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Chiral and Nonchiral [OsX_2(diphosphane)(diamine)] (X: Cl, OCH_2CF_3) Complexes for Fast Hydrogenation of Carbonyl Compounds

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Dedicated to Professor Fausto Calderazzo on the occasion of his 80th birthday

Abstract: The osmium complexes *trans*-[$OsCl_2$(dppf)(diamine)] (dppf: 1,1′-bis(diphenylphosphino)ferrocene; diamine: ethylenediamine in **3**, propylenediamine in **4**) were prepared by the reaction of [$OsCl_2(PPh_3)_3$] (**1**) with the ferrocenyl diphosphane, dppf and the corresponding diamine in dichloromethane. The reaction of derivative **3** with $NaOCH_2CF_3$ in toluene afforded the alkoxide *cis*-[$Os(OCH_2CF_3)_2$(dppf)-(ethylenediamine)] (**5**). The novel precursor [$Os_2Cl_4(P(m\text{-tolyl})_3)_5$] (**2**) allows the synthesis of the chiral complexes *trans*-[$OsCl_2$(diphosphane)(1,2-diamine)] (**6–9**; diphosphane: (*R*)-[6,6′-dimethoxy(1,1′-biphenyl)-2,2′-diyl]bis-[1,1-bis(3,5-dimethylphenyl)phosphane] (xylMeOBiphep) or (*R*)-(1,1′-binaphthalene)-2,2′-diylbis[1,1-bis(3,5-dimethylphenyl)phosphane] (xylbinap); diamine = (*R*,*R*)-1,2-diphenylethylenediamine (dpen) or (*R*,*R*)-1,2-diaminocyclohexane (dach)), obtained by the treatment of **2** with the diphosphane and the 1,2-diamine in toluene at reflux temperature. Compounds **3–5** in ethanol and in the presence of NaOEt catalyze the reduction of methyl aryl, dialkyl, and diaryl ketones and aldehydes with H_2 at low pressure (5 atm), with substrate/catalyst (S/C) ratios of 10000–200000 and achieving turnover frequencies (TOFs) of up to $3.0\times10^5\ h^{-1}$ at 70 °C. By employment of the chiral compounds **6–9**, different ketones, including alkyl aryl, bulky *tert*-butyl, and cyclic ketones, have successfully been hydrogenated with enantioselectivities up to 99% and with S/C ratios of 5000–100000 and TOFs of up to $4.1\times10^4\ h^{-1}$ at 60 °C.

Keywords: amino ligands · asymmetric catalysis · hydrogenation · osmium · phosphane ligands

Introduction

The ruthenium system *trans*-[$RuCl_2$(diphosphane)-(diamine)], developed by Noyori et al. for the catalytic reduction of simple ketones to chiral alcohols,[1] represents one of the most significant breakthroughs of both academic and industrial relevance in transition-metal-mediated asymmetric hydrogenation.[2] In addition to the most frequently used (1,1′-binaphthalene)-2,2′-diylbis(1,1-diphenylphosphane) (binap) diphosphane and (*R*,*R*)-1,2-diphenylethylenediamine (dpen) N–H diamine ligands, a large number of bidentate chiral P and N ligands have been developed to achieve both high enantioselectivity and productivity, as well as broad scope.[3,4] No universal catalysts exist on account of the structural diversity of ketones, so a high level of selectivity has been attained through fine tuning of the stereoelectronic properties of the diphosphanes and diamines. By contrast, the influence of the nature of the metal in the system [MCl_2(diphosphane)(diamine)] has not been investigated, with the chiral and achiral Fe and Os complexes being unexplored. It is worth noting that the PPh_3 osmium derivative [$OsHCl(PPh_3)_2(NH_2CMe_2CMe_2NH_2)$],[5] described by Clapham and Morris, was found to catalyze the hydrogenation[6] of acetophenone. A comparative DFT study on the hydrogenation of acetone with M–PH_3–ethylenediamine complexes (M: Fe, Ru, or Os) has also been reported.[7] Although osmium-based catalysts are usually considered less active than the ruthenium analogues,[8] we recently found that Os complexes containing the 1-(pyridin-2-yl)methanamine motif[9] are highly efficient catalysts for both the hydrogenation and transfer hydrogenation of ketones, with the CNN pincer complexes being active in enantioselective hydrogenation.[9a] Preliminary experiments showed that the system comprising [$OsCl_2(PPh_3)_3$] (**1**)/diphosphane/N–H diamine shows catalytic activity in the hy-

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drogenation of ketones, so the chemistry of the diphosphane/diamine–osmium species has been investigated.

We describe herein a novel class of complexes $[OsX_2(diphosphane)(diamine)]$ (X: Cl, OR), which were successfully prepared from **1** and the new precursor $[Os_2Cl_4(P(m\text{-tolyl})_3)_5]$ (**2**); this gives access to the chiral complexes. These derivatives were found to be the most active and productive osmium catalysts reported to date for the hydrogenation of simple ketones and aldehydes (turnover frequency (TOF) and substrate/catalyst (S/C) values of up to $3\times10^5\ h^{-1}$ and 2×10^5, respectively) at low dihydrogen pressure. With chiral diphosphanes and diamines, the asymmetric hydrogenation of ketones has been achieved with up to 99% enantiomeric excess (*ee*).

