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VIP

Enantioselective Reduction of Ketones and Imines Catalyzed by (CN-Box)Re^{V}–Oxo Complexes**

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Abstract: The development and application of chiral, non-racemic Re^{V}–oxo complexes to the enantioselective reduction of prochiral ketones is described. In addition to the enantioselective reduction of prochiral ketones, we report the application of these complexes to 1) a tandem Meyer–Schuster rearrangement/reduction to access enantioenriched allylic alcohols and 2) the enantioselective reduction of imines.

Keywords: enantioselective reduction · hydrosilylation · rearrangement · rhenium

Introduction

Transition metal–oxo complexes are amongst the most important catalysts for oxidative transformations.[1] In contrast, we reported the use of $[(PPh_3)_2Re(O)_2I]$ as a catalyst in the hydrosilylation of aldehydes and ketones[2]—an overall reduction of these functional groups. This methodology and those subsequently reported[3] have highlighted the air-, moisture-, and reagent tolerant nature of these oxidized transition-metal complexes. As a result, this class of complexes have become an attractive and practical alternative to many low oxidation state transition-metal complexes that are more commonly employed as catalysts in reduction reactions.

A number of rhenium[4] and molybdenum[5] complexes have been shown to be efficient catalysts for hydrosilylation reactions. Despite these recent reports, enantioselective metal–oxo catalyzed reductions are still rare.[6] Having previously developed a catalytic system for the hydrosilylation of carbonyls using a rhenium(V)–dioxo complex to yield chiral, racemic silyl ethers, we focused our efforts on expanding this reactivity to enantioselective reductions.

The enantioselective reduction of prochiral ketones and imines by hydrogenation, hydroboration or hydrosilylation has been extensively studied.[7] A number of different transition metals, including Zn,[8] Fe,[9] Ru,[10] Ir,[11] Ti,[12] Rh,[13] and Cu,[14] have successfully been employed in the enantioselective hydrosilylation of prochiral ketones. A similar array of transition-metal complexes have been employed as catalysts for the enantioselective hydrosilylation of imines.[15] Common to the majority of these catalysts is that they are derived from low-valent transition metals. In this report, we describe the development and application of chiral, non-racemic Re^{V}–oxo complexes to the enantioselective reduction of prochiral ketones and imines. This new class of hydrosilylation catalyst offers opportunities for the creation of novel transformations that take advantage of the unique reactivity of the metal–oxo functionality.[16] To this end, we also report the application of metal–oxo complexes to a tandem Meyer–Schuster rearrangement/reduction to access enantioenriched allylic alcohol.

Results and Discussion

Catalyst design: Evaluation of the mechanistic of the hydrosilylation of carbonyl compounds catalyzed by $[(PPh_3)_2(O)_2ReI]$ revealed that an open coordination site must be available to allow for the complexation of the carbonyl.[17] Consistent with this hypothesis is the failure of Re–oxo complexes with bidentate phosphine ligands to affect the transformation. These neutral, bidentate phosphine ligands, which occupy all available dative (L-type) coordination sites on the metal center, are not conducive to

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[**] CN-Box = Cyanobis(oxazoline).

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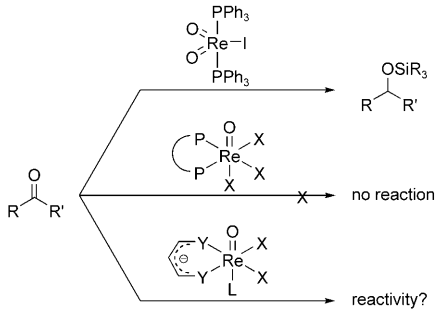
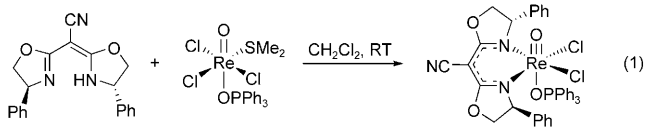
the necessary ligand dissociation. This restriction was considered in the design of a chiral Re^{V}–oxo complex for the enantioselective hydrosilylation of ketones. As a result, chiral monoanionic ligands were hypothesized to be suitable ligands for the asymmetric Re^{V}–oxo catalyzed hydrosilylation (Scheme 1).



Scheme 1. Catalyst design.

