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Osmium Pyme Complexes for Fast Hydrogenation and Asymmetric Transfer Hydrogenation of Ketones

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Dedicated to Professor Wolfgang A. Herrmann on the occasion of his 60th birthday

Abstract: The osmium compound *trans*,*cis*-[$OsCl_2(PPh_3)_2$(Pyme)] (**1**) (Pyme = 1-(pyridin-2-yl)methanamine), obtained from [$OsCl_2(PPh_3)_3$] and Pyme, thermally isomerizes to *cis*,*cis*-[$OsCl_2(PPh_3)_2$(Pyme)] (**2**) in mesitylene at 150 °C. Reaction of [$OsCl_2(PPh_3)_3$] with $Ph_2P(CH_2)_4PPh_2$ (dppb) and Pyme in mesitylene (150 °C, 4 h) leads to a mixture of *trans*-[$OsCl_2$(dppb)(Pyme)] (**3**) and *cis*-[$OsCl_2$(dppb)(Pyme)] (**4**) in about an 1:3 molar ratio. The complex *trans*-[$OsCl_2$(dppb)(Pyet)] (**5**) (Pyet = 2-(pyridin-2-yl)ethanamine) is formed by reaction of [$OsCl_2(PPh_3)_3$] with dppb and Pyet in toluene at reflux. Compounds **1**, **2**, **5** and the mixture of isomers **3**/**4** efficiently catalyze the transfer hydrogenation (TH) of different ketones in refluxing 2-propanol and in the presence of NaO*i*Pr (2.0 mol %). Interestingly, **3**/**4** has been proven to reduce different ketones (even bulky) by means of TH with a remarkably high turnover frequency (TOF up to $5.7\times10^5\ h^{-1}$) and at very low loading (0.05–0.001 mol %). The system **3**/**4** also efficiently catalyzes the hydrogenation of many ketones (H_2, 5.0 atm) in ethanol with KO*t*Bu (2.0 mol %) at 70 °C (TOF up to $1.5\times10^4\ h^{-1}$). The in-situ-generated catalysts prepared by the reaction of [$OsCl_2(PPh_3)_3$] with Josiphos diphosphanes and (±)-1-alkyl-substituted Pyme ligands, promote the enantioselective TH of different ketones with 91–96 % *ee* (*ee* = enantiomeric excess) and with a TOF of up to $1.9\times10^4\ h^{-1}$ at 60 °C.

Keywords: asymmetric catalysis · hydrogen transfer · hydrogenation · osmium · phosphane ligands

Introduction

The development of new more-efficient catalysts for the stereoselective reduction of carbonyl compounds represents a current subject of industrial and academic research. Several transition-metal complexes have been found to catalyze the enantioselective hydrogenation (HY) of ketones with dihydrogen under pressure.[1] In addition to this atom-efficient methodology, the catalytic transfer hydrogenation (TH), by using 2-propanol or formic acid as hydrogen donors, represents a powerful strategy because of the ease of performance and the broad applicability.[2] Homogeneous Rh, Ru, and to a lesser degree Ir catalysts have successfully been employed for the both asymmetric HY and TH.[1a,2] A fundamental contribution to the development of new catalysts for these two reactions has been given by Noyori and coworkers, who observed that the activity of ruthenium complexes can be enhanced by using primary amine ligands (bifunctional catalysis).[3,4] Interestingly, we have observed that a dramatic increase of activity in TH with ruthenium-based catalysts is achieved by using the ligand 1-(pyridin-2-yl)methanamine (Pyme).[5] By employment of 1-substituted Pyme ligands (RPyme; R = Me, *t*Bu, Ph), we have recently isolated the complexes *cis*-[$RuCl_2$(Josiphos)(RPyme)] which are among the most active catalysts for the asymmetric TH of a variety of aryl ketones.[6]

It is worth noting that few compounds, namely [$RuCl_2$(PP)(NN)] (PP = diphosphane; NN = Pyme,[5d,7] diamine[3,8]), [RuCl(NN)(arene)],[4b,9] [$RuCl_2$-(PPh_3)(oxazoline)],[10] Ru–Binap,[11] and (cyclopentadienone)Ru carbonyl complexes,[12] catalyze both the asymmetric TH and HY of carbonyl compounds. Despite the extensive work on ruthenium-based catalysts, much less attention has been directed towards iron[13] and osmium[13e,14] congeners, the activity of which appears lower than that of the well-established ruthenium catalysts. As regards osmium, catalytic TH of ketones has been reported for [$Os(CO)HX(PR_3)_n$] (X = Cl, H; n = 2, 3) and related complexes,[14a,b] as well as

