ketones (Scheme 39).

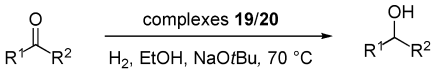
We also showed that complex *trans*-**22** (Scheme 12) was catalytically active in the HY of aldehydes and ketones in a methanol/ethanol mixture and in the presence of KO*t*Bu, showing TOFs of up to 1.0×10^4 h^{-1} (Scheme 40).[9] Comparison of the results for Os catalyst **22** and the related Ru catalyst[11] suggested that osmium is a valid complement to ruthenium for both HY and TH reactions, taking into account the fact that osmium is more robust, allowing reactions to be run at higher temperature.

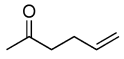
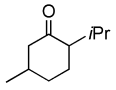
3.3. Osmium Complexes with Tridentate Ligands

In 2008, we found that the pincer TH catalysts **40**, **42**, and **43** (Scheme 16) were also extremely active for the HY of ketones in methanol when a very low amount of base (0.05 mol % KO*t*Bu) was used.[16] Thus, a number of ketones were quantitatively converted into the related alcohols within 1–2

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363–379

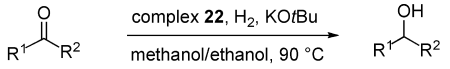
Scheme 39



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

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

Scheme 40



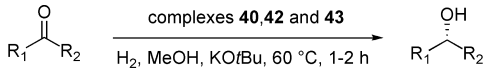
R^1	R^2	conv (%)	time (min)	TOF (h^{-1})
Ph	H	97	10	1.0×10^4
4-MeOC_6H_4	H	97	30	4.7×10^3
$PhCH_2$	H	91	8 h	1.0×10^3
PhCH=CH	H	90	30	4.6×10^3
Ph	Me	98	10	9.0×10^3
4-MeOC_6H_4	Me	95	30	3.7×10^3
Ph	4-ClC_6H_4	97	30	4.6×10^3
		99	15	6.8×10^3
		90	2 h	3.7×10^3

Reaction conditions: carbonyl compound (0.5 M), KO*t*Bu (2 mol %) in methanol/ethanol (3/1, v/v) with the Os-complex

h in the presence of 0.005 mol % catalyst (TOFs of up to 5.2×10^4 h^{-1}) (Scheme 41). Efficient AHY of methyl aryl ketones was also possible with the chiral derivatives **42** and **43** (0.005–0.002 mol %), which afforded enantioselectivities of up to 98% ee (Scheme 41). Complexes **42** and **43** were the first examples of Os catalysts for AHY of ketones and still remain the most active and productive systems.

We also prepared osmium complex **84** containing a chiral benzo[*h*]quinoline-based pincer ligand by treatment of $[OsCl_2(PPh_3)_3]$ with (*S*,*R*)-Josiphos followed by ortho metalation of **83a** (Scheme 42).[32] Moreover, according to our previous studies of Ru complexes showing that (*S*,*R*)-Josiphos correctly matched with chiral CNN ligands having the *R* configuration,[33] we prepared complex **85** as a single stereoisomer by the reaction of $[OsCl_2(PPh_3)_3]$ with (*S*,*R*)-Josiphos* and (*R*)-**83b** (Scheme 42).[32] The Os complexes **47** (Scheme 20) **84** and **85** were found to be active in the hydrogenation of C=O bonds with H_2 at low pressure (Scheme 43). Os

Scheme 41



complex	R^1	R^2	conv (%)	time (h)	TOF (h^{-1})	ee (%)
40	Me	Ph	99	1	2.5×10^4	
40	Me	3-MeOC_6H_4	99	1	2.6×10^4	
40	-$CH_2(CH_2)_3CH_2$-		99	0.5	3.3×10^4	
40	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 (0.05 mol%), MeOH. [a]0.002 mol% Os.

complex **47** catalyzed the quantitative ketone HY at 70 °C (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}. The chiral complexes **84** and **85** showed to hydrogenate acetophenone at 70 °C with 86 and 92% ee, respectively, and with good rates (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 43). 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 several ketones were successfully reduced (up to 99% ee) (Scheme 43). The comparison of the catalytic activity of the Os complexes with the Ru analogous in ketone HY shows that osmium generally requires a higher temperature and a lower base amount to work, while much the same enantioselectivity is achieved by using the identical set of chiral ligands.