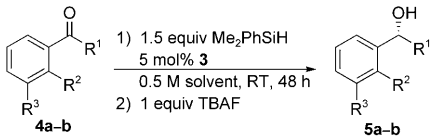
C_2-Symmetric bis(oxazoline) ligands are a privileged class of ligands that have been utilized in numerous transition-metal-catalyzed enantioselective transformations resulting in high levels of selectivity.[18] However, these ligands are most often coordinated to the metal centers as bidentate, neutral ligands.[19] We envisioned that the addition of an electron-withdrawing group on the bridging carbon of the bis(oxazoline) would increase the acidity of the ligand allowing for facile deprotonation and complexation as the corresponding anion ligand. Our investigations began with the commercially available cyanobis(oxazoline) ligand (4*S*)-(+)-phenyl-α-[(4*S*)-phenyloxazolidin-2-ylidene]-2-oxazoline-2-acetonitrile (**1**). Stirring **1** with $[Re(O)Cl_3(OPPh_3)(SMe_2)]$ (**2**) in CH_2Cl_2 at room temperature yielded (CN-box)Re^{V}–oxo complex **3** as a emerald green solid [Eq. (1)].



(1)

Initial optimization: The ability of **3** to catalyze the asymmetric hydrosilylation of ketones was examined. At room temperature, 5-methoxytetralone (**4**) was reduced with 5 mol% **3** and 1.5 equivalents of Me_2PhSiH in 0.5 M CH_2Cl_2. After TBAF deprotection of the silyl ether, the corresponding alcohol was isolated in 90% yield with 88% enantiomeric excess[20] (Table 1, entry 1).[21] In aromatic solvents, the reaction proved sluggish with only 36% yield of **5a** after 48 h (entry 2). Good reactivity was observed in ethyl acetate; however, the excellent selectivity observed with the reduction of **4a** (93% *ee* entry 3) did not extend to acyclic ketone **4b** (40% *ee*, entry 6). A higher level of enantiomeric enrichment was obtained when acetophenone was reduced in CH_2Cl_2 (57% yield and 70% *ee*, entry 5). The neat reduction of **4b** yielded the corresponding alcohol in excellent yield, but with low enantioselectivity (22% *ee*, entry 8). With improved yield compared to dichloromethane, 1,4-dioxane was identified as the optimal solvent for the reduction of both substrates furnishing the resulting alcohols in high enantiomeric excess (entries 4 and 7).

Table 1. Solvent Studies of ketone reductions.



4a–b 5a–b

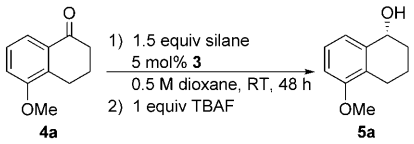
Entry	R^1	R^2	R^3	Substrate	Solvent	Yield [%]	Product	*ee* [%]
1	-$(CH_2)_3$-		OMe	**4a**	CH_2Cl_2	90	**5a**	88
2	-$(CH_2)_3$-		OMe	**4a**	benzene	36	**5a**	86
3	-$(CH_2)_3$-		OMe	**4a**	EtOAc	71	**5a**	93
4	-$(CH_2)_3$-		OMe	**4a**	dioxane	95	**5a**	89
5	Me	H	H	**4b**	CH_2Cl_2	57	**5b**	70
6	Me	H	H	**4b**	EtOAc	79	**5b**	40
7	Me	H	H	**4b**	dioxane	90	**5b**	77
8	Me	H	H	**4b**	neat	97	**5b**	22

A number of mono- and polyhydridic silanes were examined in the enantioselective hydrosilylation of 5-methoxytetralone (Table 2). High enantiomeric excess was also attained with Et_3SiH (60% yield and 85% *ee*, entry 2); however, a significant rate reduction was observed relative to the reaction with Me_2PhSiH (95% yield and 89% *ee*, entry 1). Attenuation of reactivity was more pronounced with Ph_2MeSiH (23% yield and 82% *ee*, entry 3). The use of dihydride Ph_2SiH_2 led to formation of **5a** albeit in lower yield and enantiomeric enrichment (43% yield and 72% *ee*, entry 4). None of the desired product was observed when bulky silanes (*i*Pr_3SiH and *t*$BuMe_2SiH$), PMHS or the polyhydridic phenyl silane were incorporated as reducing agents. Me_2PhSiH was found to be the optimal stoichiometric reducing agent and, based on these results, was utilized during further reaction optimization.

