Amidato complexes of ruthenium, rhodium and iridium from concise N-H bond activation: exploration in catalysis

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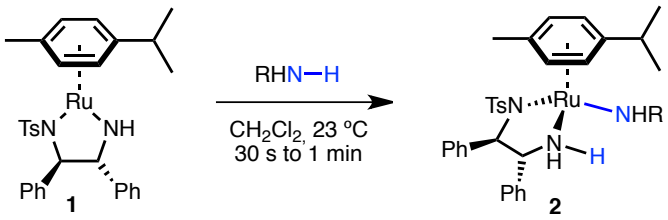
ABSTRACT

Acceptor-substituted N-H groups as found in carbamides and sulfonamides are readily activated through suitable unsaturated metal complexes applying the concept of metal-ligand bifunctionality. This process constitutes the basis for an enantioselective intramolecular addition of N-H groups onto activated alkenes. The resulting compounds can also be employed as catalyst precursors for transferhydrogenation.

1 Introduction

The transition metal catalyzed hydroamination of alkenes represents a versatile approach toward the synthesis of alkyl-nitrogen bonds.[1] In particular, the intramolecular version[2] of this reaction provides an efficient entry towards aminated cycloalkanes and derivatives thereof, which are of interest as building blocks in the synthesis of molecules with pharmaceutical, medicinal or biological interest.[3]
These reactions are also considered to be of perfect atom economic nature,[4] as the addition of an N-H bond across an alkene essentially does not generate any by-products. In the best of all cases, enantioselective catalytic hydroamination reactions do only require the presence of the corresponding catalyst in the presence of otherwise neutral conditions.[4]
Within the many concepts to activate N-H bonds in order to generate the required reactivity for addition to an alkene, unsaturated transition metal complexes have been demonstrated to be competent centers to carry out the activation of N-H bonds.[5] As a result, such concepts are widely sought after and have been explored to an impressive extent using engineered metal ligand frameworks[6] and related transition metal reactivity.[7]

One of the best activation-transfer systems known in literature is the seminal transfer-hydrogenation system of Noyori.[8] The employed ruthenium catalyst simultaneously transfers a proton and a hydride anion of secondary alcohols by formation of a hydridic H-metal bond and a protic N-H bond at the ligand. The formed species is then capable to enantioselectively and *reversibly* transfer this activated "hydrogen" to prochiral ketones, achieving high ee and high turnover numbers at room temperature. Some time ago, we reported on the application of this system for a selective metal-ligand bifunctional N-H bond activation making use of the parent coordinatively unsaturated ruthenium complexes **1**.[9] The ruthenium center in **1** results to be Lewis-acidic enough to accept the nucleophilic nitrogen while the activated nitrogen of the ligand-backbone displays sufficient basicity to deprotonate the N-H group of the substrate within the metal ligand coordination sphere. The corresponding chiral-at-ruthenium complexes **2** were formed as single diastereoisomers in good isolated yields and within comparably short reaction times (Scheme 1).



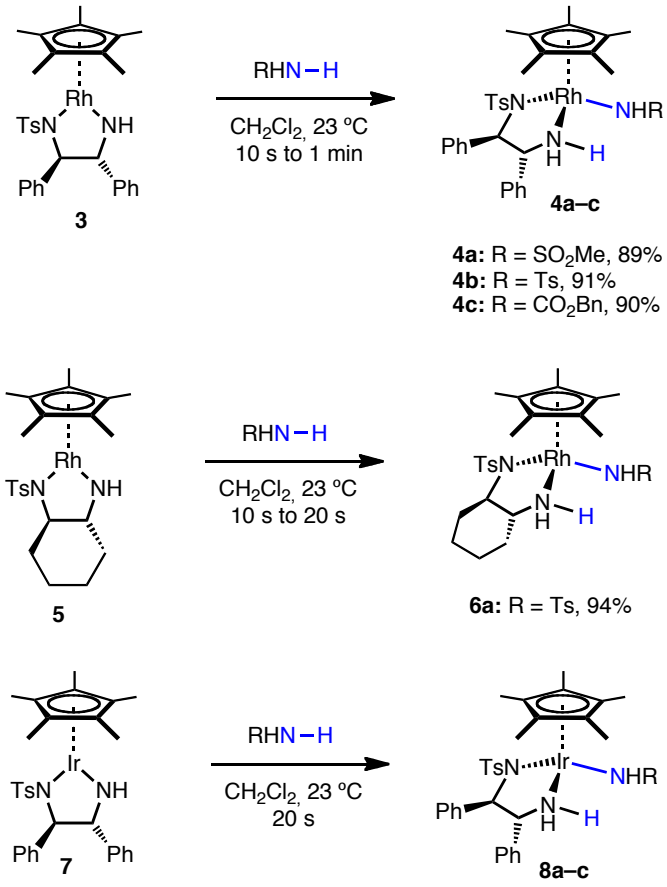
Scheme 1. Application of the metal ligand bifunctionality towards N-H activation.

Complexes of type **2** were then shown to be involved as suitable catalyst states in new intramolecular C-N bond forming reactions.[9] We here give a full account on the synthesis of additional amidato metal complexes based on central rhodium and iridium atoms and their exploration in aza-michael addition reactions. In addition, we discuss the application of amidato complexes of ruthenium, rhodium and iridium as catalyst precursors in the Noyori transferhydrogenation.

2. Results and Discussion

A logical extension of the use of pseudo-tetrahedral ruthenium complexes consists in investigating the behavior of structurally related rhodium and iridium complexes. These complexes could indeed be accessed following a general two-step approach that consists of a preformation of the coordinatively unsaturated complexes **3**, **5** and **7** containing rhodium and iridium as metal centers and different monotosylated diamine ligands in order to demonstrate the structural diversification that can be employed for ligand-metal bifunctional N-H activation.[10] In contrast to the facile synthesis of the parent ruthenium complexes **1**,[9] rhodium complexes **3** (green color) and **5** (yellow-red color) are less stable both thermically and in the presence of air, respectively, and should be submitted to reaction within short periods after their synthesis. Unlike the rhodium precursors, iridium complex **7** (deep purple color) can be handled with less care. All these activated complexes are formally of unsaturated coordination and undergo rapid and irreversible N-H bond activation in solution, which is complete within seconds. No change in reactivity is observed and the complexes **4a-c**, **6a** and **8a-c** are isolated by simple evaporation of solvent. Although in isolated form these products are stable at room temperature over at least one week, the rhodium derivatives **4a-c** and **6a** are unstable in solution and sensitive to column chromatography and need to be purified by crystallization if impurities had formed over time.