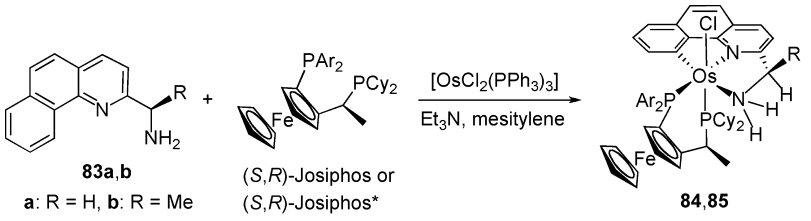
The proposed mechanism for the catalytic hydrogenation with pincer Os complexes in basic alcohol media is depicted in Scheme 23. According to the studies on the analogous pincer Ru complexes, Os–chloride complex **53** reacts with alkali alkoxide, leading to Os–alkoxide complex **54**, which is converted into hydride complex **55** via H_2 cleavage.[21] The reaction with the ketone substrate leads to the alcohol product with formation of an Os–amide alcohol adduct, which reacts with H_2 to afford the Os–hydride complex, closing the cycle. While in the catalytic TH the hydride is generated from the Os–isopropoxide complex, in the HY the metal hydride is formed by heterolytic H_2 splitting. As in the TH, in the HY the NH_2 group plays a key role in enhancing the rate of the reaction, allowing hydrogen bonding with the alcohol medium and facilitating the overall proton transfer. In addition, the nature of the alcohol also plays a crucial role, with methanol and ethanol showing better performance than 2-propanol.

4. HYDROGENATION OF IMINES

Complex **71** and its precursor **70** (Scheme 32) were used for the HY of quinoline to 1,2,3,4-tetrahydroquinoline (Scheme 44).[28,29] The cationic complex **71** was a more efficient catalyst than **70** (Scheme 44) and also proved to be an efficient and regioselective catalyst for the hydrogenation of the nitrogen-containing rings of quinoline, isoquinoline, 5,6- and 7,8-benzoquinoline, and acridine (Table 3).[34] The high activity and stability of the Os complex allowed the authors to carry out kinetic and mechanistic studies of the imine HY, which

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363–379

Scheme 42



83a,b
a: R = H, **b**: R = Me

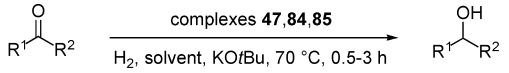
(*S*,*R*)-Josiphos or
(*S*,*R*)-Josiphos*

84,85

(*S*,*R*)-Josiphos: Ar = Ph
(*S*,*R*)-Josiphos*: Ar = 4-MeO-3,5-$Me_2C_6H_2$

84: Ar = Ph, R = H
85: Ar = 4-MeO-3,5-$Me_2C_6H_2$, R = Me

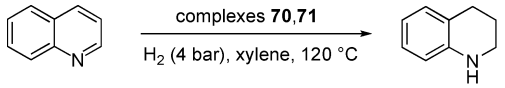
Scheme 43



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]	Me	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[d]
85[b]	Me	Ph	97	60	1.4×10^4	92[d]
in situ[c]	Me	Ph	99	30	2.4×10^4	90[d]
in situ[c]	Me	3-$MeOC_6H_4$	99	30	2.2×10^4	91[d]
in situ[c]	Me	2-naphthyl	99	30	1.6×10^4	94[d]
in situ[c]	Et	Ph	99	60	1.3×10^4	99[d]

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. [d]Alcohols with *S* configuration were obtained.

Scheme 44



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

[a]Complex = 0.5 mol%
[b]Turnover number in 1 h

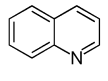
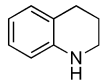
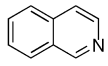
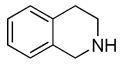
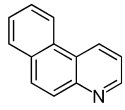
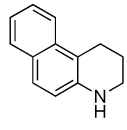
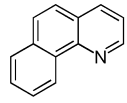
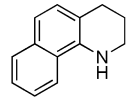
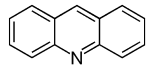
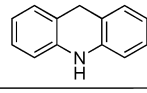
indicated that the addition of the second molecule of hydrogen was the rate-determining step.

The four Os(II)−arene complexes **86**−**89** were synthesized by the reaction of $[Os(\eta^6\text{-}p\text{-cymene})X_2]_2$ (X = Cl, I) and the chiral ligand (*S*)- or (*R*)-1-phenyl-*N*-(pyridin-2-ylmethylene)-ethanamine (Scheme 45).[35] These complexes were obtained as mixtures of two diastereomers differing in the configuration at the metal (R_{Os} or S_{Os}) and were isolated as single isomers. The catalytic activities of **87** and **89** for the reduction of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline were evaluated, and these two complexes afforded reasonable conversions (20−76%) but low ee (22−23%) (Scheme 46).