The effect of temperature was probed in the reduction of **4a** with Me_2PhSiH catalyzed by **3**. At 0 °C, no catalytic activity was observed (Table 2, entry 7). An erosion of enantioselectivity as well as reactivity was observed when the reaction was heated to 60 °C (entry 8). At this elevated temperature, a substantial amount of disilane and disiloxane through silane decomposition was observed.[22]

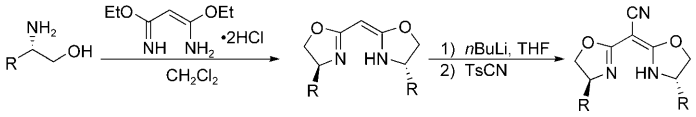
Ligand optimization: In an effort to increase the enantioselectivity of the reaction, the effect of changes to steric and electronic composition of the cyanobis(oxazoline) ligand were investigated using the optimized reaction conditions (Me_2PhSiH and **3** in dioxane at room temperature). To do so, a number of differentially substituted bis(oxazoline) compounds were synthesized. The synthesis of these com-

Table 2. Effect of silane on ketone reductions.



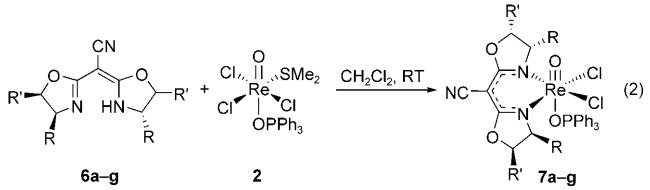
Entry	Silane	*T*	Yield [%]	*ee* [%]
1	Me_2PhSiH	RT	95	89
2	Et_3SiH	RT	60	85
3	Ph_2MeSiH	RT	23	82
4	Ph_2SiH_2	RT	43	72
5	iPr_3SiH	RT	nr	n/a
6	$tBuMe_2SiH$	RT	nr	n/a
7	Me_2PhSiH	0 °C	nr	n/a
8	Me_2PhSiH	60 °C	71	76

pounds was accomplished in two steps from the corresponding chiral, non-racemic amino alcohol (Scheme 2). The amino alcohols were 1) obtained through the reduction of the corresponding amino acid or 2) synthesized by the methods developed by Sharpless[23] or Ellman.[24] The amino alcohols were condensed with diethyl malonimidate dihydrochloride to produce the corresponding bis(oxazoline). Following protocol developed by Corey and Wang, the bis(oxazoline) was deprotonated with *n*BuLi and treated with *p*-toluenesulfonyl cyanide to yield the aryl and alkyl substituted cyanonbis(oxazolines) (Scheme 2).[25]



Scheme 2. Cyanobis(oxazoline) synthesis.

Complexation of the cyanobis(oxazolines) **6a–g** (Figure 1) was accomplished through dropwise addition[26] of the ligand as a concentrated solution in CH_2Cl_2 to a dilute suspension of **2** in CH_2Cl_2 [Eq. (2)]. The reaction underwent a gradual color change to become a clear, emerald green solution. Upon trituration with Et_2O or hexanes, the corresponding CN-box Re^V–oxo complexes **7a–g** were isolated as green solids. While formation of complexes **7a–g** proceeded readily, complexation of cyanobis(oxazolines) **6h–k** to the metal center was unsuccessful. Under the above described conditions, these complexation reactions resulted in the formation of unidentifiable black solids that were isolated and found to be catalytically inactive.[27]



(2)

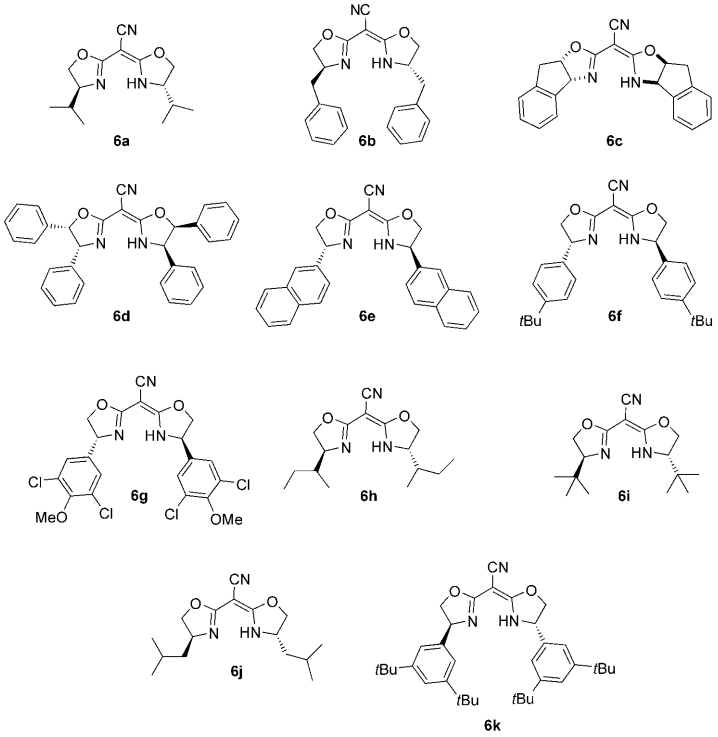
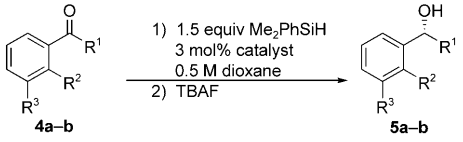


Figure 1. Cyanobis(oxazoline) ligands.