Results and Discussion

Preparation of $[OsX_2(diphosphane)(diamine)]$ complexes: The thermally stable complex *trans*-$[OsCl_2(dppf)(en)]$ (**3**; dppf: 1,1′-bis(diphenylphosphino)ferrocene, en: ethylenediamine) was easily obtained in 86% yield by treatment of **1** with the flexible diphosphane dppf[10] in dichloromethane at 40°C (3 h), followed by the addition of ethylenediamine (1 h; Scheme 1).

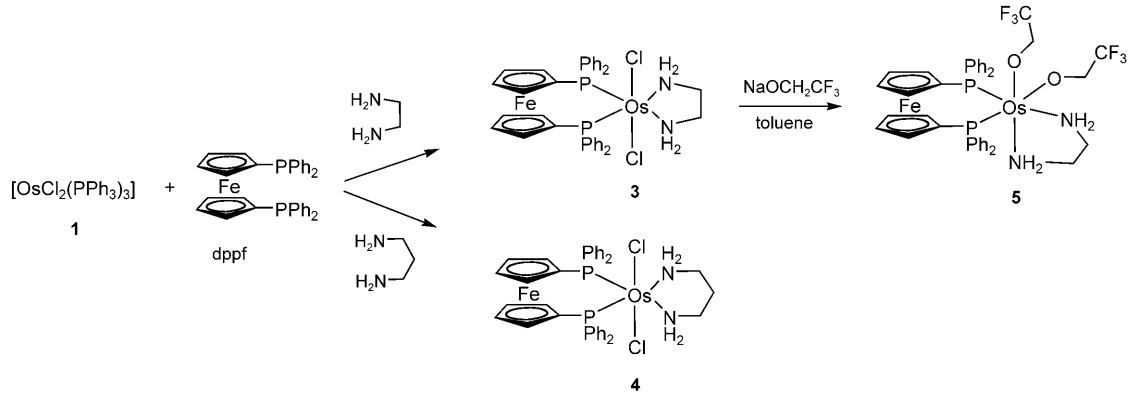
Derivative **4** was obtained similarly to **3** by using 1,3-propylenediamine. The *trans* configuration of both complexes was confirmed by the presence of one singlet in the ^{31}P NMR spectra. Treatment of **3** in toluene with two equivalents of $NaOCH_2CF_3$, prepared from 2,2,2-trifluoroethanol and NaOEt, afforded the osmium alkoxide[9a,11] *cis*-$[Os(OCH_2CF_3)_2(dppf)(en)]$ (**5**), according to the presence of two doublets at $\delta=1.6$ and -20.6 ppm ($^2J(P,P)=19.8$ Hz) in the ^{31}P NMR spectrum and two singlets at $\delta=-34.5$ and -36.1 ppm in the ^{19}F NMR spectrum (Scheme 1).

The reaction of **1** with more rigid and bulkier chiral diphosphanes, such as (*R*)-[6,6′-dimethoxy(1,1′-biphenyl)-2,2′-diyl]bis(1,1-diphenylphosphane) (MeObiphep) or (*R*)-binap and 1,2-diamines resulted in the formation of a mixture of *trans*-$[OsCl_2(diphosphane)(diamine)]$ and *trans*-$[OsCl_2(PPh_3)_2(diamine)]$ in about 1:1 ratio by incomplete PPh_3 substitution, as inferred from NMR spectroscopy measurements. The problem of synthesizing the chiral derivatives *trans*-$[OsCl_2(diphosphane)(diamine)]$ has been overcome through the preparation of novel precursor **2**, which contains the bulkier P(*m*-tolyl)$_3$ phosphane that allows higher reactivity. The orange osmium(II) compound **2** was obtained in 75% yield from the reaction of $[(NH_4)_2OsCl_6]$ with P(*m*-tolyl)$_3$ in a *t*BuOH/H_2O mixture at reflux temperature (1 day; Scheme 2).

The $^{31}P\{^1H\}$ NMR spectrum of **2** in C_6D_6 shows two doublets at $\delta=-15.4$ and -16.8 ppm ($^2J(P,P)=17.2$ Hz) and three triplets at $\delta=-13.4$, -18.1, and -19.6 ppm ($^2J(P,P)=11.5$ Hz); this is consistent with the proposed arrangement and in agreement with the related ruthenium complexes $[Ru_2Cl_4(PR_3)_5]$.[12] For osmium, the related dinuclear species $[Os_2Cl_4(L)(PPh_3)_4]$ (L: H_2O, =C=CH[C(OH)Ph$_2$]) have been reported.[13] Compound **2** reacts cleanly with several diphosphanes and diamines in toluene ($T>90$°C), as established by ^{31}P NMR spectroscopy. On the basis of the catalytic results carried out by using in situ generated catalysts (see below), the derivatives containing xylbinap-type diphosphanes and 1,2-diamines have been isolated. The reaction of precursor **2** with (*R*)-xylMeObiphep in toluene at reflux temperature for 4 h followed by treatment with (*R*,*R*)-dpen (1 h) led to the complex *trans*-$[OsCl_2((R)\text{-xylMeObiphep})((R,R)\text{-dpen})]$ (**6**), which was isolated in 54% yield (Scheme 2). In a similar way, derivatives **7**–**9** were obtained (47–66% yields) by using the appropriate ligands. The ^{31}P NMR spectra of derivatives **6**–**9** containing C_2 symmetry ligands show one singlet and are consistent with a *trans* geometry.