5. HYDROGENTION OF ESTERS

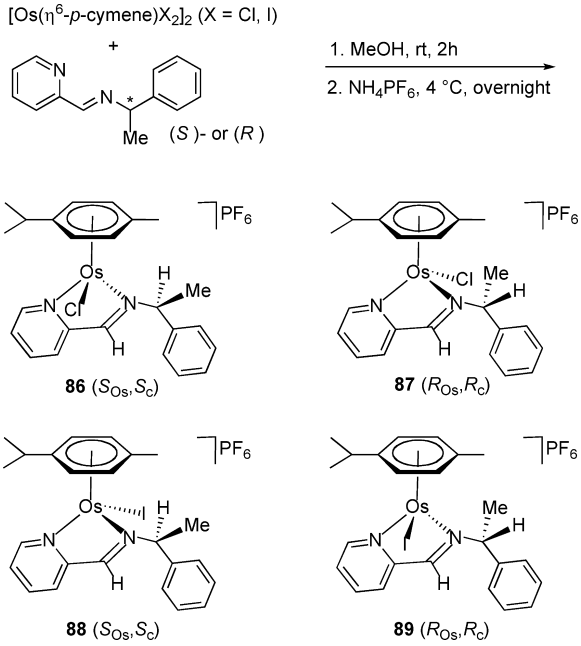
Catalytic HY of esters is an attractive green method for the synthesis of alchohols.[36] The hydrido carbonyl Os complex **90**

Table 3. Hydrogenation of Nitrogen-Containing Rings by Complex 71

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

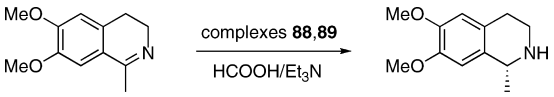
Reaction conditions: Os = 1.7×10^{-3} M, substrate = 0.17 M, H_2 = 4 atm, xylene, 125 °C. [a]TON = turnover number (1 h).

Scheme 45



DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

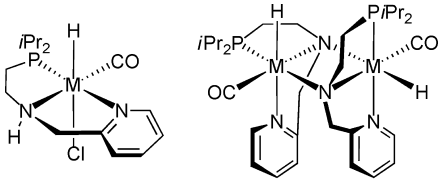
Scheme 46



complex	temp (°C)	time (h)	conv (%)	ee (%)
88	45	22	40	22
88	60	18	76	22
89	28	23	20	23

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

containing a tridentate PNN ligand was treated with KO*t*Bu to afford the unusual dimer **91** (Figure 5).[37] The catalytic



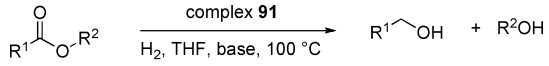
90 (M = Os)
92 (M = Ru)

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

Figure 5. Structures of mononuclear complexes **90** and **92** and the corresponding dimers **91** and **93**.

activities of **90** and **91** under H_2 (50 bar) were first tested in the HY of methyl benzoate. The Os dimer **91** was an efficient catalyst, but the reaction was slower than with the corresponding Ru complex **93** (Figure 5). Moreover, **90** and the corresponding Ru complex **92** (Figure 5) displayed similar activities in the presence of KO*t*Bu. Complex **91** was further investigated in the HY of a series of esters (Scheme 47) and

Scheme 47

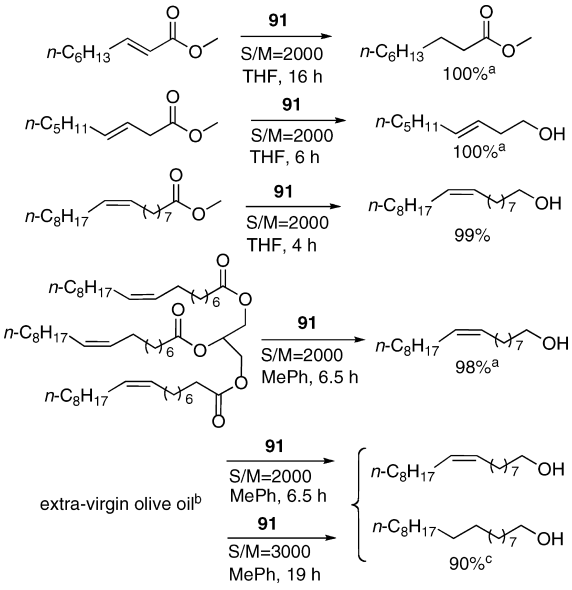


R^1	R^2	time (h)	conv (%)
Ph	Et	1.6	99
Ph	*i*Bu	1.5	93
2-BrC_6H_5	*i*Pr	17	0
n-C_5H_{11}	Me	2	100
Me	Et	3	100
-$(CH_2)_5$-		1.4	99
MeCH(OH)	Me	9	72
MeOC(O)	Me	23	0