Scheme 2. Application of the metal-ligand bifunctional N-H activation in the synthesis of novel amidato complexes of rhodium and iridium.

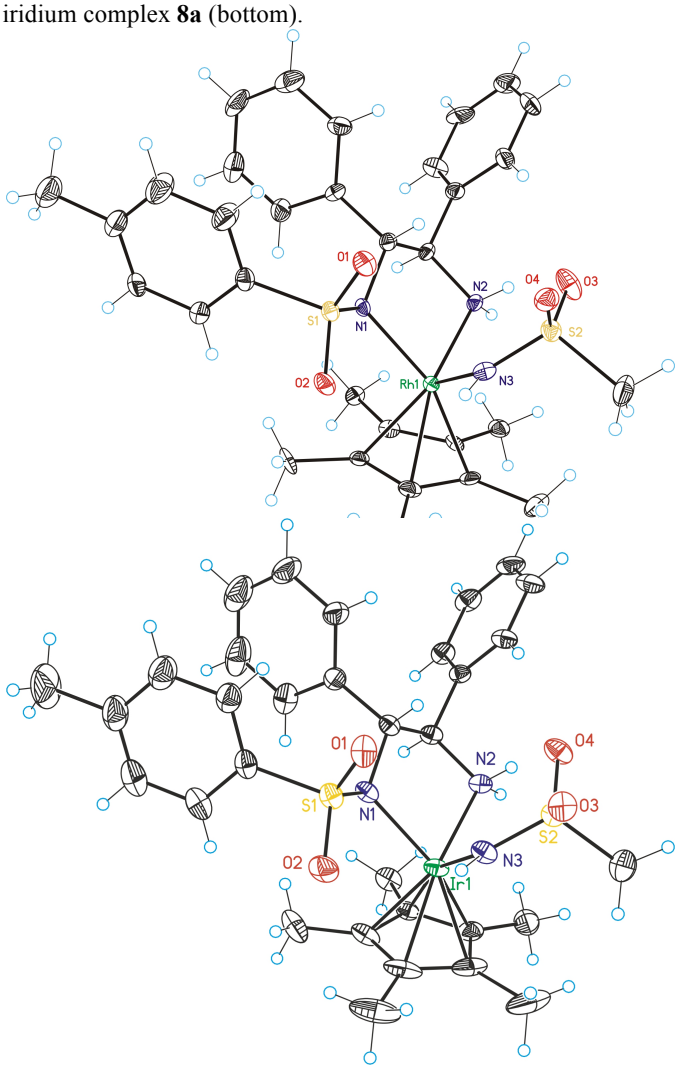


It is noteworthy that all rhodium and iridium complexes are formed as single diastereoisomers. As the step of N-H activation within the metal ligand bifunctional motif results in the formation

of additional stereogenicity at the metal center, the present approach provides a unique entry into chiral-at-metal complexes with defined absolute chirality.

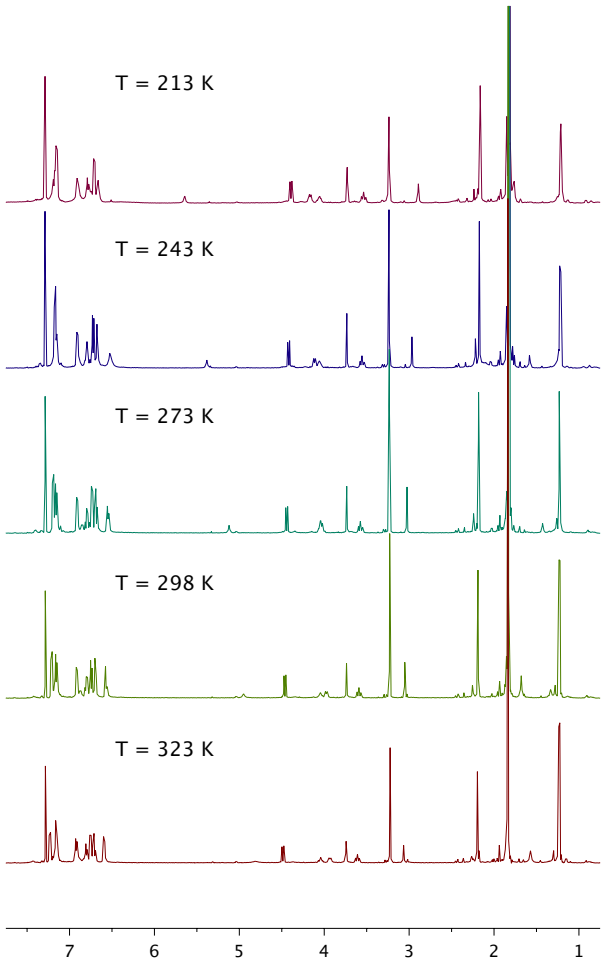
To confirm the expected relative stereochemistry at the newly created metal stereocentres, two of the product complexes were submitted to X-ray analysis. As expected, both compounds **4a** and **8a** displayed an (*S*)-configuration in dependence of the (*R*,*R*)-ethylene diamine ligand (Figure 1).[11] This outcome matches the one from the N-H activation products of the corresponding ruthenium series that had been reported earlier by our group. Obviously, these results are reminiscent of the seminal investigation of Noyori on the stereochemical basis of chiral-at-ruthenium hydride complexes that are the active catalysts in transferhydrogenation and hydrogenation reactions.[12] In addition, it confirms that the motif of unsaturated compounds **1**, **3**, **5** and **7** does exercise efficient control within the activation of polar groups within the metal-ligand bifunctional activation.

Figure 1. Solid state structures of rhodium complex **4a** (top) and iridium complex **8a** (bottom).



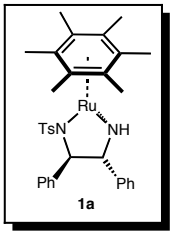
The single stereoisomeric products are configurationally stable within the common temperature range. To demonstrate this context, variable temperature ^{1}H NMR spectra were recorded for iridium complex **8a**. Figure 2 displays representative spectra from temperature range between T = 213 to 323 K. At all these temperatures, only a single set of signals was observed, which is in agreement with the expected stereochemical stability at the metal center (Figure 2).