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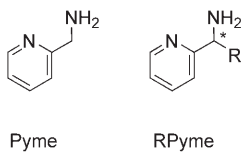
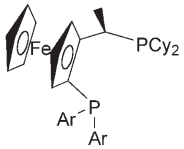
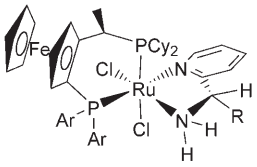
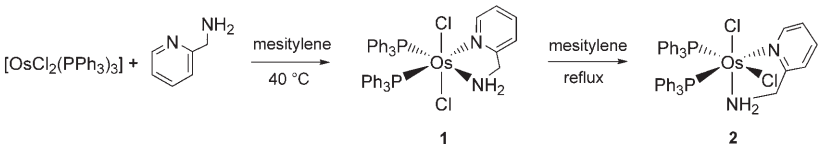






[OsCl(ON)(arene)] (ON = amino acidates).[14c] The compounds $[Os(CO)H(NCMe)_2(PPh_3)_2][BF_4]$,[14d] $[OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2]$[14e] and phosphane-based osmium complexes[14f] have been found active for HY of ketones and aldehydes, whereas the derivatives of formula $[Os(CO)HCl(PPh_3)P_2]$ (P = phosphane or P_2 = diphosphane) have been proven to catalyze both TH and HY of carbonyl compounds.[14a,g,h] Highly enantioselective reduction of ketones (up to 92% *ee)* has been obtained with the system generated in situ from $[Os(cymene)Cl_2]_2$ and β-amino alcohols.[14i] However, the low activity (Os > 0.1 mol%) and the relative slow rate of these osmium systems may limit their employment in organic synthesis. On the other hand, because of the high thermal and oxidative stability observed for osmium complexes, more robust catalysts are expected than those derived from other metals. This advantage should lead to systems displaying high TON values which may counter the higher cost involved in the case of osmium.[14a,15] Furthermore, this enhanced stability of osmium complexes can allow kinetic and mechanistic studies through detecting intermediates which may lead to a better understanding of the catalytic cycle.

We describe here that the osmium complexes $[OsCl_2P_2(Pyme)]$ ($P = PPh_3$ or $P_2 = Ph_2P(CH_2)_4PPh_2$) efficiently catalyze the rapid reduction of different ketones by means of both TH and HY in basic alcohol media. High enantioselectivity (up to 96%) has been reached in the TH by using catalysts prepared in situ from $[OsCl_2(PPh_3)_3]$, Josiphos diphosphanes, and racemic mixtures of RPyme ligands.

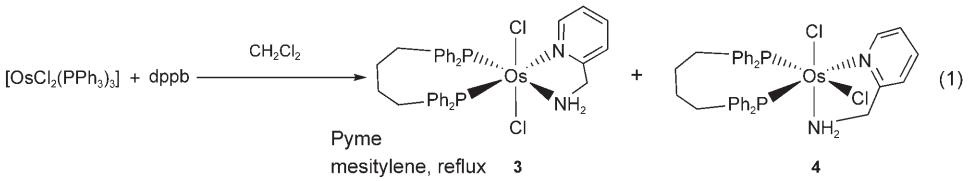


Scheme 1. Preparation of **1** and **2**.

Results and Discussion

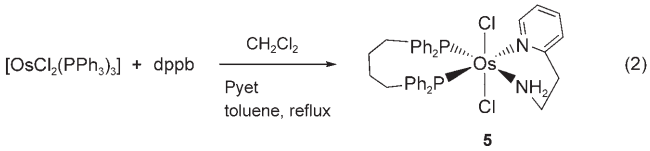
Synthesis of osmium complexes: Treatment of $[OsCl_2(PPh_3)_3]$ with one equivalent of Pyme in mesitylene at 40°C promptly leads to the compound *trans,cis*-$[OsCl_2(PPh_3)_2(Pyme)]$ (**1**) in 93% yield (Scheme 1).

The $^{31}P\{^1H\}$ NMR spectrum (CD_2Cl_2) shows two doublets at $\delta = -11.5$ and -16.3 ppm with $^2J(P,P) = 11.7$ Hz, typical of a *cis* arrangement of the P atoms. In the ^1H NMR spectrum, the CH_2 protons appear as a triplet at $\delta = 4.54$ ppm ($^3J(H,H) = 5.7$ Hz), whereas the NH_2 ones give a broad signal at $\delta = 3.70$ ppm, in agreement with a geometry with two *trans* chloride atoms. Heating of **1** in mesitylene at 150°C for 4 h affords the poorly soluble compound *cis,cis*-$[OsCl_2(PPh_3)_2(Pyme)]$ (**2**), the $^{31}P\{^1H\}$ NMR spectrum of which reveals two doublets at $\delta = -8.0$ and -8.5 ppm ($^2J(P,P) = 15.9$ Hz). The NH_2 group gives two ^1H NMR signals at $\delta = 4.51$ and 2.68 ppm, consistent with the formation of a complex with a *cis* $RuCl_2$ arrangement. The isomerization of **1** into **2** agrees with the behavior of the ruthenium analogue *trans,cis*-$[RuCl_2(PPh_3)_2(Pyme)]$, which converts into the *cis* derivative under milder conditions.[5d] Reaction of $[OsCl_2(PPh_3)_3]$ with one equivalent of $Ph_2P(CH_2)_4PPh_2$ (dppb) in CH_2Cl_2 and subsequent reaction with Pyme in mesitylene at 150°C leads to a mixture of *trans*-$[OsCl_2(dppb)(Pyme)]$ (**3**) and *cis*-$[OsCl_2(dppb)(Pyme)]$ (**4**) in about an 1:3 molar ratio [Eq. (1)].