Catalytic results: The osmium complexes **3**–**5** in basic ethanol are extremely active and productive catalysts for the hydrogenation of ketones and aldehydes at low H_2 pressure (5 atm). Acetophenone (**10a**; 0.5 M) is rapidly and quantitatively converted into 1-phenylethanol in 10 min at 70°C, by using **3** with a S/C ratio of 10000 and in the presence of 1 mol% NaOEt (Scheme 3; Table 1).

At higher S/C ratios (50000–100000), the reduction is straightforward, and complete conversion of **10a** was at-



Scheme 1. Synthesis of the complexes $[OsX_2(dppf)(diamine)]$ (X: Cl, OR).

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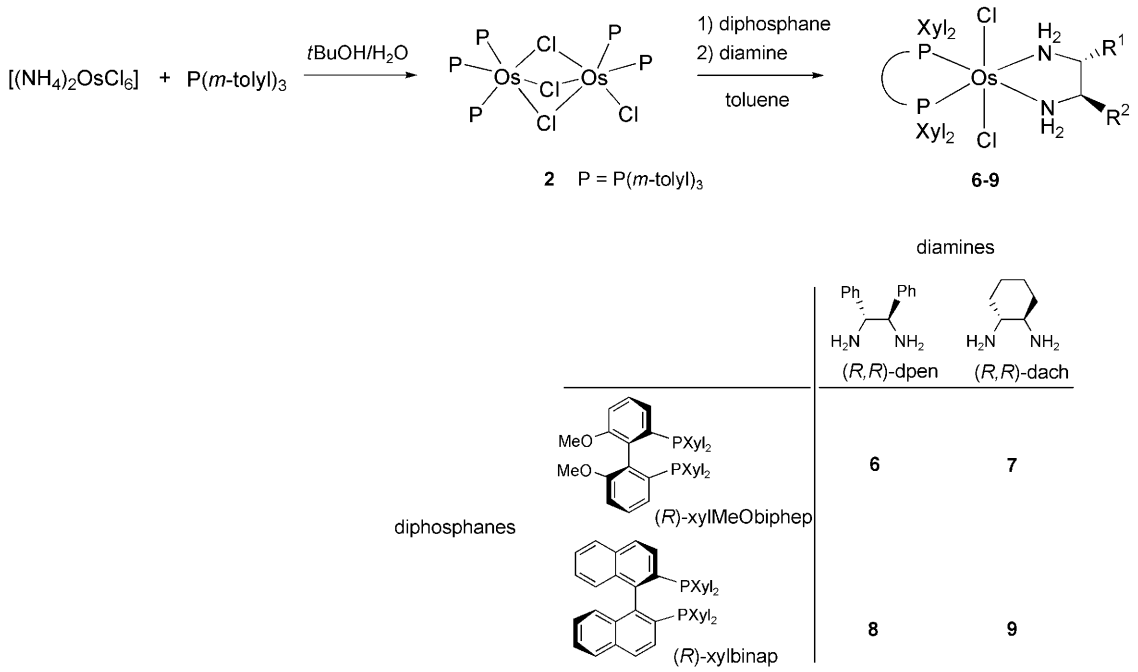
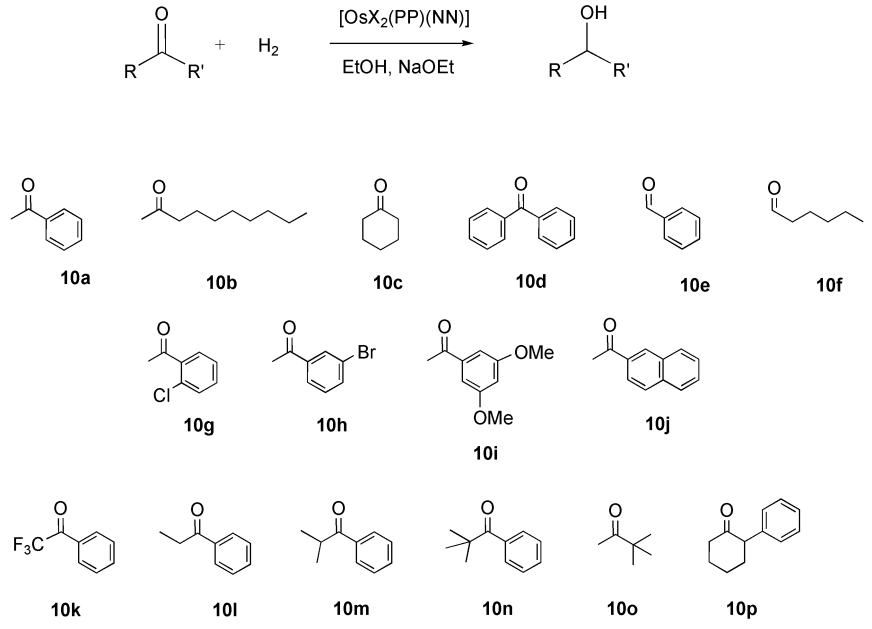


Scheme 2. Synthesis of the novel osmium precursor **2** and the chiral complexes *trans*-**6**–**9**.