Figure 2. Variable temperature ^{1}H NMR spectra for iridium complex **8a** (500 MHz, values in ppm).

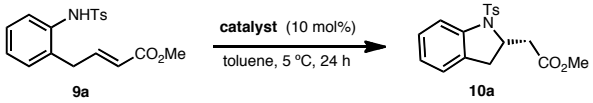


In order to explore the capability of the new complexes as chiral catalyst states in the previously described intramolecular aza-Michael reaction,[9] they were screened for the cyclization of the standard substrate **9a** to **10a**. For this particular transformation, the corresponding ruthenium complex **1a** yielded **10a** in 90% yield and 45% ee (Table 1, entry 1). The corresponding unsaturated rhodium complexes **3** and **5** gave very good chemical yields, but comparably low enantioselectivities (entries 2 and 3, respectively). Attempts to employ the preformed amido complexes **4a** and **6a**, respectively, did not result in any reactivity (entries 4,5). In contrast, the iridium complex **7** catalyzed the formation of **10** in excellent yield and already 36% ee (entry 6). Interestingly, a similar result was obtained when the reaction was started from the amido complex **8a** (entry 7), which under the conditions obviously is capable of reverting back to complex **7**. This behavior is not observed for related ruthenium and rhodium complexes.[9] Finally, at lower temperature of -15 ºC, the iridium complex **7** catalyses the C-N bond formation to **10a** in a slightly higher enantioselectivity than the parent ruthenium complex **1a** (entries 8,9).

Table 1. Screening of catalytic efficiency of rhodium and iridium complexes in intramolecular C-N bond forming reactions of **9a**.



1a



9a **10a**

Entry	Catalyst	Yield [%][a]	Ee [%][b]
1	**1a**	90	45
2	**3**	88	22
3	**5**	76	12
4	**4a**	n.r.[c]	
5	**6a**	n.r.[c]	
6	**7**	92	36
7	**8a**	76	36
8[d]	**7**	52	56
9[e]	**1a**	69	53

[a] Isolated yield after purification.

[b] Ee values determined by analytical HPLC at a chiral stationary phase.

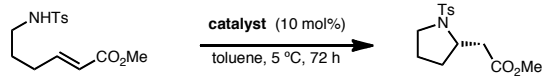
[c] n.r. = no reaction.

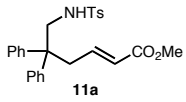
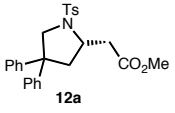
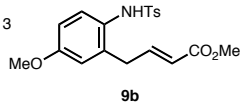
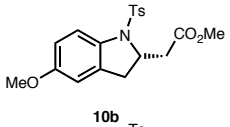
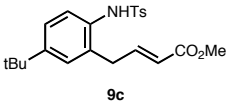
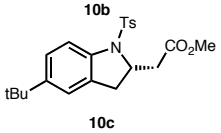
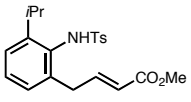
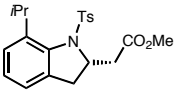
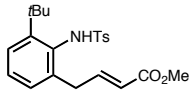
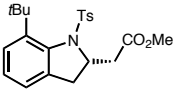
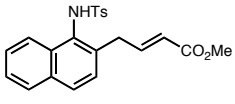
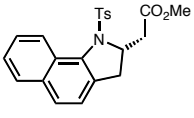
[d] Reaction at -15 °C with 96 h reaction time.

[e] Reaction at -15 °C.

As a result, complex **7** was screened in the catalytic aza-Michael reaction of several substrates (Table 2). These reactions lead to very good chemical yields and acceptable enantiomeric inductions. For the acyclic substrate **11a**, an enantiomeric excess of 32% was obtained for the cyclized product **12a**, which is significantly higher than the 15% that are obtained with the corresponding ruthenium complex **1a** (entries 1,2). Still, this type of substrate appears to contain too much flexibility in order to generate a defined stereodetermining transition state for the C-N bond formation (vido infra). To this end, arene derivatives **9b-f** performed better and led to formation of the corresponding amination products **10b-f** with enantiomeric excesses of 59-90%. As in the case of ruthenium catalysts, *para*-substitution to the aniline nitrogen does not guarantee high enantiomeric induction (entries 3,4), while an alkyl substituent in the remaining *ortho*-position influences a positive effect (entries 5,6). A related effect is obtained for the naphthalene core (entry 7). Product **10f** is initially obtained in 84% ee, but can be conveniently crystallized to enantiopurity upon crystallization from methanol solution.

Table 2. Screening of catalytic efficiency of iridium complex **7** in intramolecular C-N bond forming reactions.



Entry	Substrate	Catalyst	Product	Yield [%][a]	Ee [%][b]
1	 **11a**	**7**	 **12a**	67	32
2		**1a**		58	15
3	 **9b**	**7**	 **10b**	61	67
4	 **9c**	**7**	 **10c**	61	59
5	 **9d**	**7**	 **10d**	65	90
6	 **9e**	**7**	 **10e**	76	86
7	 **9f**	**7**	 **10f**	68	84 (99)[c]

[a] Isolated yield after purification.

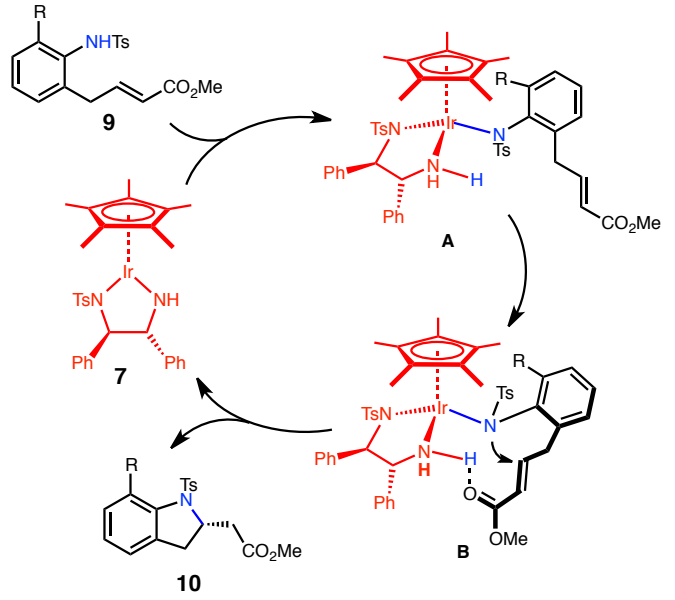
[b] Ee values determined by analytical HPLC at a chiral stationary phase.