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

alkenoates (Scheme 48). This complex was equally active for the HY of ethyl, isobutyl, and methyl benzoate and ε-caprolactone but failed with isopropyl 2-bromobenzoate and dimethyl oxalate. The activity and selectivity were also tested with substrates containing C=C bonds. The results showed significant differences between the Os and Ru catalysts. Os dimer **91** successfully catalyzed the reduction of methyl 3-nonenoate to 3-nonenol, whereas the related Ru dimer **93** proved to be inactive in this reaction. Methyl oleate was hydrogenated using **91** with retention of the C=C bond to give (*Z*)-octadec-9-enol, while **93** afforded a mixture of octadecanol and (*E*)- and (*Z*)-octadec-9-enol. The authors indicated that both the Noyori-type outer-sphere and classical

Scheme 48



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

inner-sphere hydrogenation mechanisms were possible with complexes **91** and **93** (Scheme 49). The superior activity of **91** versus $[RuH_2(CO)(PNHPiPr)]$[23] for the hydrogenation of methyl benzoate suggested an important role of the hemilability of the NNHP*i*Pr-coordinated catalysts.[37]

6. DEHYDROGENATION OF ALCOHOLS TO KETONES

In 2011, we reported that Os complexes can also be used in the DHY of alcohols to ketones.[38] Complex **94** was prepared as a trans/cis/cis = 2:6:1 mixture by the reaction of $[OsCl_2(PPh_3)_3]$ with dppb and (±)-*trans*-1,2-diaminocyclohexane (*trans*-dach), while complex **95** was obtained as a single trans isomer by treatment of $[OsCl_2(PPh_3)_3]$ with dppf and *trans*-dach (Scheme 50). The diamino derivatives **94**, **95**, and **75** (Scheme 36), Ampy complex **22** (Scheme 12), and the pincer Os complexes **40** (Scheme 16) and **47** (Scheme 20) were assessed in the acceptorless dehydrogenation of 1,2,3,4-tetrahydro-1-naphthol (α-tetralol). Complexes **22**, **75**, **94**, and **95** efficiently catalyzed the dehydrogenation of α-tetralol to afford almost complete conversion (93–98%), whereas the pincer complexes **40** and **47** displayed significantly lower activity (Scheme 51). The best activity was obtained with complex **75**, which gave 98% conversion in 6 h. This complex was also an efficient catalyst for the dehydrogenation of a number of alcohols (Table 4) and sterols (Scheme 52).

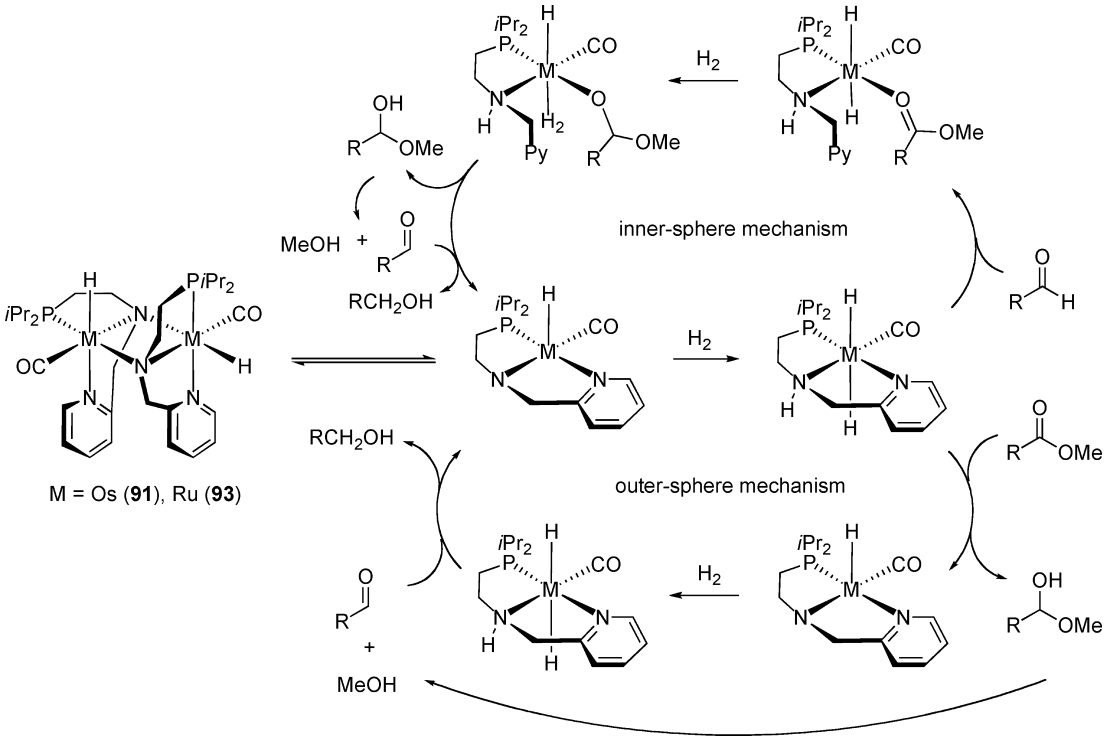
More recently, we found that Os–Ampy complex **22** (Scheme 12) shows good efficiency in alcohol DHY,[11] affording 98% conversion of sterol **96a** in 1 h, whereas the analogous diamine derivative **95** requires 20 h.[38]