Cyanobis(oxazoline) ligands of varying electronic and steric composition (**6a–g**) were readily synthesized from the corresponding amino alcohols and complexed to the metal center, as described above, to yield (CN-box) Re^V–oxo complexes (**7a–g**). These complexes were examined in the reduction of 5-methoxytetralone and acetophenone. Moderate enantiomeric excesses were obtained in the hydrosilylation reactions catalyzed by rhenium complexes incorporating cyanobis(oxazoline) ligands with alkyl (53% *ee*, Table 3, entry 1), benzyl (53% *ee*, entry 2), and indenyl (30% *ee*, entry 3) substitution. Tetraphenyl substituted ligand **6d** led to slightly improved levels of enantioenrichment of **5a**

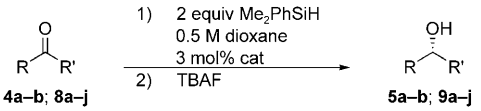
Table 3. Ligand effects on ketone reductions.

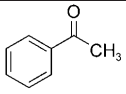
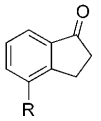
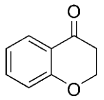
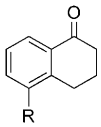
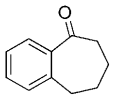
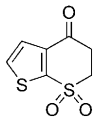
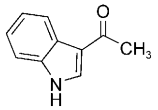
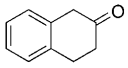
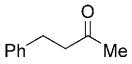


Entry	R^1	R^2	R^3	Ligand	Catalyst	Yield [%]	Product	*ee* [%]
1	$-(CH_2)_3-$		OMe	**6a**	**7a**	23	**5a**	53
2	$-(CH_2)_3-$		OMe	**6b**	**7b**	88	**5a**	53
3	$-(CH_2)_3-$		OMe	**6c**	**7c**	71	**5a**	30
4	$-(CH_2)_3-$		OMe	**6d**	**7d**	26	**5a**	67
5	$-(CH_2)_3-$		OMe	**6e**	**7e**	83	**5a**	96
6	$-(CH_2)_3-$		OMe	**1**	**3**	95	**5a**	89
7	$-(CH_2)_3-$		OMe	**6f**	**7f**	97	**5a**	94
8	Me	H	H	**6d**	**7d**	35	**5b**	73
9	Me	H	H	**6e**	**7e**	68	**5b**	82
10	Me	H	H	**1**	**3**	90	**5b**	77
11	Me	H	H	**6f**	**7f**	87	**5b**	86
12	Me	H	H	**6g**	**7g**	60	**5b**	71

(67% *ee*, entry 3) and good selectivity in the reduction of **4b** (73%, entry 8). A substantial increase in selectivity was achieved with 2-napthyl cyanobis(oxazoline) Re-oxo complexes **7e** (82% and 96% *ee*, entries 5 and 9). However, markedly improved reactivity was observed with the phenyl and 4-*tert*-butylphenyl catalysts with consistently high level of enantioselectivity (77–94% *ee*, entries 6, 7, 10 and 11).

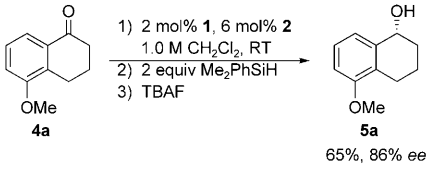
Table 4. Asymmetric reduction of aryl ketones.



Entry	Ketone	Substrate	Catalyst	Yield [%]	Product	*ee* [%]
1		**4b**	(*S*)-**3**	90	**5b**	78 (*R*)
			(*R*)-**7f**	92		86 (*S*)
2		**8a**: R = H	(*S*)-**3**	59	**9a**	88 (*R*)
			(*R*)-**7f**	89		86 (*S*)
3		**8b**: R = OTs	(*S*)-**3**	70	**9b**	83 (*R*)
4		**8c**	(*S*)-**3**	69	**9c**	87 (*R*)
			(*R*)-**7f**	61		86 (*S*)
5		**4a**: R = OMe	(*S*)-**3**	71	**5a**	93 (*R*)
			(*R*)-**7f**	97		94 (*S*)
6		**8d**: R = H	(*S*)-**3**	84	**9d**	89 (*R*)
7		**8e**	(*S*)-**3**	70	**9e**	75 (*R*)
			(*R*)-**7f**	82		88 (*S*)
8		**8f**	(*S*)-**3**	83	**9f**	78 (*R*)
			(*R*)-**7f**	96		81 (*S*)
9		**8g**	(*S*)-**3**	51	**9g**	93 (*R*)
			(*R*)-**7f**	64		82 (*S*)
10		**8h**	(*R*)-**7f**	80	**9h**	84 (*S*)
11		**8i**	(*S*)-**3**	94	**9i**	15 (*R*)
12		**8j**	(*R*)-**7f**	67	**9j**	6 (*S*)