[c] After crystallization from MeOH.

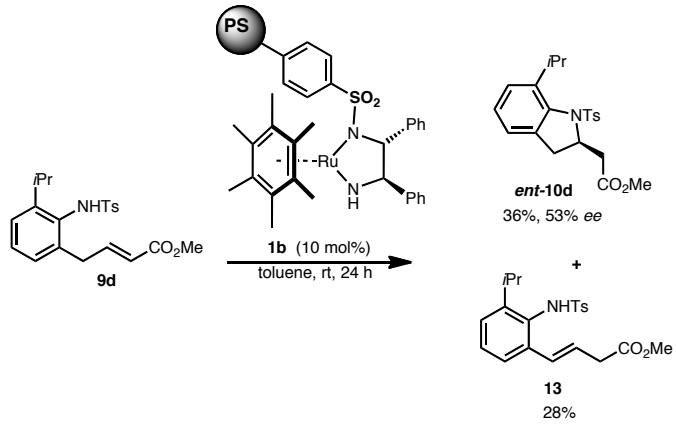
These reactions are understood to follow the general catalytic cycle that was previously postulated for catalyses with ruthenium complexes generated from complex **1**.[9] Again, the present reactions are based on an efficient N-H activation reaction of substrates **9** within the iridium-diamine framework of complex **7** (Figure 3). The resulting amidato iridium complexes **A** should form as a single chiral-at-iridium diastereoisomers as deduced from the studies on formation of related complexes **8a-c** (Scheme 2). At the stages **A**, the interaction between the amidate nitrogen and the alkene will generate cyclic transition states **B** for the C-N bond formation, which is possibly aided by a hydrogen bonding between the NH_2-group of the ligand and the carbonyl group of the ester. The present transition state **B** characterizes the hydroamination process as an aza-Michael reaction.[15] A structurally related mode of activation and transfer had been reported by Ikariya for a metal-ligand bifunctional Michael addition of malonates to enones.[16] It furthermore confirms the strategy of a dual activation mode within the alkene amination process, which combines classical approaches of metal-mediated hydroamination through discrete [M]-N intermediates and carbonyl acitivation to render the conjugated alkene more susceptible for conjugate amination. C-N Bond formation at stages **B** lead to formation of the indoline products **10** with concomitant regeneration of the active catalyst state **7**. As previously noted for the corresponding ruthenium complexes, substitution at the 6-position of the aniline ring of the substrate

greatly enhances the enantioselectivity of the reaction (cf., Table 2). This is the result of an effective steric repulsion between the Cp* substituent of the chiral iridium catalyst and the aryl substituent of the substrate. Consequential to the stereogenic iridium center, these groups are placed in proximity at stage **B** of the reaction, and their repulsion accelerates the enantioselective product formation.

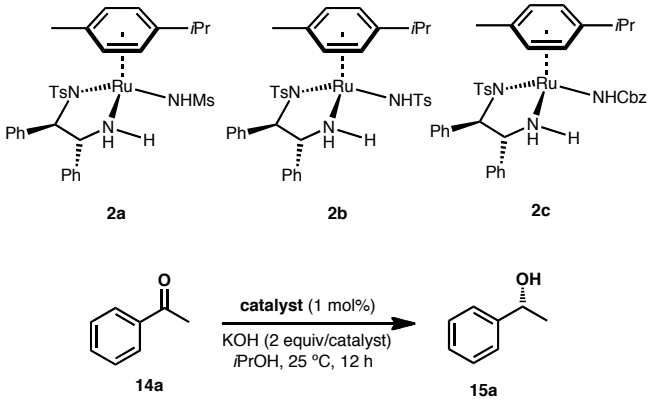
Figure 3. Catalytic cycle for the iridium-catalyzed aza-Michael addition.



Scheme 3. Heterogeneous catalysis for the enantioselective aza-Michael reaction using a polystyrene (PS)-supported diamine ligand.



One of the major disadvantages of the present approach may be the irreversible loss of the catalysts during the work-up process. To be able to recover and reuse the metal catalyst, we were interested to introduce a heterogeneous version of the developed bifunctional metal-ligand catalyzed aza-Michael reaction by attaching the corresponding catalyst to a resin surface. Previously, Pericàs developed an efficient polystyrene-supported version of the Noyori–Ikariya catalyst,[17] that could be successfully used for the highly enantioselective transfer hydrogenation of alkyl aryl ketones with formic acid/triethylamine in the presence of a small amount of dichloromethane. We applied the described procedure for the preparation of the active 16e$^-$ amido-ruthenium complex attached to the surface of the polystyrene resin. Unfortunately, despite a number of reactions that were performed in order to optimize the reaction, the heterogeneous catalyst turned out to be less reactive and less chemoselective (Scheme 3). An unexpected side reaction of alkene isomerisation was observed, although the enantiomeric excess of the desired cyclic product was relatively high (compare to the performance of **1a** in Table 1, entry 9).



Entry	Catalyst	Yield [%][a]	Ee [%][b]
1	**2a**	90	97
2	**2b**	89	97
3	**2c**	95	96
4	**4c**	90	93
5	**6a**	50	95
6	**8a**	33	90

Table 3. Exploration of ruthenium, rhodium and iridum amidato complexes in the transferhydrogenation of acetophenone.

[a] Isolated yield after purification.

[b] Ee values determined by analytical HPLC at a chiral stationary Chiralcel OD phase (*n*-hexane/*i*PrOH, 98/2, v/v, 1 mL/min).