The $^{31}P\{^1H\}$ NMR spectra (CD_2Cl_2) recorded during the reaction reveal the formation of the two isomers, with **3** ($\delta = -14.3$ and -16.3 ppm, $^2J(P,P) = 10.5$ Hz) which partially converts into **4** ($\delta = -3.9$ and -13.1 ppm, $^2J(P,P) = 13.2$ Hz).[16] As a matter of fact, prolonged heating of this mixture inhibited the isolation of **4** as a single product. Compound **3** gives a signal at $\delta = 2.63$ ppm for the NH_2 group in its ^1H NMR spectrum (CD_2Cl_2), whereas the resonance at $\delta = 4.30$ ppm is for the CH_2N moiety, the ^{13}C NMR signal of which is at $\delta = 50.4$ ppm, according to the values of the analogue *trans*-$[RuCl_2(dppb)(Pyme)]$.[5d] The NH_2 group of **4** gives two ^1H NMR signals at $\delta = 4.54$ and 2.77 ppm, whereas the CH_2N ^{13}C NMR resonance is at $\delta = 56.2$ ppm, close to the corresponding *cis* ruthenium compound.[5d] Employment of 2-(pyridin-2-yl)ethanamine (Pyet), which displays a longer

CH_2 chain than Pyme, results in the formation of the *trans* isomer. Treatment of $[OsCl_2(PPh_3)_3]$ with dppb in CH_2Cl_2, followed by addition of Pyet in refluxing toluene (3 h) gives *trans*-$[OsCl_2(dppb)(Pyet)]$ (**5**) [Eq. (2)].

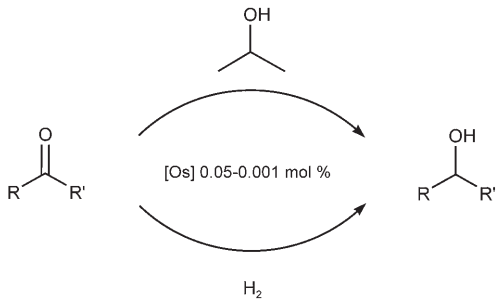


(2)

5

The $^{31}P\{^1H\}$ NMR spectrum of **5** exhibits two doublets at $\delta = -10.1$ and -15.9 ppm with $^2J(P,P) = 12.3$ Hz, whereas the NH_2 moiety gives a ^1H NMR signal at $\delta = 4.09$ ppm, consistent with a *trans* geometry. At variance with **3**, no isomerization has been observed by subsequent heating of **5**, indicating that the length of the pyridine CH_2 chain affects the geometry of the complex. With Pyme, the *trans*-$[OsCl_2P_2(Pyme)]$ compounds are initially formed and thermally convert (partially) to the most-stable *cis* analogues. This behavior resembles that observed for ruthenium Pyme complexes, even though the isomerization occurs with osmium under harsher conditions and no complete *cis* isomerization has been obtained with **3**.

Catalytic results: The osmium compounds **1**, **2**, and **5** have been proven to be catalytically active for the reduction of acetophenone by means of TH in refluxing 2-propanol. Importantly, with the system **3/4** (1/3 molar ratio) many ketones have been quickly converted into alcohols by means of fast TH and also HY with dihydrogen (Scheme 2).



Scheme 2. Reduction of ketones catalyzed by osmium complexes by means of TH or HY.

When compound **1** (Os 0.05 mol%) is added to acetophenone (0.1 M) in refluxing 2-propanol that contains NaO*i*Pr (2 mol%), quantitative formation of 1-phenylethanol is achieved in 5 min, leading to a turnover frequency (TOF) of $7.5 \times 10^4\ h^{-1}$. Employment of the isomer **2** gives a slightly higher rate ($TOF = 8.6 \times 10^4\ h^{-1}$; Table 1).

With the mixture **3/4**, the TH of MeCOPh occurs in 30 s, leading to a TOF of $5.7 \times 10^5\ h^{-1}$. This rate is surprisingly high and can be compared with that of the most active catalysts for TH-based on ruthenium.[5,17] Actually, the activity of **3/4** appears higher than that of the analogue *cis*-$[RuCl_2(dppb)(Pyme)]$ ($TOF = 3.0 \times 10^5\ h^{-1}$),[5d] showing that osmium systems may be used as fast catalysts for the reduction of carbonyl compounds, a result which has not been previously reported. Compound **5**, containing a longer pyridine chain, is also catalytically active, with a low rate ($TOF = 1.4 \times 10^4\ h^{-1}$) relative to **3/4**, indicating that the use of Pyme is crucial to achieve high activity with osmium, as observed for ruthenium.[18] It should be noted that with **3/4**, the complete reduction of MeCOPh has been obtained at extremely low catalyst loading. At variance with the ruthenium analogues ($TON = 10^4$), **3/4** is catalytically active even at 0.001 mol% ($TON \approx 1.8 \times 10^5$) with a gradual decrease of the rate by reducing the osmium concentration ($TOF = 5.5 \times 10^5$ to $3.4 \times 10^5\ h^{-1}$ at 0.02 to 0.001 mol%, respectively; Table 2).