7. CONCLUSIONS

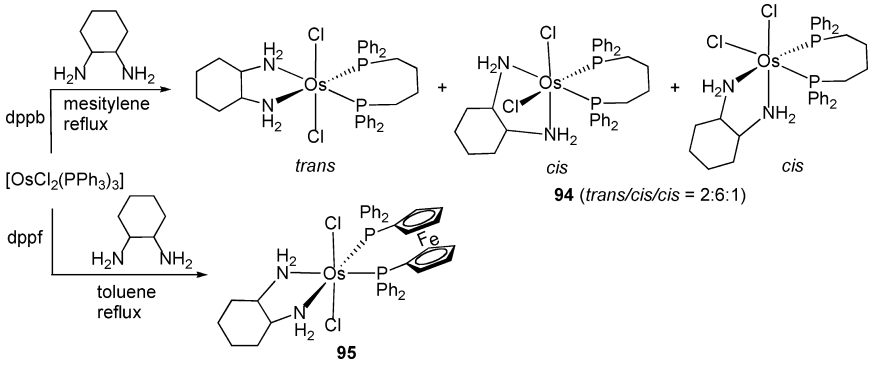
The work described in this Account demonstrates that Os complexes have recently shown remarkably high catalytic activity in the hydrogenation (HY) and transfer hydrogenation (TH) of ketones, aldehydes, esters, and imines, allowing the

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363–379

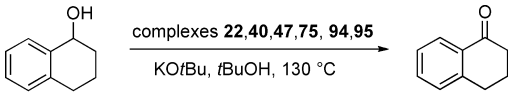
Scheme 49. Inner- and Outer-Sphere Mechanisms for Ester Hydrogenation Catalyzed by Complex 91 or 93



Scheme 50



Scheme 51



complex	time (h)	conversion (%)
22	20	87
40	24	44
47	24	36
75	6	98
94	22	93
95	24	96

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

Table 4. Dehydrogenation of Alcohols with Complex 75

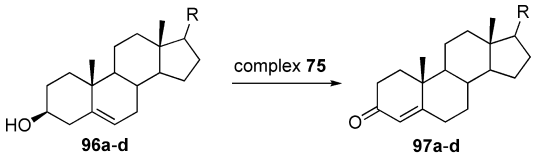
alcohol	conv (%)	time (h)	TOF (h^{-1})
1,2,3,4-tetrahydronaphthalen-1-ol	98	6	80
2,3-dihydro-1*H*-inden-1-ol	98	6	50
9*H*-fluoren-9-ol	88[a]	20	20
1-phenylethanol	96	40	20
1-(4-methoxyphenyl)ethanol	68	–	20
3-methylcyclohex-2-enol	82	20	30
3,5,5-trimethylcyclohex-2-enol	97	20	70
cyclohex-2-enol	91[b]	2	220
heptan-2-ol	91[c]	0	15
heptan-3-ol	40	30	–
diphenylmethanol	41	30	–

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

synthesis of chiral and nonchiral alcohols and amines in high yields and very short reaction times. Moreover, the high productivity and thermal stability and simple syntheses of Os complexes may offset their higher cost compared with their Ru analogues. Importantly, Os complexes are able to catalyze both TH and HY reactions as well as dehydrogenation of alcohols with efficiencies comparable and in some cases superior to

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Scheme 52



a: R = CH(Me)$(CH_2)_3$*i*Pr, **b**: R = CH(Me)CH=CHCH(Et)*i*Pr, **c**: R = =O, **d**: R = 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%), KO*t*Bu (4 mol%) in *t*BuOH/toluene (2:1, v/v) at 145 °C.

those reported for the analogous ruthenium systems. These results give a glimpse of the potential of Os for the design of new highly productive and robust catalysts for the synthesis of chiral and nonchiral alcohols and amines as well as carbonyl compounds from alcohols. Thus, we hope that this report will promote increased interest in the chemistry of osmium catalysts, opening novel opportunities for new catalytic processes as well as the improvement of existing ones.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: chelucci@uniss.it.
*E-mail: walter.baratta@uniud.it.