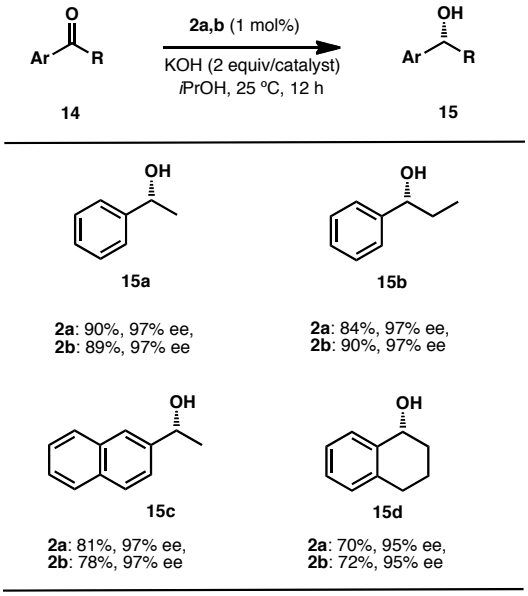
As could be expected, rhodium and iridium complexes **4c**, **6a** and **8a** are versatile precatalysts for the standard metal-ligand bifunctional transferhydrogenation of ketones. In contrast to the aza-Michael reactions from Table 2, where presence of any base catalyses the undesired background reaction of a racemic C-N bond formation, presence of base does not constitute a detrimental effect in the case of transferhydrogenation with 2-propanol. The capacity of various complexes to catalyse the transferhydrogenation of standard substrate acetophenone **14a** to the corresponding secondary alcohol (*R*)-1-phenyl ethanol **15a** was probed. Enantioselective alcohol formation was accomplished in high yields and with high enantioselectivities (Table 3). In particular, our previously reported amido ruthenium complexes **2a-c** gave conversions and enantiomeric excesses that are comparable to the ones obtained with the corresponding chloride complexes introduced by Noyori (entries 1-3). This observation can be rationalized by the assumption that the initial base-mediated formation of the unsaturated complex **1** from Scheme 1 is independent of the anion that is removed in the

elimination reaction. As a result, the transferhydrogenation contains the retro-N-H activation as the initial step of the catalysis.

The same is observed for rhodium and iridium complexes. For example, rhodium complexes **4c** and **6a** gave good, albeit lower conversion of **14a** to **15a** (entries 4,5). For **4c**, the observed ee value of 93% is in good agreement with literature reports reporting on the related chloride complex as catalyst precursor (90% ee).[13] In addition, **6a** gives a slightly lower ee than reported in the literature for the corresponding chloride complex (97% ee).[14] This reaction was terminated after 24h to allow for comparison in relative rate, when it had not reached full conversion. However, the reaction remained of complete chemoselectivity at this stage as only product **15a** and unreacted starting material **14a** were present. Finally, the iridium complex **8a** showed the common reduced reactivity that is common in iridium hydrides.[13] Despite the low yield after 24h, the enantioselectivity was high as expected (90% ee, entry 6).

To fully confirm this context, the ruthenium complexes **2a** and **2b** were employed in additional transferhydrogenation reactions of ketones (Table 4). Again, the obtained results compare well with literature data on the related chloride precursor. It demonstrates that the amido metal complexes obtained from N-H activation can serve as bench-stable catalyst precursors for the present transferhydrogenation reactions.

Table 4. Exploration of ruthenium amidato complexes **2a**,**b** in the transferhydrogenation of ketones.



[a] Isolated yield after purification.

[b] Ee values determined by analytical HPLC at a chiral stationary phase.

3. Conclusion

We have reported the synthesis of new chiral-at-metal amido complexes of rhodium and iridium, which are formed through a stereoselective N-H activation reaction making use of the metal-ligand bifunctionality concept. The resulting complexes can be employed as catalysts or catalyst precursors in enantioselective transition metal catalysis as demonstrated for the case of an intramolecular C-N bond forming reaction and for the case of established transfer hydrogenation reactions for the synthesis of enantioenriched secondary alcohols from ketones.

4. Experimental section

All solvents, reagents and all deuterated solvents were purchased from Aldrich and TCI commercial suppliers. Column chromatography was performed with silica gel (Merck, type 60, 0.063-0.2 mm). NMR spectra were recorded on a Bruker Avance 400 MHz or 500 MHz spectrometers, respectively. All chemical shifts in NMR experiments were reported as ppm downfield from TMS. The following calibrations were used: $CDCl_3$ δ = 7.26 and 77.0 ppm, CD_2Cl_2 δ = 5.32 and 54.00 ppm. MS (ESI-LCMS) experiments were performed using an Agilent 1100 HPLC with a Bruker micro-TOF instrument (ESI). A Supelco C8 (5 cm x 4.6 mm, 5 μm particles) column was used with a linear elution gradient from 100% H_2O (0.5% HCO_2H) to 100% MeCN in 13 min at a flow rate of 0.5 mL/min. MS (EI) and HRMS experiments were performed on a Kratos MS 50 within the service centers at ICIQ. IR spectra were taken in a Bruker Alpha instrument in the solid state. Ruthenium complexes **2a-c,** amination precursors **9a-f** were synthesized as described previously.[10,12] Amination products **10a-f**[10] and **12a**[18] are known compounds.

General procedure A for the N-H activation and resulting formation of the amidato metal complexes: A solution of 0.1 mmol of the corresponding 16e$^-$-metal complex in 5 mL abs. dichloromethane was kept under an argon atmosphere and stirred at room temperature. 1 eq. of a solution of the desired amide (0.1 mmol in 1 mL CH_2Cl_2) was added dropwise until the solution color change remained permanently. The final complex was isolated by removal of solvent under reduced pressure and isolated as crystalline material.