Table 1. Catalytic TH of acetophenone (0.1 M) with **1**–**5** (Os 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 82 °C.

Compound	Conv. [%][a]	*t* [min]	TOF [h^{-1}][b]
1	98	5	7.5×10^4
2	98	5	8.6×10^4
3/4	98	30 s	5.7×10^5
5	94	10	1.4×10^4

[a] The conversion was determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

Table 2. Catalytic TH of acetophenone (0.1 M) at different loadings of **3/4** and NaO*i*Pr (2 mol%) in 2-propanol at 82 °C.

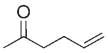
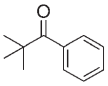
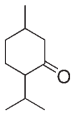
Mol% of **3/4**	Conv. [%][a]	*t* [min]	TOF [h^{-1}][b]
0.02	98	2	5.5×10^5
0.01	98	5	4.8×10^5
0.005	97	5	4.5×10^5
0.002	99	30	3.7×10^5
0.001	98	120	3.4×10^5

[a] The conversion was determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

These data indicate that **3/4** is more robust compared to the ruthenium analogues, that is, the deactivation process is retarded, and, therefore, this osmium system can be employed in the synthesis of alcohols on a preparative scale. Interestingly, the mixture **3/4** enables the fast chemoselective reduction of unsaturated dialkyl ketones, such as 5-hexen-2-one ($TOF = 3.2 \times 10^5\ h^{-1}$), without reduction or isomerization of the terminal olefinic bond (Table 3).

Most importantly, *tert*-butyl ketones, which are feebly reactive in the TH leading to low conversion or requiring severe reaction conditions,[13e,19] are here efficiently reduced to alcohols with **3/4**. As a matter of fact, 3,3-dimethyl-2-butanone and 2,2-dimethylpropiophenone are quantitatively converted to alcohols in minutes by using 0.05 mol% of **3/4**, with $TOF = 8.0 \times 10^3$ and $1.7 \times 10^4\ h^{-1}$, respectively (Table 3). The lower rate observed for these substrates relative to that of acetophenone is in agreement with the less-favorable

Table 3. Catalytic TH of unsaturated and bulky ketones (0.1 M) with **3/4** (Os 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 82 °C.

Ketone	Conv. [%][a]	*t* [min]	TOF [h^{-1}][b]
	96	2	3.2×10^5
	98	30	1.7×10^4
	93	30	8.0×10^3
	99	30	2.7×10^4

[a] The conversion was determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

access of the carbonyl group to the metal center as a result of steric factors. Under these catalytic conditions, complete conversion of menthone has also been obtained. It is worth noting that when the system $[OsCl_2(dppb)(Pyme)]$ is generated in situ by refluxing a 2-propanol solution of $[OsCl_2(PPh_3)_3]$ with dppb (1 h) and Pyme (2 h), it promotes the TH of acetophenone with the same activity of **3/4**.

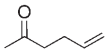
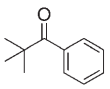
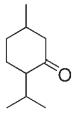
As ruthenium complexes $[RuCl_2(PP)(Pyme)]$[5d,7] have been proven to catalyze both TH and HY, we have investigated the catalytic activity of **3/4** in the HY of ketones at low dihydrogen pressure. Among the different alcohols (ROH; R = Me, Et, *i*Pr), ethanol has been found to give the best performance in the presence of the base KO*t*Bu. Thus, when an ethanol solution of acetophenone (0.5 M) containing **3/4** (Os 0.05 mol%) and KO*t*Bu (2 mol%) was stirred under 5 atm of H_2 in a 100 mL glass autoclave at 70 °C, complete reduction of the ketone was achieved in 10 min (TOF = 1.5×10^4 h^{-1}; Table 4).

At a lower loading of osmium (0.01 and 0.005 mol%), the reduction occurs completely with almost the same rate, indicating that **3/4** should be considered a robust catalytic system for HY (Table 4). The system **3/4** promotes the efficient HY of 5-hexen-2-one to the corresponding unsaturated alcohol with high rates and no reduction of the C=C bond has been observed. Importantly, the osmium system (**3/4** 0.01 mol% and 5 atm of H_2) also enables the reduction of the bulky *tert*-butyl substrates 3,3-dimethyl-2-butanone and 2,2-dimethylpropiophenone with almost the same rate of acetophenone (Table 4). This is a remarkable result as the HY of these types of compounds is described to occur at a lower rate, due to the bulkiness of the *tert*-butyl group.[20] A point to note is that the related ruthenium complex $[RuCl_2(PP)(Pyme)]$ (PP = (*S*)-tolbinap) was found to efficiently catalyze the asymmetric HY of *tert*-butyl ketones.[7] With **3/4**, also the cyclic ketones 2-methyl-cyclohexanone and menthone have been reduced to alcohols under these catalytic conditions and with high rates of reaction. A comparison of the results obtained with **3/4** in TH with those achieved in HY show that while in the TH, the rate strongly depends on the bulkiness of the substrates, in HY, the rate is apparently slightly affected by the steric properties of the ketone, suggesting that the H_2 activation is likely to be the rate-determining step.