Scheme 3. Hydrogenation of ketones and aldehydes **10** with the *trans* and *cis* Os complexes **3**–**9** (S/C = 10000–200000).

tained within 2 h at S/C = 200000 (TOF = 2.3×10^5 h^{-1}), which indicates that deactivation is retarded. Derivative **4**, containing the 1,3-diamine, shows a higher rate with a TOF value of 3.0×10^5 h^{-1} (S/C = 50000). The alkoxide **5** of *cis* configuration displays a similar activity to that of the *trans*-configured chloride **3** (TOF = 1.5×10^5 and 1.7×10^5 h^{-1}, respectively); this suggests that, under these catalytic conditions, both precursors rapidly generate the catalytically active osmium species. These high values of rate and productivity of Os in hydrogenation are unprecedented[5,6,9a,b] and rely on a combination of the accelerating N–H effect[1] with the robust metal frame. In the absence of H_2 in ethanol, these osmium complexes led to poor conversion of **10a** (less than 30% after 2 h), in accordance with the unfavorable redox potential of ethanol for ketone reduction,[14] which indicates that transfer hydrogenation is a less important pathway when H_2 is used. Complex **3** has been proven to efficiently catalyze the hydrogenation of linear and cyclic aliphatic ketones **10b** and **10c** (S/C = 50000) and the diaryl ketone **10d** (S/C = 10000) in less than 1 h. Also, the aromatic and aliphatic aldehydes **10e** and **10f** were easily and quantitatively reduced to primary alcohols within 10 min at 60 °C by using 0.5 mol% NaOEt.

The chiral complexes **6**–**9** rapidly catalyze the enantioselective hydrogenation of **10a** in EtOH at 60 °C in the presence of 1 mol% NaOEt. With derivative **6**, containing (*R*)-xylMeObiphep, (*S*)-1-phenylethanol (90% *ee*) has been obtained with S/C = 10000–100000, without deactivation or erosion of enantioselectivity (Table 2). An increase in the *ee*

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Table 1. Catalytic hydrogenation of ketones and aldehydes (0.5 M) in the presence of **3–5** and NaOEt (1 mol %) in ethanol under 5 atm H_2.

Complex	Substrate	S/C	T [°C]	Conv. [%][a]	t [min]	TOF [h^{-1}][b]
3	**10a**	10000	70	>99	10	1.7×10^5
3	**10a**	50000	70	99	30	1.8×10^5
3	**10a**	100000	70	98	60	1.5×10^5
3	**10a**	200000	70	98	120	2.3×10^5
4	**10a**	10000	70	>99	10	1.8×10^5
4	**10a**	50000	70	>99	30	3.0×10^5
5	**10a**	10000	70	98	10	1.5×10^5
3	**10b**	50000	60	95	60	8.0×10^4
3	**10c**	50000	60	97	60	9.0×10^4
3	**10d**	10000	60	>99	30	3.0×10^4
3[c]	**10e**	10000	60	99	10	9.0×10^4
3[c]	**10f**	10000	60	>99	10	5.7×10^4

[a] The conversion were determined by GC analysis. [b] Turnover frequency (moles of ketone converted into alcohol per mole of catalyst per hour) at 50% conversion. [c] With 0.5 mol% NaOEt.

Table 2. Catalytic asymmetric hydrogenation of ketones (0.5 M) in the presence of **6–9** and NaOEt (1 mol %) in ethanol under 5 atm H_2 at 60 °C.

Complex	Ketone	S/C	Conv. [%][a]	t [h]	TOF [h^{-1}][b]	*ee* [%][a]
6	**10a**	10000	96	0.5	2.0×10^4	90 (*S*)
6[c]	**10a**	50000	94	2	2.1×10^4	90 (*S*)
6[c,d]	**10a**	100000	90	15	1.0×10^4	90 (*S*)
7	**10a**	10000	>99	2	1.8×10^4	86 (*S*)
8	**10a**	10000	>99	0.5	2.5×10^4	97 (*S*)
9	**10a**	10000	99	0.5	4.1×10^4	94 (*S*)
8	**10g**	10000	>99	2	7.0×10^3	90 (*S*)
8	**10h**	10000	>99	1	1.0×10^4	99 (*S*)
8	**10i**	10000	>99	0.5	2.0×10^4	99 (*S*)
8	**10j**	10000	99	0.3	2.0×10^4	95 (*S*)
8	**10k**	10000	>99	1	1.2×10^4	87 (*R*)
8	**10l**	10000	>99	0.5	1.9×10^4	99 (*S*)
8	**10m**	10000	99	3	5.0×10^3	99 (*S*)
8	**10n**	10000	85	24	1.0×10^3	90 (*S*)
8	**10o**	10000	92	15	1.2×10^3	71 (*R*)
8	**10p**	5000	>99	2	2.5×10^3	92 (1*S*,2*S*); *cis*/*trans* = 97:3

[a] The conversion and *ee* value were determined by GC analysis. [b] Turnover frequency (moles of ketone converted into alcohol per mole of catalyst per hour) at 50% conversion. [c] With 2 mol% NaOEt. [d] T = 50 °C.

value (97 and 94% *ee*, respectively) was observed with the (*R*)-xylbinap derivatives **8** and **9**, containing (*R*,*R*)-dpen and (*R*,*R*)-dach, with **9** being more rapid (TOF = 4.1×10^4 h^{-1}).