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, five book chapters, and three patents, centers on the design, synthesis, and catalytic applications of chiral ligands, with particular interest toward those based on the pyridine framework, and on metal-catalyzed reactions.

Salvatore Baldino received his laurea degree in chemistry from Sassari University in 2005 and his Ph.D. from Sassari University under the supervision of Dr. Giorgio Chelucci in 2009. Currently he is conducting postdoctoral research with Prof. Walter Baratta at the University of Udine. His research focuses on the synthesis of chiral and nonchiral ligands and their application in metal-catalyzed reactions.

Walter Baratta attended the SNS of Pisa and graduated in chemistry in 1989. Starting in 1994 he spent two years in the group of Prof. W. A. Herrmann at TU München. He became a Research Associate in 1996 at the University of Udine and in 2005 was appointed Associate Professor. His research interests are mainly focused on Ru and Os catalysts for the reduction of carbonyl compounds. In 2008 he was awarded the Solvias Prize "In recognition of the development of Os-Josiphos catalysts".

ACKNOWLEDGMENTS

Financial support from Fondazione Banco di Sardegna is gratefully acknowledged.

REFERENCES

(1) For a review of TH, see: Ito, J.; Nishiyama, H. Recent Topics of Transfer Hydrogenation. *Tetrahedron Lett.* **2014**, *55*, 3133−3146 and references therein.
(2) For a review of HY, see: *Handbook of Homogeneous Hydrogenation*; de Vries, J. G., Elsevier, C. J., Eds.; Wiley-VCH: Weinheim, Germany, 2007.
(3) For reviews of Os complexes in catalysis, see: (a) Sánchez-Delgado, R. A.; Rosales, M.; Esteruelas, M. A.; Oro, L. A. Homogeneous Catalysis by Osmium Complexes. A Review. *J. Mol. Catal. A: Chem.* **1995**, *96*, 231−243. (b) Morris, R. H. Ruthenium and Osmium. In *Handbook of Homogeneous Hydrogenation*; de Vries, J. G., Elsevier, C. J., Eds.; Wiley-VCH: Weinheim, Germany, 2007; pp 45−70.
(4) Jung, M.-K.; Huh, S.; Lee, W.-Y.; Jun, M.-J. Hydrogenation of *trans*-Cinnamaldehyde with Hydrido−Carbonyl Osmium(II) Complexes of Chelating Phosphine Ligands. *Bull. Korean Chem. Soc.* **1997**, *18*, 806−810.
(5) Faller, J. W.; Lavoie, A. R. Enantioselective Routes to Both Enantiomers of Aryl Alcohols with a Single Catalyst Antipode: Ru and Os Transfer Hydrogenation Catalysts. *Org. Lett.* **2001**, *3*, 3703−3706.
(6) Faller, J. W.; Lavoie, A. R. Enantioselective Syntheses of Nonracemic Benzyl-*α*-*d* Alcohols via Catalytic Transfer-Hydrogenation with Ru, Os, Rh, and Ir Catalysts. *Organometallics* **2002**, *21*, 3493−3495.
(7) Schlünken, C.; Esteruelas, M. A.; Lahoz, F. J.; Oro, L. A.; Werner, H. Synthesis, Molecular Structure and Catalytic Activity of Six-Coordinate Chloro(hydrido)- and Dihydridoruthenium(II) and -osmium(II) Complexes with the Chiral Ligands P*i*Pr_2NH(Me)Ph, (*S*,*S*)-Chiraphos and (*S*,*S*)-Diop. *Eur. J. Inorg. Chem.* **2004**, 2477−2487.
(8) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. *trans*-[$RuCl_2$(phosphane)$_2$(1,2-diamine)] and Chiral *trans*-[$RuCl_2$(diphosphane)(1,2-diamine)]: Shelf-Stable Precatalysts for the Rapid, Productive, and Stereoselective Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **1998**, *37*, 1703−1707.
(9) Baratta, W.; Ballico, M.; Del Zotto, A.; Siega, K.; Magnolia, S.; Rigo, P. Osmium Pyme Complexes for Fast Hydrogenation and Asymmetric Transfer Hydrogenation of Ketones. *Chem.—Eur. J.* **2008**, *14*, 2557−2563.
(10) Baratta, W.; Chelucci, G.; Herdtweck, E.; Magnolia, S.; Siega, K.; Rigo, P. Highly Diastereoselective Formation of Ruthenium Complexes for Efficient Catalytic Asymmetric Transfer Hydrogenation. *Angew. Chem., Int. Ed.* **2007**, *46*, 7651−7654.
(11) Putignano, E.; Bossi, G.; Rigo, P.; Baratta, W. MCl_2(ampy)(dppf) (M = Ru, Os): Multitasking Catalysts for Carbonyl Compound/Alcohol Interconversion Reactions. *Organometallics* **2012**, *31*, 1133−1142.
(12) Baratta, W.; Siega, K.; Rigo, P. Fast and Chemoselective Transfer Hydrogenation of Aldehydes Catalyzed by RuCl(CNN)(dppb). *Adv. Synth. Catal.* **2007**, *349*, 1633−1636.
(13) Carmona, D.; Lahoz, F. J.; García-Orduña, P.; Oro, L. A. Half-Sandwich Complexes of Osmium(II) with L-*α*-Amino Carboxylate Ligands as Asymmetric Transfer Hydrogenation Catalysts. On the Origin of the Enantioselectivity. *Organometallics* **2012**, *31*, 3333−3345.
(14) Carmona, D.; Lamata, M. P.; Viguri, F.; Dobrinovich, I.; Lahoz, F. J.; Oro, L. A. On the Sense of the Enantioselection in Hydrogen Transfer Reactions from 2-Propanol to Ketones. *Adv. Synth. Catal.* **2002**, *344*, 499−502.
(15) Baratta, W.; Chelucci, G.; Gladiali, S.; Siega, K.; Toniutti, M.; Zanette, M.; Zangrando, E.; Rigo, P. Ruthenium(II) Terdentate CNN Complexes. Superlative Catalysts for the Hydrogen Transfer