*4.1. Mesylamidato rhodium complex (**4a**)*

Synthesized according to general procedure A. Isolated as a red solid. $[\alpha]^{25}_D$ = -13 (c = 0.288 g/100 mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.80 (s, 15H, C*H*$_3$-Cp*), 2.14 (s, 3H, C*H*$_3$-Ts), 3.16 (s, 3H, C*H*$_3$-Ms), 3.22 (s, 1H, N*H*), 3.50 (d, *J* = 11.0 Hz, 1H, C*H*), 3.63 (ddd, *J* = 13.6, 10.6, 3.0 Hz, 1H, C*H*), 4.18 (d, *J* = 10.6 Hz, 1H, N*H*), 6.13 (t, *J* = 11.7 Hz, 1H, N*H*), 6.52 (d, *J* = 8.3 Hz, 2H, Ar-*H*), 6.59-6.90 (m, 7H, Ar-*H*), 7.05-7.10 (m, 3H, Ar-*H*), 7.17 (d, *J* = 8.3 Hz, 2H, Ar-*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 9.4 (*C*H$_3$-Cp*), 21.0 (*C*H$_3$-Ts), 45.8 (*C*H$_3$-Ms), 69.5 (*C*H), 72.1 (*C*H), 94.0 (*Cp**), 94.1 (*Cp**), 126.0, 127.1, 127.4, 127.9, 128.1, 128.5, 128.4, 138.9, 139.5, 139.6, 141.4. IR (KBr): ν(cm^{-1}) = 3304, 3247, 068, 3027, 2966, 2935, 1603, 1506, 1465, 1337, 1270, 1163, 1127, 1112, 1086, 989, 917, 830, 718, 579. MS**:** m/z (MALDI) calcd for $C_{31}H_{36}N_2O_2SRh$ [M – $NHSO_2CH_3$]$^+$ 618.2, found 618.2.

*4.2. Tosylamidato rhodium complex (**4b**)*

Synthesized according to general procedure A. Isolated as a red solid. $[\alpha]^{25}_D$ = -12 (c = 0.448 g/100 mL, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 15H, C*H*$_3$-Cp*), 2.14 (s, 3H, C*H*$_3$-Ts), 2.41 (s, 3H, C*H*$_3$-Ts), 3.33 (s, 1H, N*H*), 3.46 (d, *J* = 9.3 Hz, 1H, C*H*), 3.65 (ddd, *J* = 12.1, 11.1, 3.0 Hz, 1H, C*H*), 4.20 (d, *J* = 11.1 Hz, 1H, N*H*), 5.66 (t, *J* = 12.1 Hz, 1H, N*H*), 6.55 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 6.64-6.68 (m, 5H, Ar-*H*), 6.74 (d, *J* = 8.6 Hz, 2H, Ar-*H*), 7.02- 7.11 (m, 5H, Ar-*H*), 7.17 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 7.26 (d, *J* = 8.6 Hz, 2H, Ar-*H*). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 9.5 (*C*H$_3$-Cp*), 21.0 (*C*H$_3$-Ts), 21.4 (*C*H$_3$-Ts), 69.5 (*C*H), 72.1 (*C*H), 94.1 (*Cp**), 94.2 (*Cp**), 126.0, 126.1, 126.9, 126.9, 127.1, 127.4, 127.8, 128.1, 128.4, 129.0, 139.0, 139.4, 139.4, 141.4, 142.9, 144.6. IR (KBr): ν(cm^{-1}) = 3350, 3304, 3242, 3068, 3032, 2966, 2919, 1603, 1511, 1460, 1337, 1271, 1168, 1132, 1086, 917, 820, 702, 579. MS**:** m/z (MALDI) calcd for $C_{31}H_{36}N_2O_2SRh$ [M – $NHSO_2C_7H_7$]$^+$ 618.2, found 618.2.

*4.3. Benzyl carbamidato rhodium complex (**4c**)*

Synthesized according to general procedure A. Isolated as a red solid. $[\alpha]^{25}_D$ = -26 (c = 0.116 g/100 mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 15H, C*H*$_3$-Cp*)), 2.16 (s, 3H, C*H*$_3$-Ts), 3.08 (d, *J* = 10.0 Hz, 1H, N*H*), 3.64 (ddd, *J* = 13.8, 10.8, 3.0 Hz, 1H, C*H*), 3.97 (s, 1H, N*H*), 3.97-3.98 (m, 1H, C*H*), 4.02 (d, *J* = 11.0 Hz, 1H, N*H*), 5.14 (d, *J* = 3.0 Hz, 2H, C*H*$_2$), 6.56 (d, *J* = 7.4 Hz, 2H, Ar-*H*), 6.65-7.41 (m, 15H, Ar-*H*), 7.52 (d, *J* = 7.4 Hz, 2H, Ar-*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 9.1 (*C*H$_3$-Cp*), 21.1 (*C*H$_3$-Ts), 66.8 (*C*H$_2$), 69.8 (*C*H), 72.1 (*C*H), 93.2 (*Cp**), 93.3 (*Cp**), 125.9, 126.9, 127.1, 127.3, 127.7, 128.0, 128.1, 128.1, 128.2, 128.5, 128.6, 138.9, 139.5, 139.9, 142.0, 156.6, 163.4 (CO). IR (KBr): ν(cm^{-1}) = 3380, 3293, 3063, 3027, 2960, 2925, 1721, 1639, 1460, 1404, 1352, 1271, 1132, 1086, 912, 825, 702, 584. MS**:** m/z (MALDI) calcd for $C_{31}H_{36}N_2O_2SRh$ [M – $NHO_2C_8H_7$]$^+$ 618.2, found 618.1.

*4.4. Tosylamidato rhodium complex (**6a**)*

Synthesized according to general procedure A. Isolated as a red solid. $[\alpha]^{25}_D$ = -20.6 (c = 0.507 g/100 mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.67-1.18 (m, 4H, C*H*$_2$), 1.35 (d, *J* = 12.5 Hz, 1H, C*H*$_2$), 1.50 (d, *J* = 12.5 Hz, 1H, C*H*$_2$), 1.70 (s, 15H, C*H*$_3$-Cp*), 1.86-1.87 (m, 1H, C*H*$_2$), 1.94-1.95 (m, 1H, C*H*$_2$), 2.35 (s, 6H, C*H*$_3$-Ts), 2.38-2.39 (m, 1H, C*H*), 2.48 (ddd, *J* = 14.0, 10.8, 3.2 Hz, 1H, C*H*), 2.72 (s, 1H, N*H*), 3.32 (d, *J* = 11.3 Hz, 1H, N*H*), 4.37 (t, *J* = 11.3 Hz, 1H, N*H*), 7.12 (d, *J* = 8.3 Hz, 2H, Ar-*H*), 7.19 (d, *J* = 8.3 Hz, 2H, Ar-*H*), 7.76 (d, *J* = 8.3 Hz, 2H, Ar-*H*), 7.81 (d, *J* = 8.3 Hz, 2H, Ar-*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 9.4 (*C*H$_3$-Cp*), 21.3 (*C*H$_3$-Ts), 24.4, 24.7, 34.6, 36.3, 63.4 (*C*H), 64.6 (*C*H), 93.7 (*Cp**), 93.8 (*Cp**), 126.0, 126.7, 128.7, 128.9, 140.2, 140.4, 144.8. IR (KBr): ν(cm^{-1}) = 3355, 3278, 3165, 3063, 3022, 2930, 2858, 1271, 1132, 1096, 902, 715, 671, 579, 554. MS**:** m/z (MALDI) calcd for $C_{24}H_{37}N_2O_2SRh$ [M – $NHSO_2C_7H_7$]$^+$ 520.2, found 520.2.