With complex **8**, several methyl aryl ketones, namely, **10g–j**, are efficiently reduced to the corresponding (*S*)-alcohols in 0.3–2 h with 90, 99, 99, and 95% *ee*, respectively (S/C = 10000 and TOF values of up to 2.0×10^4 h^{-1}). The ketone **10k**, containing the electron-withdrawing CF_3 group, is also quickly reduced to the *R* enantiomer (87% *ee*). Interestingly, the alkyl aryl ketones **10l**[15] and **10m** and the *tert*-butyl substrates **10n** and **10o** are hydrogenated to the corresponding alcohols with 99, 99, 90, and 71% *ee*, respectively. It is worth noting that although the catalytic activity of **8** for **10n** and **10o** is lower than that with the other substrates, the related complexes *trans*-[$RuCl_2$(binap)(1,2-diamine)] were shown to be poorly active and enantioselective,[16] which indicates that the Os system is more active for bulky ketones[9b] than the Ru system. In addition, the configurationally labile α-substituted ketone **10p** has been hydrogenated to (1*S*,2*S*)-2-phenylcyclohexanol with high diastereoselectivity (*cis*/*trans* = 97:3) and an *ee* value of 92%.[1a] These are the highest *ee* values to date for asymmetric ketone hydrogenation based on Os catalysts,[9a] a field that has been practically unexplored.

The complexes *trans*-[$OsCl_2$(diphosphane)(diamine)] can also be generated in situ from **2** and the appropriate ligands. Thus, complex **8**, prepared by the treatment of **2** with (*R*)-xylbinap in toluene at 110 °C (3 h) and (*R*,*R*)-dpen (1 h), catalyzes the hydrogenation of **10a** to the corresponding (*S*)-alcohol in EtOH at 60 °C (S/C = 10000, TOF = 20000 h^{-1}, 96% *ee*) with much the same activity as that of the isolated complex. Employment of (*R*)-binap in place of (*R*)-xylbinap afforded the *S* enantiomer with 89% *ee*. In addition, if (*S*)-xylbinap is combined with (*R*,*R*)-dpen, compound **10a** is reduced to the (*R*)-alcohol at a lower rate and with lower enantioselectivity (TOF = 15000 h^{-1}, 54% *ee*). Finally, attempts to prepare **8** in situ from **1** instead of **2** resulted in the incomplete formation of **8** (about 40% conversion) and the hydrogenation of **10a** to the (*S*)-alcohol with 60% *ee*.

With regard to the catalytic cycle, it is likely that the *trans*-dichloride complexes react with sodium ethoxide in the presence of dihydrogen to afford the catalytically active osmium dihydride species[5] through a mechanism similar to that reported for the related ruthenium complexes.[17]

The stronger bonding and different electronic properties of the 5d metal osmium, with respect to the 4d metal ruthenium, result in the formation of more stable catalysts, which can work at higher temperature, in more protic solvents (ethanol versus 2-propanol), and with less base. This suggests that the chiral complexes *trans*-[$OsCl_2$(diphosphane)(diamine)], despite the higher metal cost, may be a valid complement to the analogous Ru derivatives.

Conclusion

We have prepared a novel class of osmium(II) complexes, *trans*- and *cis*-[OsX_2(diphosphane)(diamine)] (X: Cl, OR). Whereas the derivatives with the flexible diphosphane dppf were prepared from [$OsCl_2(PPh_3)_3$], the synthesis of the complexes containing more rigid chiral diphosphanes (such as the binap type) has been achieved by using the novel precursor [Os_2Cl_4(P(*m*-tolyl)$_3$)$_5$]. These complexes exhibit remarkably high activity and productivity in the hydrogenation of ketones and aldehydes (S/C and TOF values of up to 2.0×10^5 and 3.0×10^5 h^{-1}, respectively). The enantioselective reduction of ketones (up to 99%) has been performed with the correctly matched chiral diphosphane and diamine ligands. The straightforward preparation and high modularity

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of the system [OsX_2(diphosphane)(diamine)] holds promise for the broad application of osmium in asymmetric hydrogenation.