Scope of enantioselective reduction of ketones: The scope of the hydrosilylation was probed using two equivalents of Me_2PhSiH, in dioxane, and 3 mol% of catalyst **3** or **7f**. Good to excellent enantioselectivities were obtained in the reduction of aromatic ketones. Acetophenone was reduced with good selectivity (Table 4, entry 1). Good to excellent enantiomeric excess was obtained in the reduction of five-, six-, and seven-membered cyclic ketones (83–94% *ee*) (entries 2–7). Heteroaromatic ketones were also well tolerated under the reaction conditions; for example, alcohol **9g** was obtained in 93% *ee* (entry 9). In most cases, the 4-*tert*-butylphenyl catalyst **7f** produced greater enantioselectivities than phenyl catalyst **3**, although, in some cases, the observed enhancement was not dramatic and the effect can even be reversed (entry 9). The reduction of non-aryl ketones proceeded in good to excellent yield, however, with modest enantioenrichment of the resultant alcohols (6–15% *ee*, entries 11 and 12).

A convenient, alternate protocol for the hydrosilylation entails the in situ generation of the chiral catalyst. This was achieved by pre-stirring 2 mol% of **2** and 6 mol% of the desired cyanobis(oxazoline) ligand in CH_2Cl_2 for two hours prior to addition of the ketone and silane. Under these conditions, **4a** was hydrosilylated and deprotected yielding the corresponding alcohol **5a** with identical enantioselectivity to that observed with the pre-formed catalyst **3** [Eq. (3)].

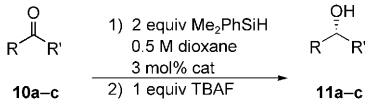


(3)

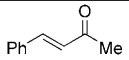
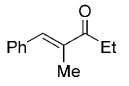
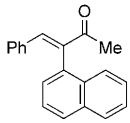
The Re^V–oxo catalyzed enantioselective hydrosilylation of ketones was extended to the synthesis of chiral allylic alcohols. Modest enantioselectivities, 45–55% *ee*, were observed in the hydrosilylation of α,β-unsaturated conjugated ketone **10a** (Table 5, entry 1). Higher enantiomeric excesses, 55–63% *ee*, were obtained with α-substituted enone **10b** (entry 2). It should be noted that 1,4-reduction of the enones was not observed under these conditions.

Tandem 3,3-rearrangement–asymmetric reduction: In the course of examining Re^V–oxo complexes as catalysts in the

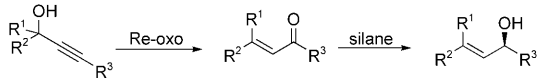
Table 5. Asymmetric reduction of enones.



10a–c 11a–c

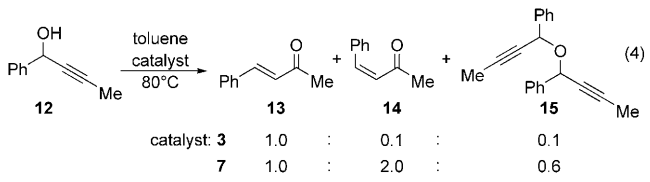
Entry	Ketone	Substrate	Catalyst	Yield [%]	Product	*ee* [%]
1		**10a**	(*R*)-**7f**	90	**11a**	55 (*S*)
			(*S*)-**3**	87		63 (*R*)
2		**10b**	(*R*)-**7f**	47	**11b**	55 (*S*)
3		**10c**	(*R*)-**7f**	71	**11c**	95 (*S*)

etherification of propargyl alcohols,[16e] rearrangement of the alcohol to enone, the Meyer–Schuster rearrangement, was observed to be the prevailing reactivity in non-polar and aromatic solvents.[28] It was envisioned that a Re^{V}–oxo catalyzed Meyer–Schuster rearrangement could be coupled with the asymmetric reductions in a one-pot synthesis of chiral allylic alcohols from racemic propargyl alcohols (Scheme 3).