As regards the asymmetric reduction of ketones with osmium, fast enantioselective TH in basic 2-propanol has been observed with the catalytic system generated in situ by the reaction of $[OsCl_2(PPh_3)_3]$, (*S*,*R*)-Josiphos in refluxing 2-propanol (1 h), and Pyme (1 h) in 1:1.5:2 molar ratios, respectively. This system enables the quantitative TH of PhCOMe (30 min at 60 °C) to (*S*)-1-phenylethanol (91% *ee*) by using a low-catalyst loading (Os 0.05 mol%) and NaO*i*Pr (2 mol%), affording a TOF of 9.7×10^3 h^{-1} (Table 5).

According to our studies on the asymmetric TH of ketones with ruthenium by using racemic RPyme ligands, which afforded higher *ee* values compared to Pyme,[6] employment of (±)-MePyme in the reduction of acetophenone gives the (*S*)-alcohol with both a higher enantiomeric excess (95%) and reaction rate (TOF = 1.5×10^4 h^{-1}) (Table 5). Furthermore, a high *ee* (94% (*S*)) and reaction rate (TOF = 1.9×10^4 h^{-1}) have also been obtained with the racemic mixture of *t*Bu-Pyme. When the bulkier (*S*,*R*)-

Table 4. Catalytic HY of ketones (0.5 M) with **3/4** and KO*t*Bu (2 mol%) in ethanol under 5 atm H_2 at 70 °C.

Mol% of **3/4**	Ketone	Conv. [%][a]	*t* [h]	TOF [h^{-1}][b]
0.05		>99	10 min	1.5×10^4
0.01		>99	1	1.4×10^4
0.005		>99	4	1.3×104
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	7.0×10^3
0.01		>99	2	1.4×10^4

[a] The conversion was determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

Table 5. Enantioselective catalytic TH of acetophenone (0.1 M) with the system $[OsCl_2(PPh_3)_3]$/PP/(±)-RPyme (Os: 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 60°C.

PP	Ar of PP	R of Pyme	Conv. [%][a]	*t* [min]	*ee* [%][a]	TOF [h^{-1}][b]
(*S*,*R*)−Josiphos	Ph	H	96	30	91 *S*	9.7×10^3
(*S*,*R*)-Josiphos	Ph	Me	96	30	95 *S*	1.5×10^4
(*S*,*R*)-Josiphos	Ph	*t*Bu	97	10	94 *S*	1.9×10^4
(*S*,*R*)-Josiphos*	4-OMe-3,5-$Me_2C_6H_2$	H	97	40	92 *S*	1.1×10^4
(*S*,*R*)-Josiphos*	4-OMe-3,5-$Me_2C_6H_2$	Me	92	30	95 *S*	8.0×10^3
(*S*,*R*)-Josiphos*	4-OMe-3,5-$Me_2C_6H_2$	*t*Bu	98	30	93 *S*	1.3×10^4

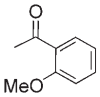
[a] The conversion and *ee* were determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

Josiphos*, which contains the 4-OMe-3,5-$Me_2C_6H_2$ groups instead of Ph ones, is used in combination with Pyme or (±)-RPyme (R = Me, *t*Bu), reduction of acetophenone is quickly achieved (TOF values 8.0×10^3–1.3×10^4 h^{-1}) with formation of (*S*)-1-phenylethanol in 92–95% *ee* (Table 5). With the catalyst generated in situ from $[OsCl_2(PPh_3)_3]$, (*S*,*R*)-Josiphos, and (±)-*t*Bu-Pyme, asymmetric TH of the aryl-substituted ketones 2′-methyl- 2′-chloro- and 2′-methoxyacetophenone has been observed, affording (*S*)-alcohols with 94–96% *ee*, indicating that this osmium system can be efficiently used for the preparation of chiral alcohols (Table 6).

The ^{31}P NMR analysis of the reaction mixtures of the $[OsCl_2(PPh_3)_3]$/PP/(±)-RPyme system reveals the formation of numerous stereoisomers. Attempts to obtain a single catalytic precursor by using different solvents at high temperature failed. These results can be compared with those obtained with ruthenium which showed that $[RuCl_2(PPh_3)_3]$, (*S*,*R*)-Josiphos, and (±)-RPyme led in refluxing toluene to the single stereoisomer *cis*-$[RuCl_2(PP)(RPyme)]$ through a highly diastereoselective reaction.[6] Interestingly, with (*S*,*R*)-Josiphos and (±)-RPyme-based systems, similar values of *ee* have been obtained in the catalytic TH of ketones by using the structurally well-defined ruthenium complexes as well as the in-situ-prepared osmium system as catalytic precursors.