Experimental Section

General: All reactions were carried out under an argon atmosphere by using standard Schlenk techniques. The solvents and ketones were carefully dried by standard methods and distilled under argon before use. The diphosphane ligands and all other chemicals were purchased from Aldrich and Strem and used without further purification. Compound **1** was prepared according to the literature procedure.[18] NMR spectroscopy measurements were recorded on a Bruker AC200 spectrometer and the chemical shifts (in ppm) are relative to tetramethylsilane for ^{1}H and ^{13}C{^{1}H} spectra and to 85% H_3PO_4 for ^{31}P{^{1}H} spectra. 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 2: [$(NH_4)_2OsCl_6$] (1.50 g, 3.42 mmol) and P(*m*-tolyl)$_3$ (4.20 g, 13.8 mmol) were added to a solution of *tert*-butanol (130 mL) and water (55 mL). The suspension was heated at reflux temperature for 24 h to afford an orange precipitate, which was washed with water (2×15 mL), heptane (3×15 mL), and pentane (1×15 mL) and then dried under reduced pressure (2.61 g, 75%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): δ = 9.72 (m, 1H; aromatic proton), 8.82 (brs, 1H; aromatic proton), 8.24 (t, J(H,H) = 5.4 Hz, 1H; aromatic proton), 8.10–5.95 (m, 57H; aromatic protons), 2.26 (s, 3H; Me), 2.15–1.81 (m, 33H; Me), 1.71 (s, 3H; Me), 1.67 (s, 3H; Me), 1.26 ppm (s, 3H; Me); ^{13}C{^{1}H} NMR (50.3 MHz, $C_6D_5CD_3$, 20°C): δ = 141.9–124.2 (m; aromatic carbon atoms), 22.5–20.9 ppm (m; Me); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): δ = −13.4 (t, ^2J(P,P) = 11.5 Hz), −15.4 (d, ^2J(P,P) = 17.2 Hz), −16.8 (d, ^2J(P,P) = 17.2 Hz), −18.1 (brt ^2J(P,P) = 11.5 Hz), −19.6 ppm (t, ^2J(P,P) = 11.5 Hz); elemental analysis calcd (%) for $C_{105}H_{105}Cl_4OsP_5$: C 61.70, H 5.18; found: C 61.90, H 5.23; ESI-MS (MeOH): m/z (%): 2042.8 (100) [M−Cl+MeOH]$^+$, 1139.3 (26) [OsCl(P(*m*-tolyl)$_3$)$_3$]$^+$.

Synthesis of 3: Complex **1** (150 mg, 0.143 mmol) and dppf (87 mg, 0.157 mmol) were dissolved in dichloromethane (3.0 mL) and the solution was heated at 40°C for 3 h. Ethylenediamine (9.6 μL, 0.143 mmol) was added at room temperature and the solution was heated at reflux for 1 h. The resulting solution was concentrated (1.5 mL) and the addition of diethyl ether (4 mL) afforded a yellow precipitate, which was washed with diethyl ether (2×3 mL) and dried under reduced pressure (108 mg, 86%). ^{1}H NMR (200.1 MHz, CD_2Cl_2, 20°C): δ = 7.79–7.28 (m, 20H; Ph), 4.58 (m, 4H; C_5H_4), 4.16 (t, J = 1.7 Hz, 4H; C_5H_4), 3.12 (brs, 4H; CH_2), 2.65 ppm (brs, 4H; NH_2); ^{13}C{^{1}H} NMR (50.3 MHz, CD_2Cl_2, 20°C): δ = 140.7 (dd, J(C,P) = 53.1, 8.6 Hz; *ipso* Ph), 134.5 (t, J(C,P) = 4.9 Hz; Ph), 129.0 (t, J(C,P) = 0.9 Hz; Ph), 127.4 (pseudo t, J(C,P) = 4.5 Hz; Ph), 89.9 (d, J(C,P) = 55.5 Hz; *ipso* C_5H_4), 76.3 (t, J(C,P) = 3.8 Hz; C_5H_4), 70.2 (t, J(C,P) = 2.9 Hz; C_5H_4), 44.0 ppm (s; CH_2); ^{31}P{^{1}H} NMR (81.0 MHz, CD_2Cl_2, 20°C): δ = −10.1 ppm (s); elemental analysis calcd (%) for $C_{36}H_{36}Cl_2FeN_2OsP_2$: C 49.38, H 4.14, N 3.20; found: C 48.86, H 4.10, N 3.18.

Synthesis of 4: Complex **4** was prepared by following the procedure used for **3**, with 1,3-propylenediamine (12 μL, 0.144 mmol) in place of ethylenediamine (111 mg, 87%). ^{1}H NMR (200.1 MHz, CD_2Cl_2, 20°C): δ = 7.75–7.28 (m, 20H; Ph), 4.57 (m, 4H; C_5H_4), 4.15 (t, J = 1.8 Hz, 4H; C_5H_4), 3.32 (brs, 4H; NCH_2), 2.81 (brs, 4H; NH_2), 1.68 ppm (brm, 2H; CH_2); ^{13}C{^{1}H} NMR (50.3 MHz, CD_2Cl_2, 20°C): δ = 139.0 (dd, J(C,P) = 51.8, 8.6 Hz; *ipso* Ph), 135.0 (t, J(C,P) = 4.8 Hz; Ph), 129.2 (t, J(C,P) = 0.9 Hz; Ph), 127.4 (pseudo t, J(C,P) = 4.4 Hz; Ph), 88.6 (dd, J(C,P) = 61.8, 5.5 Hz; *ipso* C_5H_4), 76.2 (t, J(C,P) = 3.8 Hz; C_5H_4), 70.4 (t, J(C,P) = 2.9 Hz; C_5H_4), 38.6 (s; NCH_2), 29.1 ppm (s; CH_2); ^{31}P{^{1}H} NMR (81.0 MHz, CD_2Cl_2, 20°C): δ = −10.5 ppm (s); elemental analysis calcd (%) for $C_{37}H_{38}Cl_2FeN_2OsP_2$: C 49.95, H 4.31, N 3.15; found: C 49.99, H 4.47, N 2.98.