*4.5. Mesylamidato iridium complex (**8a**)*

Synthesized according to general procedure A. Isolated as yellow solid in 97% yield. $[\alpha]^{25}_D$ = 50.3 (c = 0.16 g/100 mL, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 15H, C*H*$_3$-Cp*), 2.16 (s, 3H, C*H*$_3$-Ts), 3.20 (s, 3H, C*H*$_3$-Ms), 3.56 (ddd, *J* = 13.9, 11.0, 3.2 Hz, 1H, C*H*), 3.71 (s, 1H, N*H*), 3.95 (brd, 1H, N*H*), 4.44 (d, *J* = 11.0 Hz, 1H, C*H*), 6.54 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 6.65-6.78 (m, 6H, Ar-*H*), 6.85-6.91 (m, 2H, Ar-*H*), 7.12-7.15 (m, 2H, Ar-*H*), 7.19 (d, *J* = 8.2 Hz, 2H, Ar-*H*). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 9.5 (*C*H$_3$-Cp*), 21.1 (*C*H$_3$-Ts), 45.6 (*C*H$_3$-Ms), 69.9 (*C*H), 74.8 (*C*H), 85.6 (*Cp**), 126.3, 127.0, 127.2, 127.6, 128.0, 128.4, 128.7, 138.1, 138.8, 139.7, 140.9. IR: ν(cm^{-1}) = 3277, 2960, 2921, 2853, 1493, 1454, 1378, 1260, 1228, 1185, 1116, 1082, 1029, 987, 903, 807, 794, 767, 749, 729, 697, 681, 652, 574. MS**:** m/z (MALDI) calcd for $C_{31}H_{36}N_2O_2SIr$ [M – $NHSO_2C_2H_6$]$^+$ 693.2, found 693.2.

*4.6. Tosylamidato iridium complex (**8b**)*

Synthesized according to general procedure A. Isolated as an orange solid in 97% yield. $[\alpha]^{25}_D$ = 44.7 (c = 0.500 g/100 mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$, MeOD): δ = 1.70 (s, 15H,

CH_3-Cp*), 2.16 (s, 3H, CH_3-Ts), 2.42 (s, 3H, CH_3-Ts), 3.52 (d, *J* = 11.0 Hz, 1H, C*H*), 4.16 (s, 2H, NH_2), 4.35 (d, *J* = 11.0 Hz, 1H, C*H*), 6.50 (d, *J* = 7.2 Hz, 2H, Ar-*H*), 6.63-6.83 (m, 7H, Ar-*H*), 7.02-7.17 (m, 5H, Ar-*H*), 7.30 (d, *J* = 7.9 Hz, 2H, Ar-*H*), 7.90 (d, *J* = 8.3 Hz, 2H, Ar-*H*). ^{13}C-NMR (75 MHz, $CDCl_3$, MeOD): δ = 9.5 (*C*H_3-Cp*), 21.2 (*C*H_3-Ts), 21.5 (*C*H_3-Ts), 70.2 (*C*H), 74.9 (*C*H), 86.2 (*Cp**), 125.9, 126.3, 126.7, 127.2, 127.5, 127.6, 128.4, 128.5, 128.7, 128.8, 129.4, 129.6, 138.2, 139.3, 140.5, 140.7, 141.7, 144.3. IR (KBr): ν(cm^{-1}) = 3284, 3259, 3064, 3030, 2965, 2922, 2869, 1459, 1262, 1210, 1159, 1130, 1087, 909, 816, 702, 669, 569, 501. MS**:** m/z (MALDI) calcd for $C_{32}H_{39}N_2O_2SIr$ $[M - NHSO_2C_7H_7]^+$ 708.2, found 708.2.

*4.7. Benzyl carbamidato iridium complex (**8c**)*

Synthesized according to general procedure A. Isolated as an orange solid in 95% yield. $[\alpha]^{25}_D$ = -41 (c = 0.054 g/100 mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.67 (s, 15H, CH_3-Cp*), 2.08 (s, 3H, CH_3-Ts), 3.49 (ddd, *J* = 13.6, 10.6, 3.2 Hz, 1H, C*H*), 4.18 (d, *J* = 10.9 Hz, 1H, C*H*), 4.29 (s, 1H, N*H*), 4.99 (s, 2H, CH_2), 5.05 (d, *J* = 4.0 Hz, 2H, NH_2), 6.48 (dd, *J* = 7.0, 1.6 Hz, 2H, Ar-*H*), 6.61-6.72 (m, 7H, Ar-*H*), 6.97- 7.22 (m, 8H, Ar-*H*), 7.42 (d, *J* = 7.7 Hz, 2H, Ar-*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 9.7 (*C*H_3-Cp*), 21.7 (*C*H_3-Ts), 66.5 (*C*H_2), 70.7 (*C*H), 75.4 (*C*H), 85.5 (*Cp**), 126.7, 127.6, 127.6, 127.7, 127.8, 128.1, 128.4, 128.6, 128.7, 128.8, 129.0, 129.1, 129.3, 139.4, 139.8, 139.9, 139.9, 141.9, 164.2 (*C*O). IR (KBr): ν(cm^{-1}) = 3388, 3060, 3027, 2960, 2911, 1718, 1646, 1456, 1410, 1261, 1087, 1028, 911, 799, 702, 581. MS**:** m/z (MALDI) calcd for $C_{32}H_{39}N_2O_2SIr$ $[M - NHO_2C_8H_7]^+$ 708.2, found 708.2.