As regards the species which form during catalysis, it is likely that osmium hydrides are generated when $[OsCl_2P_2(Pyme)]$ complexes are treated with alkali metal alkoxides in 2-propanol. Reaction of **1** with NaO*i*Pr (three equivalents) in C_6D_6/2-propanol at room temperature leads to the formation of two *trans* OsP_2 hydride species which, after evaporation of the solvent mixture, show two $^{31}P\{^1H\}$ NMR singlets at $\delta = 23.9$ and 23.0 ppm, in a 3:1 molar ratio. The ^1H NMR spectrum of the main product in C_6D_6 shows a triplet at $\delta = 3.10$ ppm ($^3J(H,H) = 6.0$ Hz) for CH_2N, a broad signal for NH_2 ($\delta = 2.37$ ppm), and two signals at $\delta = -7.80$ (pseudo q, $J = 8.8$ Hz) and -10.8 ppm (broad signal) for two hydrides, which are consistent with a *cis*,*trans*-$[OsH_2(PPh_3)_2(Pyme)]$ dihydride compound, similar to the analogous ruthenium complex.[5d] Employment of **2** in place of **1** leads to identical results, indicating that in basic 2-propanol, the *trans* and *cis* osmium precursors give the same hydride species. These data suggest that in the catalytic TH mediated by *trans* or *cis* osmium Pyme complexes, the species $[OsHXP_2(Pyme)]$ (X = H, OR′) are the intermediates involved in β-hydrogen elimination versus ketone-insertion reaction, according to the studies on ruthenium-hydride/alkoxide complexes.[21]

Table 6. Enantioselective catalytic TH of ketones (0.1 M) with the system $[OsCl_2(PPh_3)_3]$/(*S*,*R*)-Josiphos/(±)-*t*BuPyme (Os 0.05 mol%) and NaO*i*Pr (2 mol%) in 2-propanol at 60°C.

Ketone	Conv. [%][a]	*t* [min]	*ee* [%][a]	TOF [h^{-1}][b]
	99	30	94 *S*	1.2×10^4
	98	60	95 *S*	9.1×10^3
	99	60	96 *S*	8.6×10^3

[a] The conversion and *ee* were determined by GC analysis. [b] Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion.

Conclusion

We have found that the novel osmium complexes of general formula $[OsCl_2P_2(Pyme)]$ (P = P phosphane or P_2 = diphosphane) are active catalysts for the reduction of ketones in basic alcohol media with remarkably high reaction rates (TOF up to 5.7×10^5 h^{-1}). The osmium system **3**/**4** has been proven to rapidly catalyze both the TH and HY of different ketones at very low loading of catalyst (0.001 and 0.005 mol%). With the catalysts generated in situ from $[OsCl_2(PPh_3)_3]$, (*S*,*R*)-Josiphos, and (±)-RPyme ligands, efficient asymmetric TH of methyl–aryl ketones (up to 96% *ee*) and good rates of reaction have been observed. Work is in progress to establish the structure of the in-situ-generated chiral osmium compounds and the species involved in the catalytic TH and HY reactions. These results clearly show that when a suitable set of ligands is employed, osmium complexes may display extremely high catalytic activity in reduction processes, comparable to other elements, including ruthenium, with the advantage that deactivation is retarded. This study may help in the design of new efficient homogeneous osmium catalysts and to stimulate research in this relatively less-studied area of chemistry.

Experimental Section

General: All reactions were carried out under an argon atmosphere by using standard Schlenk techniques. The solvents and the ketones were carefully dried by standard methods and distilled under argon before use.

The diphosphane, Pyme, and Pyet ligands and all other chemicals were purchased from Aldrich and were used without further purification. The complex $[OsCl_2(PPh_3)_3]$ was prepared according to the literature procedure.[22] NMR measurements were recorded on a Bruker AC 200 spectrometer and chemical shifts, in ppm, are relative to TMS for ^1H and $^{13}C\{^1H\}$ NMR, whereas 85% H_3PO_4 was used for $^{31}P\{^1H\}$ NMR spectroscopy. Elemental analyses (C, H, N) were carried out with a Carlo Erba 1106 elemental analyzer, whereas the GC analyses were performed with a Varian GP-3380 gas chromatograph equipped with a MEGADEX-ETTBDMS-β chiral column.