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379

Reduction of Ketones via Reversible Carbonyl Group Insertion into the Ru−H Bond. *Angew. Chem., Int. Ed.* **2005**, *44*, 6214−6219.
(16) Baratta, W.; Ballico, M.; Chelucci, G.; Siega, K.; Rigo, P. Osmium(II) CNN Pincer Complexes as Efficient Catalysts for Both Asymmetric Transfer and H_2 Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **2008**, *47*, 4362−4365.
(17) Baratta, W.; Benedetti, F.; Del Zotto, A.; Fanfoni, L.; Felluga, F.; Magnolia, S.; Putignano, E.; Rigo, P. Chiral Pincer Ruthenium and Osmium Complexes for the Fast and Efficient Hydrogen Transfer Reduction of Ketones. *Organometallics* **2010**, *29*, 3563−3570.
(18) Baratta, W.; Ballico, M.; Baldino, S.; Chelucci, G.; Herdtweck, E.; Siega, K.; Magnolia, S.; Rigo, P. New Benzo[*h*]quinoline-Based Ligands and their Pincer Ru and Os Complexes for Efficient Catalytic Transfer Hydrogenation of Carbonyl Compounds. *Chem.—Eur. J.* **2008**, *14*, 9148−9160.
(19) Baratta, W.; Ballico, M.; Esposito, G.; Rigo, P. Role of the NH_2 Functionality and Solvent in Terdentate CNN Alkoxide Ruthenium Complexes for the Fast Transfer Hydrogenation of Ketones in 2-Propanol. *Chem.—Eur. J.* **2008**, *14*, 5588−5595.
(20) Baratta, W.; Siega, K.; Rigo, P. Catalytic Transfer Hydrogenation with Terdentate CNN Ruthenium Complexes: The Influence of the Base. *Chem.—Eur. J.* **2007**, *13*, 7479−7486.
(21) Baratta, W.; Baldino, S.; Calhorda, M. J.; Costa, P. J.; Esposito, G.; Herdtweck, E.; Magnolia, S.; Mealli, C.; Messaoudi, A.; Mason, S. A.; Veiros, L. F. CNN Pincer Ruthenium Catalysts for Hydrogenation and Transfer Hydrogenation of Ketones: Experimental and Computational Studies. *Chem.—Eur. J.* **2014**, *20*, 13603−13617.
(22) Bertoli, M.; Choualeb, A.; Gusev, D. G.; Lough, A. J.; Major, Q.; Moore, B. PNP Pincer Osmium Polyhydrides for Catalytic Dehydrogenation of Primary Alcohols. *Dalton Trans.* **2011**, *40*, 8941−8949.
(23) Bertoli, M.; Choualeb, A.; Lough, A. J.; Moore, B.; Spasyuk, D.; Gusev, D. G. Osmium and Ruthenium Catalysts for Dehydrogenation of Alcohols. *Organometallics* **2011**, *30*, 3479−3482.
(24) Vega, E.; Lastra, E.; Gamasa, M. P. Asymmetric Transfer Hydrogenation of Ketones Catalyzed by Enantiopure Osmium(II) Pybox Complexes. *Inorg. Chem.* **2013**, *52*, 6193−6198.
(25) Cuervo, D.; Gamasa, M. P.; Gimeno, J. New Chiral Ruthenium(II) Catalysts Containing 2,6-Bis(4′-(*R*)-phenyloxazolin-2′-yl)pyridine (Ph-pybox) Ligands for Highly Enantioselective Transfer Hydrogenation of Ketones. *Chem.—Eur. J.* **2004**, *10*, 425−432.
(26) Pattanayak, P.; Patra, D.; Pratihar, J. L.; Burrows, A.; Mahon, M. F.; Chattopadhyay, S. Osmium and Cobalt Complexes Incorporating Facially Coordinated N,N,O Donor Azo-imine Ligands: Redox and Catalytic Properties. *J. Chem. Sci.* **2013**, *125*, 51−62.