Scheme 3. Tandem Meyer–Schuster rearrangement hydrosilylation.

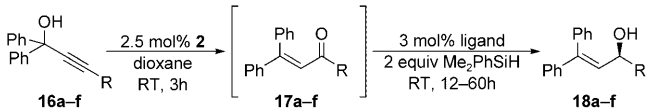
Chiral complexes **3** and **7f** were tested for there ability to facilitate the Meyer–Schuster rearrangement. Propargyl alcohol **12** was treated with CN-box Re complexes **3** and **7f** in toluene at 80 °C.[29] The reaction resulted in the formation of *cis* and *trans* isomers of the desired enone (**13** and **14**) as well as a dimerized by-product (**15**) [Eq. (4)].



(4)

Having observed that the chiral catalyst could be generated in situ (see above), we next examined Re–oxo complex **2**, the chiral catalyst precursor, as a catalyst for the Meyer–Schuster reaction.[30] Gratifyingly, **2** facilitated the rearrangement of the **16a** to the corresponding enone (**17a**). Without isolation of the enone, ligand **1** was added to the reaction solution followed by 2 equivalents of Me_2PhSiH. Allyl alcohol **18a** was isolated in 43% yield and 49% *ee* (Table 6, entry 1). After further optimization, it was found that in situ generation of chiral catalyst **7g** provided allyl alcohols **18a–f** in the highest levels of enantiomeric excess from the one-pot Meyer–Schuster rearrangement-reducion of propargyl alcohols **16b–f**.

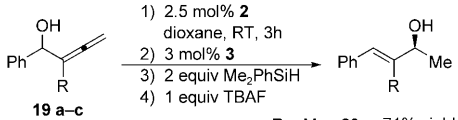
Table 6. Tandem Meyer–Schuster rearrangement–hydrosilylation.



16a–f 17a–f 18a–f

Entry	R	Substrate	Ligand	Yield [%]	Product [%]	*ee* [%]
1	Ph	**16a**	**1**	43	**18a**	49
2	Ph	**16a**	**6g**	38	**18a**	82
3	2-Nap	**16b**	**6g**	42	**18b**	92
4	2-Cl-Ph	**16c**	**6g**	85	**18c**	64
5	4-Cl-Ph	**16d**	**6g**	25	**18d**	50
6	*t*Bu	**16e**	**6g**	42	**18e**	63
7	*n*Bu	**16f**	**6g**	73	**18f**	65

To access α, β-unsaturated enones, the rearrangement of allenyl alcohols was examined. Allenyl alcohols **19a–c** were subjected to the tandem reaction conditions [Eq. (5)]. Using commercially available ligand **1**, the one-pot reactions were performed using Me_2PhSiH as the stoichiometric reducing agents. The allylic alcohols **20a–c** were obtained in good yields (63–71%) and moderate to good enantiomeric excess (56–77%). As shown above, the ability to generate the chiral catalyst in situ lends provides a highly tunable system for the enantioselective synthesis of allylic alcohols from racemic starting materials.

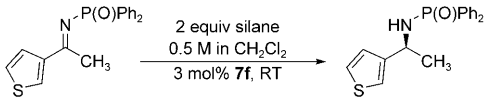


(5)

R = Me **20a** 71% yield, 65% *ee*
Ph **20b** 68% yield, 56% *ee*
*n*Bu **20c** 63% yield, 77% *ee*

Asymmetric reduction of imines: With a system in hand for the asymmetric reduction of ketones, we next turned our attention toward the reduction of imines.[6] While efficient systems have been developed, they generally utilize metals in low oxidation states. Representative systems include those catalyzed by low oxidation state late metal complexes[11,15] and titanocene complexes.[15f,31] In order to demonstrate the utility of this air and moisture tolerant catalyst for the synthesis of chiral amines via reduction of the corresponding imine, an appropriate protecting group needed to be selected. Phosphinyl imines have been shown to be stable under ambient conditions and proved suitable for the reaction conditions. The phosphinyl group can easily be cleaved under acidic conditions to yield the chiral amine.[32]

The reduction of methyl thiophene imine **21** in CH_2Cl_2 with Me_2PhSiH proceeded with excellent yield and enantioselectivity at room temperature [Eq. (6)].[33] The reaction proceeded with the same selectivity in a range of solvents including THF, EtOAc, and toluene. The substitution of Me_2PhSiH with Ph_2MeSiH did not alter the enantioselectivi-