Synthesis of 1: $[OsCl_2(PPh_3)_3]$ (135 mg, 0.129 mmol) and Pyme (17 μL, 0.165 mmol) were suspended in mesitylene (2 mL) and the mixture was heated at 40 °C for 30 min, affording a yellow precipitate, which was filtered, washed with diethyl ether (2×5 mL) and dried under reduced pressure. Yield: 107 mg (93%); ^1H NMR (200.1 MHz, CD_2Cl_2, 20 °C): $\delta = 8.41$ (d, $^3J(H,H) = 5.6$ Hz, 1H; *o*-C_5H_4N), 7.72–6.95 (m, 32H; aromatic protons), 6.54 (pseudot, $^3J(H,H) = 6.5$ Hz, 1H; aromatic proton), 4.54 (pseudot, $^3J(H,H) = 5.7$ Hz, 2H; CH_2), 3.70 ppm (brs, 2H; NH_2); $^{13}C\{^1H\}$ NMR (50.3 MHz, CD_2Cl_2, 20 °C): $\delta = 163.6$ (d, $J(C,P) = 1.9$ Hz; N*C*CH_2), 158.0 (d, $J(C,P) = 3.4$ Hz; NCH of C_5H_4N), 139.0–120.6 (m; aromatic carbon atoms), 51.3 ppm (pseudot, $J(C,P) = 2.3$ Hz; NCH_2); $^{31}P\{^1H\}$ NMR (81.0 MHz, CD_2Cl_2, 20 °C): δ −11.5 (d, $^2J(P,P) = 11.7$ Hz), −16.3 ppm (d, $^2J(P,P) = 11.7$ Hz); elemental analysis calcd (%) for $C_{42}H_{38}Cl_2N_2OsP_2$: C 56.44, H 4.29, N 3.13; found: C 56.48, H 4.41, N 3.00.

Synthesis of 2: Compound **1** (80 mg, 0.090 mmol) was suspended in mesitylene (3 mL) and the mixture was heated at 150 °C for 4 h. The dark-yellow product was filtered, washed with diethyl ether (10 mL), dichloromethane (1 mL), and dried under reduced pressure. Yield: 70 mg (88%); ^1H NMR (200.1 MHz, CD_2Cl_2, 20 °C): $\delta = 8.82$ (d, $^3J(H,H) = 5.4$ Hz, 1H; *o*-C_5H_4N), 7.68–6.82 (m, 33H; aromatic protons), 4.51 (brt, 1H; NH_2), 3.74 (dd, $J(H,H) = 16.1$, 4.7 Hz, 1H; CH_2), 3.04 (m, 1H; CH_2), 2.68 ppm (m, 1H; NH_2); $^{31}P\{^1H\}$ NMR (81.0 MHz, CD_2Cl_2, 20 °C): $\delta = -8.0$ (d, $^2J(P,P) = 15.9$ Hz), −8.5 ppm (d, $^2J(P,P) = 15.9$ Hz); elemental analysis calcd (%) for $C_{42}H_{38}Cl_2N_2OsP_2$: C 56.44, H 4.29, N 3.13; found: C 56.29, H 4.35, N 3.02.

Synthesis of 3/4: $[OsCl_2(PPh_3)_3]$ (120 mg, 0.115 mmol) and dppb (49 mg, 0.115 mmol) were dissolved in dichloromethane (4 mL), and the solution was stirred at room temperature for 2 h. After evaporation of the solvent, mesitylene (4 mL) and Pyme (14 μL, 0.136 mmol) were added, and the resulting suspension was heated at 150 °C for 4 h and stirred at room temperature overnight. The yellow–green precipitate was filtered, washed with diethyl ether (3×4 mL) and dried under reduced pressure. Yield: 76 mg (83%); ^1H NMR (200.1 MHz, $CDCl_3$, 20 °C): $\delta = 9.41$ (d, $^3J(H,H) = 5.0$ Hz; *o*-C_5H_4N, major complex), 8.83 (d, $^3J(H,H) = 5.6$ Hz; *o*-C_5H_4N, minor complex), 8.17–6.63 (m; aromatic protons), 4.60 (t, $^3J(H,H) = 11.0$ Hz; NH_2, major complex), 4.31 (t, $^3J(H,H) = 5.0$ Hz; NCH_2 minor complex), 4.10–3.95 (m; NCH_2 major complex), 3.30–3.10 (m; CH_2), 2.70–1.10 ppm (m; CH_2 and NH_2); $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$, 20 °C): $\delta = 163.8$ (s; N*C*CH_2, minor complex), 158.6 (s; N*C*CH_2, major complex), 155.1 (s; *o*-NCH, minor complex), 149.4 (s; *o*-NCH, major complex), 140.9–119.2 (m; aromatic carbon atoms), 56.0 (s; NCH_2, major complex), 50.1 (s; NCH_2, minor complex), 36.4 (d, $J(C,P) = 33.8$ Hz; PCH_2 major complex), 35.3 (d, $J(C,P) = 35.9$ Hz; PCH_2, minor complex), 28.6 (d, $J(C,P) = 35.5$ Hz; PCH_2, major complex), 27.2 (s; PCH_2CH_2, major complex), 25.6 (s; PCH_2CH_2, minor complex), 24.4 (d, $J(C,P) = 32.6$ Hz; PCH_2, minor complex), 19.1 (s; PCH_2CH_2, minor complex), 18.4 ppm (s; PCH_2CH_2, major complex); $^{31}P\{^1H\}$ NMR (81.0 MHz, $CDCl_3$, 20 °C): $\delta = -3.6$ (d, $^2J(P,P) = 13.3$ Hz; major complex), −13.2 ppm (d, $^2J(P,P) = 13.3$ Hz), −14.7 (d, $^2J(P,P) = 10.5$ Hz; minor complex), −16.1 ppm (d, $^2J(P,P) = 10.5$ Hz); elemental analysis calcd (%) for $C_{34}H_{36}Cl_2N_2OsP_2$: C 51.32, H 4.56, N 3.52, found: C 51.12, H 4.61, N 3.46.