(27) Pattanayak, P.; Patra, D.; Pratihar, J. L.; Burrows, A.; Mohan, M. F.; Chattopadhyay, S. Studies on the reactions of ruthenium(II) substrates with tridentate (N,N,O) azo ligands. *Inorg. Chim. Acta* **2010**, *363*, 2865−2873.
(28) Rosales, M.; González, A.; Navarro, J.; Soscún, H.; Zárraga, J. Synthesis and Catalytic Properties of the Complex $[OsH(CO)(NCMe)_2(PPh_3)_2]BF_4$. *Inorg. Chim. Acta* **1997**, *257*, 131−135.
(29) Rosales, M.; Gonzalez, A.; Mora, M.; Nader, N.; Navarro, J.; Sánchez, L.; Soscún, H. Kinetics and Mechanisms of Homogeneous Catalytic Reactions. Part 4. Hydrogenation of Cyclohexanone and 2-Cyclohexen-1-one Catalysed by the Complexes $[MH(CO)(NCMe)_2(PPh_3)_2]BF_4$ (M = Ru, Os). *Transition Met. Chem.* **2004**, *29*, 205−211.
(30) Clapham, S. E.; Morris, R. H. Reactions of an Amido Hydrido Complex of Osmium, $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$: HX Addition, HX Transfer, and Ketone H_2 Hydrogenation. *Organometallics* **2005**, *24*, 479−481.
(31) Baratta, W.; Barbato, C.; Magnolia, S.; Siega, K.; Rigo, P. Chiral and Nonchiral $[OsX_2(diphosphane)(diamine)]$ (X: Cl, OCH_2CF_3) Complexes for Fast Hydrogenation of Carbonyl Compounds. *Chem.—Eur. J.* **2010**, *16*, 3201−3206.
(32) Baratta, W.; Fantoni, L.; Magnolia, S.; Siega, K.; Rigo, P. Benzo[*h*]quinoline Pincer Ruthenium and Osmium Catalysts for Hydrogenation of Ketones. *Eur. J. Inorg. Chem.* **2010**, 1419−1423.
(33) Baratta, W.; Chelucci, G.; Magnolia, S.; Siega, K.; Rigo, P. Highly Productive CNN Pincer Ruthenium Catalysts for the Asymmetric Reduction of Alkyl Aryl Ketones. *Chem.—Eur. J.* **2009**, *15*, 726−732.
(34) Rosales, M.; Castillo, J.; González, A.; González, L.; Molina, K.; Navarro, J.; Pacheco, I.; Pérez, H. Kinetics and Mechanisms of Homogeneous Catalytic Reactions. Part 5. Regioselective Reduction of Heteroaromatic Nitrogen Compounds Catalysed by $[OsH(CO)(NCMe)_2(PPh_3)_2]BF_4$. *Transition Met. Chem.* **2004**, *29*, 221−228.
(35) Fu, Y.; Soni, R.; Romero, M. J.; Pizarro, A. M.; Salassa, L.; Clarkson, G. J.; Hearn, J. M.; Habtemariam, A.; Wills, M.; Sadler, P. J. Mirror-Image Organometallic Osmium Arene Iminopyridine Halido Complexes Exhibit Similar Potent Anticancer Activity. *Chem.—Eur. J.* **2013**, *19*, 15199−15209.
(36) Dub, A. P.; Ikarya, T. Catalytic Reductive Transformations of Carboxylic and Carbonic Acid Derivatives Using Molecular Hydrogen. *ACS Catal.* **2012**, *2*, 1718−1741.
(37) Spasyuk, D.; Smith, S.; Gusev, D. G. From Esters to Alcohols and Back with Ruthenium and Osmium Catalysts. *Angew. Chem., Int. Ed.* **2012**, *51*, 2772−2775.
(38) Baratta, W.; Bossi, G.; Putignano, E.; Rigo, P. Pincer and Diamine Ru and Os Diphosphane Complexes as Efficient Catalysts for the Dehydrogenation of Alcohols to Ketones. *Chem.—Eur. J.* **2011**, *17*, 3474−3481.

DOI: 10.1021/ar5003818
Acc. Chem. Res. 2015, 48, 363−379