Synthesis of 5: Sodium ethoxide (0.25 mmol), obtained by evaporation of a 0.25 M solution of NaOEt in ethanol (1 mL), was treated with 2,2,2-trifluoroethanol (42 μL, 0.576 mmol) and *trans*-[$OsCl_2$(dppf)(en)] (100 mg, 0.114 mmol) in toluene (4 mL). The suspension was stirred at 100°C for 1 h. The resulting dark orange solution was kept at −20°C for 4 h; this afforded precipitation of NaCl, which was then removed by filtration through Celite. The filtrate was concentrated (1 mL) and addition of pentane (4 mL) afforded a yellow-orange precipitate, which was filtered and dried under reduced pressure (91 mg, 80%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): δ = 8.26 (pseudo t, J(H,H) = 8.6 Hz, 3H; Ph), 7.71 (brs, 1H; Ph), 7.31–6.98 (m, 15H; Ph), 6.74 (s, 1H; Ph), 4.69 (s, 1H; C_5H_4), 4.57 (m, 1H; OCH_2), 4.35–4.25 (s, 2H; C_5H_4 and CH_2), 3.81–3.47 (s, 10H; C_5H_4, CH_2 and NH_2), 3.24 (t, J(H,H) = 10.1 Hz, 1H; CH_2), 2.93–1.51 ppm (brm, 5H; CH_2 and NH_2); ^{13}C{^{1}H} NMR (50.3 MHz, C_6D_6, 20°C): δ = 142.7 (d, J(C,P) = 38.7 Hz; *ipso* Ph), 141.8 (d, J(C,P) = 27.3 Hz; *ipso* Ph), 140.9 (d, J(C,P) = 21.8 Hz; *ipso* Ph), 139.6 (d, J(C,P) = 45.5 Hz; *ipso* Ph), 135.3–127.0 (m; aromatic carbon atoms and CF_3), 85.2 (d, J(C,P) = 53.5 Hz; *ipso* C_5H_4), 82.1 (d, J(C,P) = 52.9 Hz; *ipso* C_5H_4), 76.6 (m; C_5H_4), 75.2 (s; C_5H_4), 74.8 (d, J(C,P) = 8.2 Hz; C_5H_4), 73.8 (d, J(C,P) = 9.0 Hz; C_5H_4), 71.6 (d, J(C,P) = 5.5 Hz; C_5H_4), 71.1 (d, J(C,P) = 4.9 Hz; C_5H_4), 70.3 (q, J(C,F) = 29.5 Hz; CH_2CF_3), 69.8 (d, J(C,P) = 5.5 Hz; C_5H_4), 64.8 (q, J(C,F) = 29.3 Hz; CH_2CF_3), 50.9 (d, J(C,P) = 2.7 Hz; CH_2NH_2), 41.0 ppm (d, J(C,P) = 1.9 Hz; CH_2NH_2); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): δ = 1.6 (d, ^2J(P,P) = 19.8 Hz), −20.6 ppm (d, ^2J(P,P) = 19.8 Hz); ^{19}F{^{1}H} NMR (188.3 MHz, C_6D_6, 20°C): δ = −34.5 (s), −36.1 ppm (s); elemental analysis calcd (%) for $C_{40}H_{40}F_6FeN_2O_2OsP_2$: C 47.91, H 4.02, N 2.79; found: C 48.01, H 4.10, N 2.74.

Synthesis of 6: Complex **2** (100 mg, 0.049 mmol) and (*R*)-xylMeObiphep (75 mg, 0.108 mmol) were dissolved in toluene (1 mL) and the solution was heated at reflux temperature for 4 h. After addition of (*R*,*R*)-dpen (23 mg, 0.108 mmol), the solution was heated at reflux for 1 h. The solvent was evaporated, then heptane (5 mL) was added to the product, and was subsequently evaporated. Addition of heptane afforded a yellow precipitate, which was washed with cold heptane and dried under reduced pressure (62 mg, 54%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): δ = 8.04 (brt, J(H,H) = 8.1 Hz, 8H; aromatic protons), 7.43–6.68 (m, 16H; aromatic protons), 6.52 (s, 2H; aromatic protons), 6.01 (d, J(H,H) = 7.8 Hz, 2H; aromatic protons), 4.54 (brs, 2H; CH), 4.08 (brs, 4H; NH_2), 3.03 (s, 6H; OMe), 2.11 (s, 12H; CMe), 2.08 ppm (s, 12H; CMe); ^{13}C{^{1}H} NMR (50.3 MHz, C_6D_6, 20°C): 158.1 (pseudo t, J(C,P) = 5.3 Hz, *C*OMe), 143.3–109.9 (m; aromatic carbon atoms), 64.1 (s; NCH), 54.3 (s; OMe), 21.6 (s; C*Me*), 21.5 ppm (s; C*Me*); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): δ = −12.9 ppm (s); elemental analysis calcd (%) for $C_{60}H_{64}Cl_2N_2O_2OsP_2$: C 61.69, H 5.52, N 2.40; found: C 61.35, H 5.64, N 2.40.