Synthesis of 5: $[OsCl_2(PPh_3)_3]$ (100 mg, 0.095 mmol) and dppb (45 mg, 0.106 mmol) were dissolved in dichloromethane (2 mL) and the solution was stirred at room temperature for 2 h. After elimination of the solvent, toluene (2 mL) and Pyet (14.8 μL, 0.124 mmol) were added and the mixture was refluxed for 3 h. The resulting solution was concentrated (1 mL) and addition of diethyl ether (5 mL) afforded a green–yellow precipitate, which was washed with diethyl ether (2×5 mL) and dried under reduced pressure. Yield: 62 mg (81%); ^1H NMR (200.1 MHz, CD_2Cl_2, 20 °C): $\delta = 9.87$ (d, $^3J(H,H) = 6.0$ Hz, 1H; *o*-C_5H_4N), 8.31 (m, 2H; aromatic protons), 7.88–6.70 (m, 20H; aromatic protons), 6.28 (d, $^3J(H,H) = 7.4$ Hz, 1H; aromatic proton), 4.09 (brs, 2H; NH_2), 3.93 (m, 1H; CH_2), 3.18 (m, 4H; CH_2), 2.50–1.12 ppm (m, 7H; CH_2); $^{13}C\{^1H\}$ NMR (50.3 MHz, CD_2Cl_2, 20 °C): $\delta = 160.6$ (s; N*C*CH_2), 154.9 (s; NCH), 141.1–122.5 (m; aromatic carbon atoms), 40.3 (d, $J(C,P) = 1.8$ Hz; CH_2CH_2N), 39.9 (s; CH_2CH_2N), 36.0 (dd, $J(C,P) = 33.9$, 3.7 Hz; PCH_2), 29.8 (d, $J(C,P) = 35.9$ Hz; PCH_2), 27.6 (s; PCH_2CH_2), 18.8 ppm (t, $J(CP) = 1.8$ Hz; PCH_2CH_2); $^{31}P\{^1H\}$ NMR (81.0 MHz, CD_2Cl_2, 20 °C): $\delta = -10.1$ (d, $^2J(P,P) = 12.3$ Hz), −15.9 ppm (d, $^2J(P,P) = 12.3$ Hz); elemental analysis calcd (%) for $C_{35}H_{38}Cl_2N_2OsP_2$: C 51.92, H 4.73, N 3.46; found: C 51.93, H 4.67, N 3.48.

Typical procedure for the catalytic transfer hydrogenation of ketones: Osmium complex (2.0 μmol) was added to 2-propanol (2 mL). The ketone (2.00 mmol) was dissolved in 2-propanol and the solution (18.6 mL) was refluxed under argon. Addition of NaO*i*Pr (400 μL, 0.1 M in 2-propanol) and the solution containing the osmium complex (1.0 mL, 1.0 μmol) afforded the reduction of the ketone (osmium 0.05 mol%, NaO*i*Pr 2.0 mol%, ketone 0.1 M).

Typical procedure for the catalytic hydrogenation of ketones: The mixture **3/4** (1.4 mg, 1.76 μmol) was added to 2 mL of ethanol. The ketone (4.30 mmol) and KO*t*Bu (9.7 mg, 0.086 mmol) were dissolved in ethanol (total volume 8.1 mL) and the solution containing the osmium complex (0.49 mL, 0.43 μmol) was added. The resulting solution was transferred into a thermostated reactor at 70 °C and dihydrogen was introduced at a pressure of 5 atm, affording the reduction of the ketone (osmium 0.01 mol%, KO*t*Bu 2 mol%, ketone 0.5 M).

Typical procedure for enantioselective catalytic transfer hydrogenation of ketones: A 2-propanol (2 mL) solution of $[OsCl_2(PPh_3)_3]$ (2.1 mg, 2.0 μmol) and the (*S,R*)-Josiphos diphosphane (3.0 μmol) was refluxed for 1 h and, after addition of the (±)-RPyme ligand (4.0 μmol), for an additional 1 h. The ketone (2.00 mmol) was dissolved in 2-propanol and the solution (18.6 mL) was heated at 60 °C. Addition of NaO*i*Pr (400 μL, 0.1 M in 2-propanol) and the solution that contained the osmium complex (1.0 mL) afforded the reduction of the ketone (osmium 0.05 mol%, NaO*i*Pr 2 mol%, ketone 0.1 M).

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