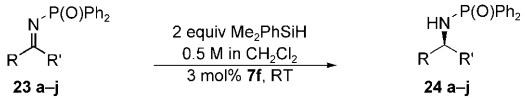


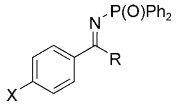
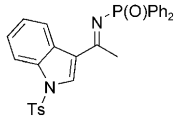
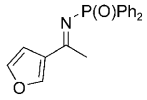
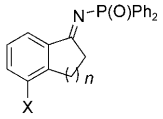
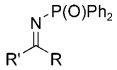
(6)

ty; however, Me_2PhSiH generally resulted in higher yield of the corresponding phosphinyl amine. No reactivity was observed with $Me_2tBuSiH$ or iPr_3SiH. Mild heating of the reaction showed no measurable decrease in enantioselectivity but did result in slightly higher yields (Me_2PhSiH at 40 °C: 81 % yield, 98 % *ee*).

The reaction successfully led to the reduction of aryl phosphinyl imines. Acyclic ketimines (Table 7, entries 1–7) reduced good yield with excellent enantioselectivity. Similar selectivity was observed with cyclic ketimines (entries 8–10). Notably, imine **23j** exists primarily as the enamine and the reduction proceeded in 71 % yield with 96 % *ee* without any additional reaction time or heating. Additionally, heteraromatic compounds performed well under the reaction conditions and were reduced in very good yield with excellent selectivity (entries 6 and 7). Interestingly, *N*-methylpyrrole methyl ketimine was unreactive when subject to the reduction conditions. Aliphatic ketimines did not display the same selectivity as the aryl imines. Cyclohexyl methyl imine **23k** and isopropyl ethyl imine **23l** were reduced with 32 and 17 % *ee*, respectively (Table 7, entries 11 and 12). The bulky *tert*-butyl methyl imine was unreactive (entry 13).

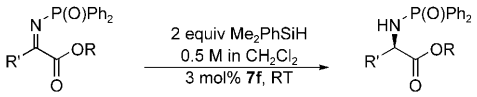
Table 7. Reduction of aryl and alkyl phosphinyl imines.

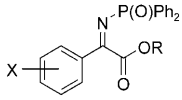
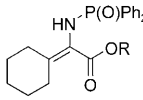
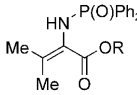
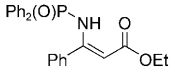


Entry	Imine	Substrate			Yield [%]	Product	*ee* [%]
1		**23a**	X = H	R = Me	51	**24a**	> 99
2		**23b**	OMe	Me	61	**24b**	98
3		**23c**	CF_3	Me	78	**24c**	98
4		**23d**	I	Me	71	**24d**	99
5		**23e**	H	Bu	68	**24e**	> 99
6		**23f**			81	**24f**	> 99
7		**23g**			76	**24g**	99
8		**23h**	*n* = 1	X = H	89	**24h**	95
9		**23i**	2	OMe	69	**24i**	95
10		**23j**	3	H	71	**24j**	96
11		**23k**	R = Me	R′ = Cy	69	**24k**	32
12		**23l**	Et	*i*Pr	73	**24l**	17
13		**23m**	Me	*t*Bu	nr	**24m**	n/a

The synthesis of phenyl glycine derivatives was achieved through the reduction of α-imino esters by **7f**. The reduction of these imines proceeded in moderate to good yield with excellent enantioselectivity (Table 8, entries 1–3). Non-aromatic α-imino esters bearing α-protons existed as the α-amino acrylate and were unreactive (entries 4 and 5). Similarly, β-imino ester **25f** did not yield the desired amine **26f** (entry 6).

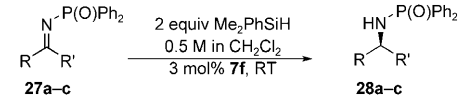
Table 8. Reduction of α-imino esters.

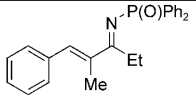
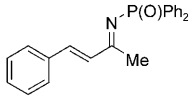
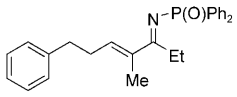


Entry	Imine	Substrate			Yield [%]	Product	*ee* [%]
1		**25a**	X = Ph	R = Et	83	**26a**	> 99
2		**25b**	4-OMePh	Me	47	**26b**	95
3		**25c**	2-MePh	Me	69	**26c**	99
4		**25d**			nr	**26d**	n/a
5		**25e**			nr	**26e**	n/a
6		**25f**			nr	**26f**	n/a

Synthesis of chiral allylic amines was achieved through chemo- and enantioselective reduction of the corresponding imine. Conjugated aromatic imines were reduced in good yield with excellent selectivity (Table 9, entries 1–2). Unconjugated vinyl imines were reduced with good enantioselectivity in moderate yield. For this substrate, extension of the reaction time led to reduction of the olefin to yield the alkyl amine.