*4.8. (E)-Methyl 6-(4-methylphenylsulfonamido)-5,5-diphenylhex-2-enoate (**11a**)*

A solution of *N*-(2,2-diphenylpent-4-en-1-yl)-4-methylbenzenesulfonamide[19] (391 mg, 1.0 mmol) was dissolved in 5 mL of freshly distilled dichloromethane. Grubbs-Hoveyda catalyst (19 mg, 0.03 mmol) and methyl acrylate (0.8 mL, 9.0 mmol) were subsequently added in single portions and the reaction was refluxed for 18h at 50 ºC (external oil bath temperature). The reaction mixture was then cooled to room temperature and all volatile material was removed under reduce pressure. The product was purified by column chromatography (silica gel, ethyl acetate/*n*-hexane, 1/4, v/v) as a white solid (418 mg, 93%). R_f = 0.3.

Obtained as a white solid. m.p. 131-132 ºC. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.77-1.84 (m, 1H, CH_2), 2.23-2.28 (m, 1H, CH_2), 2.43 (s, 3H, CH_3-Ts), 3.59 (d, *J* = 6.4 Hz, 2H, CH_2), 3.70 (s, 3H, CO_2CH_3), 4.12 (t, *J* = 6.4 Hz, 1H, NH), 5.68 (d, *J* = 15.8 Hz, 1H, CH), 6.75-6.83 (m, 1H, CH), 7.06 (psd, *J* =7.3 Hz, 4H, Ar-H), 7.18-7.31 (m, 8H, Ar-H), 7.65 (d, *J* = 8.2 Hz, 2H, Ar-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 21.7, 39.6, 49.7, 49.8, 51.5, 124.8, 127.2, 127.7, 128.8, 129.9, 136.3, 143.7, 143.8, 143.9, 166.4. IR: ν(cm^{-1}) = 3216, 2865, 1718, 1650, 1597, 1493, 1445, 1416, 1330, 1288, 1258, 1196, 1168, 1159, 1074, 1029, 994, 964, 918, 890, 814, 780, 752, 735, 698, 657, 628, 569. HRMS: m/z (ESI) calcd for $C_{26}H_{27}NO_4SNa$ $[M + Na]^+$ 472.1559, found 472.1549.

General Procedure for Intramolecular Amination

The required 16e$^-$-complexes **1a, 3, 5** and **7** were synthesized by modified literature procedures:[10,12] generally, 0.1 mmol of the corresponding chloride-complex is dissolved in 2 mL of dichloromethane. While the solution is stirred, an excess of potassium hydroxide is added to cause the solution change its color in the ways described in the text. Washing with water and quick drying over CaH_2 under argon atmosphere gives a solution of the activated complex. The mixture is filtered under argon atmosphere and washed with abs. dichloromethane. This solution containing the pure complex is concentrated to 5 mL and used immediately. The colored solution of prepared catalyst with known concentration (0.01 M) was subsequently used for catalysis. To the solution of starting material (0.05 mmol) in toluene (2 mL) at –15 ºC was added a solution with known concentration of activated catalyst (0.5 mL of the solution per reaction, 0.005 mmol, 10 mol%). The reaction was stirred at this temperature for the periods reported in Tables 1 and 2, quenched with a saturated aqueous solution of NH_4Cl (5 mL) and extracted with $CHCl_3$ (15 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to provide the crude product mixture. Purification was carried out by column chromatography as described previously.

HPLC determination: **10a**: Chiralpak-AD, 0.7 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 18.0 min (*R*-enantiomer), tR_2 = 24.2 min (*S*-enantiomer); **10b**: Chiralcel-OD, 0.5 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 27.5 min (*R*-enantiomer), tR_2 = 29.8 min (*S*-enantiomer). **10c**: Chiralpak-AD, 0.7 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 12.6 min (*S*-enantiomer), tR_2 = 19.4 min (*R*-enantiomer). **10d**: Chiralpak-AD, 0.7 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 9.5 min (*S*-enantiomer), tR_2 = 11.0 min (*R*-enantiomer). **10e:** Chiralpak-AD, 0.7 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 8.9 min (*S*-enantiomer), tR_2 = 10.4 min (*R*-enantiomer). **10f:** Chiralpak-AD, 0.7 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 21.2 min (*R*-enantiomer), tR_2 = 22.4 min (*S*-enantiomer). **12a**: Chiralcel-OD, 1 mL/min, 2-PrOH/hexane, 10/90, v/v, tR_1 = 19.3 min (*R*-enantiomer), tR_2 = 22.4 min (*S*-enantiomer).

General Procedure for transferhydrogenation

In a Schlenk tube under an argon atmosphere, the corresponding metal complex (0.5 or 5 mol%) is dissolved in 0.1 mL of iso-propanol. A solution of KOH in iso-propanol (40 μL, 0.1 M) is then added via syringe. An immediate color change occurs throughout the addition, and a solution of acetophenone (0.2 mmol) in iso-propanol (1.9 mL) is then added. The mixture is stirred at room temperature overnight. The reaction is quenched by addition of an aqueous solution of HCl (10%), and the mixture is extracted with CH_2Cl_2 (3x). The combined organic phases are dried over Na_2SO_4, filtrated over Celite® and the solvent is removed under reduced pressure. The crude mixture is purified by chromatography (silica gel, *n*-hexane/ethyl acetate, 4/1, v/v) to obtain the desired secondary alcohol.

HPLC determination: **15a**: Chiralcel-OD, 1.0 mL/min, 2-PrOH/hexane, 2/98, v/v, tR_1 = 18.0 min (*R*-enantiomer), tR_2 = 25.0 min (*S*-enantiomer); **15b**: Chiralcel-OD, 0.5 mL/min, 2-PrOH/hexane, 2/98, v/v, tR_1 = 15.5 min (*R*-enantiomer), tR_2 = 17.7 min (*S*-enantiomer). **15c**: Chiralcel-OD, 1.0 mL/min, 2-PrOH/hexane, 2/98, v/v, tR_1 = 22.6 min (*R*-enantiomer), tR_2 = 28.5 min (*S*-enantiomer); **15d**: Chiralcel-OD, 0.7 mL/min, 2-PrOH/hexane, 2/98, v/v, tR_1 = 11.5 min (*R*-enantiomer), tR_2 = 14.3 min (*S*-enantiomer).

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Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic submitted along with the manuscript and graphic files to the appropriate editorial office.