Synthesis of 7: Complex **7** was prepared by following the procedure used for **6**, with (*R*,*R*)-dach (12 mg, 0.105 mmol) in place of (*R*,*R*)-dpen (69 mg, 66%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): δ = 8.01 (m, 6H; aromatic protons), 7.43–6.69 (m, 10H; aromatic protons), 5.98 (d, J(H,H) = 8.1 Hz, 2H; aromatic protons), 3.45 (m, 2H; NH*H*), 2.99 (s, 6H; OMe), 2.67 (m, 2H; NH*H*), 2.31 (m, 2H; C*H*N), 2.16 (s, 12H; CMe), 2.11 (s, 12H; CMe), 0.92 (m, 4H; CH_2), 0.49 ppm (m, 4H; CH_2); ^{13}C{^{1}H} NMR (50.3 MHz, C_6D_6, 20°C): 158.2 (m; *C*OMe), 136.8–109.9 (m; aromatic carbon atoms), 57.0 (s; NCH), 54.2 (s; OMe), 35.5 (s; CH_2), 24.8 (s; CH_2), 21.7 (s; C*Me*), 21.2 ppm (s; C*Me*); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): δ = −14.3 ppm (s); elemental analysis calcd (%) for $C_{52}H_{62}Cl_2N_2O_2OsP_2$: C 58.36, H 5.84, N 2.62; found: C 59.00, H 5.87, N 2.84.

Synthesis of 8: Complex **8** was prepared by following the procedure used for **6**, with (*R*)-xylbinap (79 mg, 0.108 mmol) in place of (*R*)-xylMeObiphep (56 mg, 47%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): δ = 8.86 (t, J(H,H) = 6.9 Hz, 2H; aromatic protons), 8.16 (d, J(H,H) = 9.2 Hz, 4H; aromatic protons), 7.94–6.48 (m, 26H; aromatic protons), 5.94 (s, 2H; aromatic protons), 4.53 (brm, 2H; NCH), 3.96 (brm, 2H; NH_2), 3.84 (brm, 2H; NH_2), 2.08 (s, 12H; CMe), 1.82 ppm (s, 12H; CMe); ^{13}C{^{1}H} NMR (50.3 MHz, C_6D_6, 20°C): δ = 135.2–123.9 (m; aromatic carbon atoms), 63.9 (s; NCH), 21.5 (s; C*Me*), 21.3 ppm (s; C*Me*); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): δ = −12.7 ppm (s); elemental analysis calcd (%)

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for $C_{66}H_{64}Cl_2N_2OsP_2$: C 65.61, H 5.34, N 2.32; found: C 65.47, H 5.12, N 2.25.

Synthesis of 9: Complex **9** was prepared by following the procedure used for **6**, with (*R*)-xylbinap (79 mg, 0.108 mmol) and (*R*,*R*)-dach (12 mg, 0.105 mmol) in place of (*R*)-xylMeObiphep and (*R*,*R*)-dpen, respectively (64 mg, 59%). ^{1}H NMR (200.1 MHz, C_6D_6, 20°C): $\delta = 8.85$ (t, J(H,H) = 7.9 Hz, 2H; aromatic protons), 8.11 (d, J(H,H) = 7.41 Hz, 4H; aromatic protons), 7.91–6.43 (m, 16H; aromatic protons), 5.95 (s, 2H; aromatic protons), 3.38 (m, 2H; NH*H*), 2.54 (m, 2H; NH*H*), 2.30 (m, 2H; CHN), 2.17 (s, 12H; Me), 1.81 (s, 12H; Me), 0.89 (m, 4H; CH_2), 0.46 ppm (m, 4H; CH_2); ^{13}C{^{1}H} NMR (50.3 MHz, C_6D_6, 20°C): $\delta = 135.2$–123.3 (m; aromatic carbon atoms), 57.0 (s; NCH), 35.4 (s; CH_2), 24.8 (s; CH_2), 21.7 (s; C*Me*), 21.2 ppm (s; C*Me*); ^{31}P{^{1}H} NMR (81.0 MHz, C_6D_6, 20°C): $\delta = -13.7$ ppm (s); elemental analysis calcd (%) for $C_{58}H_{62}Cl_2N_2OsP_2$: C 62.75, H 5.63, N 2.52; found: C 62.47, H 5.84, N 2.42.

Typical procedure for the catalytic hydrogenation of ketones: The osmium complex (1.7 μmol) was dissolved in ethanol (2 mL). The ketone (4.3 mmol), NaOEt (0.043 mmol from a 0.25 M standard solution), and the osmium solution (500 μL, 0.43 μmol) were added to the ethanol (final volume of 8.6 mL). The resulting solution was transferred into a thermostated reactor at 60°C, and dihydrogen was introduced at a pressure of 5 atm to reduce the ketone (S/Os = 10000, 1 mol% NaOEt, 0.5 M ketone). The samples were withdrawn from the reactor at regular time intervals (2, 5, 10, 20, 30 min, and longer reaction times), in accordance with the S/C ratio and the conversion of the ketone. The solution was quickly quenched by the addition of diethyl ether (1:1 v/v), filtered over a short silica pad, and analyzed by chiral GC. The TOF values were obtained by interpolating the data at 50% conversion.

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