Table 9. Synthesis of allylic amines.



Entry	Imine	Substrate	Yield [%]	Product	*ee* [%]
1		**27a**	71	**28a**	> 99
2		**27b**	62	**28b**	75
3		**27c**	48	**28c**	83

Conclusion

In summary, a series of chiral, non-racemic (CN-box)Re^{V}–oxo complexes have been prepared and employed as versatile and efficient catalysts for the hydrosilylation of ketones and imines. These reductions proceed under an ambient air atmosphere without the need for exclusion of advantageous water. The mild reaction is highly functional group tolerant and has been extended to include the formation phenyl glycine derivative, allylic alcohol and allylic amines. The (CN-box)Re^{V}–oxo complexes can be pre-formed and isolated as benchtop stable solids or generated in situ from a single precursor. The utility of in situ generation of the chiral catalyst and the unique reactivity of metal–oxo complexes was highlighted in tandem Meyer–Schuster hydrosilylation reactions providing access to enantioenriched allylic alcohols from racemic propargyl and allenyl alcohols.

Experimental Section

General procedure for synthesis of Re^{V}–oxo complexes 3 and 7a–g: Re^{V}–dimethylsulfide (DMS) complex **2** (1 equiv) was added to a round-bottom flask charged with a magnetic stir bar. CH_2Cl_2 was added to a reaction flask to a concentration of 5 mM. In a scintillation vial, 1.2 equiv of cyanobis(oxazoline) ligand **6f** was diluted in CH_2Cl_2 (5 mM). Ligand solution was added slowly to Re suspension. Reaction solution quickly changes from light green to very dark green. Reaction stirred at RT for ~5 h at which time the solution is a bright emerald green. (Note: This reaction time can be reduced to 30 min by adding one drop of DMSO; however, isolation of the product becomes more difficult.) Solvent was evaporated and the dark green film was diluted with a small amount of CH_2Cl_2 then triturated with Et_2O. Filtration with a Buchner funnel yields Re complex **7f**, a bright green solid. The trituration was repeated 4 times or until no significant material was isolated. The resultant solid was dried in vacuo.

General procedure for asymmetric reduction of ketones with isolated asymmetric catalyst: To a 7.4 mL Fischer vial charged with a solution of ketone (50 mg, 1 equiv) in dioxane (1 M), was added silane (2 equiv) followed by catalyst **3** or **7f** (3 mol%). The reaction was monitored by TLC. Upon completion or 72 h, the reaction was quenched with 1 equiv of tetrabutylammonium fluoride (1.0 M in THF). The reaction mixture was loaded directly on to a silica gel column and chromatographed with the 10–20% ethyl acetate in hexanes (**9g**: 50% ethyl acetate in hexanes) to give the alcohol. NMR and HPLC analyses of the compounds listed below were consistent with previously reported values.[34] Absolute configuration of **5b**, **9a**, and **9d** were assigned by comparison of the optical rotation and HPLC retention times to literature values.[21]

General procedure for tandem Meyer–Schuster asymmetric reduction reaction: Re–DMS complex **2** (2.5 mol%) was added to scintillation vial charged with 1 equiv of propargyl alcohol in 0.5 M dioxane. The reaction solution is stirred at room temperature for 3 h. Upon complexation, 3 mol% of cyanobis(oxazoline) ligand was added and the reaction solution was stirred at room temperature for 5 h resulting in a clear solution then 2 equivalents of Me_2PhSiH were added. The reaction solution was stirred at room temperature and monitored by TLC. After 60 h or reaction completion, the silyl ether was deprotected with 1 equiv of tetrabutylammonium fluoride (1.0 M in THF). Direct purification reaction mixture by column chromatography on a silica gel column with the 10–20% ethyl acetate in hexanes gave the allylic alcohol. The enantiomeric excess was determined by chiral HPLC.

General procedure for asymmetric reduction of phosphinyl imines with asymmetric catalyst: To a 7.4 mL Fischer vial charged with a solution of imine (50 mg, 1 equiv) in CH_2Cl_2 (1 M), was added Me_2PhSiH (2 equiv) followed by catalyst **7f** (3 mol%). The reaction was monitored by TLC. Upon completion or 72 h, the reaction was chromatographed. The reaction mixture was loaded directly on to a silica gel column and chromatographed with the 10–50% acetone in CH_2Cl_2 to give the amine. Absolute configurations were assigned by comparison of the HPLC retention times to literature values.[33]

Acknowledgements

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