Proton-responsive pyridine-based ligands: Synthesis, coordination chemistry and catalysis

de Boer, S.Y.

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Ruthenium PNN(O) Complexes: Cooperative Reactivity and Application as Catalysts for Acceptorless Dehydrogenative Coupling Reactions

Abstract The novel tridentate pincer ligand L1 is described, featuring two different proton-responsive ligand reactive sites, i.e. a hydroxy-pyridine functionality and a phosphinomethyl side arm. This dual-mode reactive ligand is coordinated to Ru(II) to generate complex 1. Site-selective deprotonation of the hydroxy-pyridine functionality was achieved using both mild (DBU) and strong bases (KO'Bu or KHMDS), whereas the phosphinomethyl is only deprotonated by strong bases. DFT calculations suggest enhanced reactivity for this system over well-established PNN pincer complexes that do not contain the hydroxy-pyridine fragment. Application of this complex 1 in the dehydrogenation of formic acid resulted in poor turnover frequencies, however, clean and CO-free hydrogen was produced. Using a dearomatization-reprotonation strategy with complex 1 in the dehydrogenative coupling of alcohols resulted in high conversions of different esters. When used in the more challenging dehydrogenative coupling of alcohols and amines, the main product proved to be the ester, and not the amide.
3.1 Introduction

Tridentate pincer ligands that feature a reactive site have gained a lot of interest during the past decade. Especially the well-known complexes with lutidine-based PNP and PNN systems as well as bipy-PNN based motifs (Figure 1) are of particular interest because of their ability to undergo facile and reversible deprotonation of the phosphinomethyl side arm, generating a formally dearomatized N-heterocycle.

Ruthenium complexes of these types of ligand are able to activate C-H, N-H and O-H bonds, and catalyze a large variety of reactions. Examples are the acceptorless dehydrogenation of alcohols into ketones (PNP), the hydrogenation of amides into alcohols and amines and the reverse reaction, i.e. amide formation from alcohols and amines (PNN). The formation of esters is accomplished via homo-coupling of primary alcohols as well as by the cross-coupling of primary and secondary alcohols. In these catalytic reactions metal-ligand cooperativity is crucial, as reversible deprotonation of the phosphinomethyl arm is required during the catalytic cycle. The symmetrical PNP ligand can be deprotonated twice, similar as observed for structures b and c in Figure 2. These latter systems have both been applied in the catalytic transfer hydrogenation of ketones. Both the pyrazole and the hydroxypyridine fragment are more easily deprotonated than the methylene spacer in PNP systems, as they contain more acidic NH or OH groups at the β position with respect to the metal. To date, ligands with two different acidic sites have rarely been explored. Incorporating two different reactive sites in one molecule may hold benefits as it may allow the (sequential) activation of two substrates of different basicity on one metal center, which can couple together subsequently, such as the cross-dehydrogenative coupling.

An interesting example is the mono-anionic dearomatized Ru(II)PNN complex, prepared by double deprotonation of both the NH and benzylic CH position (Scheme 1). Combination of these two modes of MLC (Metal-Ligand Cooperation) in one complex, a dual-mode system, might lead to enhanced catalytic activity, due to the ability of the complex to “choose” the
pathway with the lowest activation energy. This complex proved to be an efficient catalyst for the acceptorless dehydrogenative coupling of alcohols into esters at 35 ºC, as well as the hydrogenation of esters to alcohols at room temperature and under 5 bar H₂.

![Scheme 1](image1.png)

**Scheme 1.** A dual-mode Ru(II)PNN system capable of catalysis under mild conditions.

In this chapter we introduce new ligands based on 6-(di-tert-butyl-phosphinomethyl)-6'-hydroxy-2,2'-bipyridine, which feature two different reactive side arms. These ligands combine a PNN bipyridine and a hydroxypyridine functionality (Scheme 2). One side features a tautomeric hydroxypyridine – pyridonate moiety and the other side is characterized by a phosphinomethyl-pyridine, together forming a potentially tridentate ligand.

![Scheme 2](image2.png)

**Scheme 2.** Envisioned ligand system with two reactive side arms.

The reactivity of these ligands as well as the catalytic activity of their Ru(II) complexes will be reported. We expect enhanced activity for these complexes compared to their ‘parent’ counterparts, as the hydroxyl-function that can provide protons and/or pre-coordinate substrates via hydrogen bonding, is near the metal center. The low barriers between 2-hydroxypyridine and 2-pyridone will likely diminish the necessity of high temperature, high pressures and strong bases. These complexes will be studied in the dehydrogenation of formic acid, in the acceptorless dehydrogenative coupling of alcohols into esters and the formation of amides from primary alcohols and primary and secondary amines. Both esters and amides are industrially important functional groups that appear in many useful products like polymers, plasticizers and pharmaceuticals.
3.2 Results and Discussion

3.2.1 Synthesis of tridentate PNN(O) ligands

Initially, we set out to make a small library of dual-mode tridentate ligands (ligands I-III, Figure 3). On the right side arm, they consist of an aminomethyl-pyridine or phosphinomethyl-pyridine. The left side arm contains a nitrogen-based ring structure with an OH or NH that can be deprotonated by weak bases. During the selected routes to afford I and II, we encountered problems regarding ring closure of the pyrazole and connection of the amine donor to the ligand. The synthesis of ligand III was rather straightforward, as it is quite comparable to the synthesis of bipyridine PNN ligands.\(^9\) Therefore, we focused on this ligand system, using tert-butyl as substituent on the phosphine arm.

![Figure 3. Intended library of dual-mode ligands.](image)

The synthesis of ligand III involved several synthetic steps. Intermediate A was synthesized according to a literature procedure,\(^{20}\) via a Stille coupling using 2-bromo-6-methoxypyridine and 2-methyl-6-(tributylstannyl)pyridine (Scheme 3). Subsequently, the mono-lithiation of the methyl-group was followed by phosphorylation to yield L1Me. In the last step, the removal of the methoxyl group was achieved by acid hydrolysis using concentrated HBr in acetic acid, which produced ligand L1 in 69% yield.

![Scheme 3. Synthetic route for the preparation of dual-mode ligand L1.](image)
Characterization of $\mathbf{L_1}$ by NMR spectroscopy shows a singlet at $\delta$ 37.5 in $^{31}$P NMR spectrum, while the $^1$H NMR displays a broad singlet at 10.72 ppm and a doublet ($^2J_{PH} = 3.2$ Hz) at 3.11 ppm, which correspond to the hydroxyl proton and $-\text{CH}_2\text{P}$ spacer, respectively. These spectral data are very similar to those of the well-known PNN ligand, suggesting negligible electronic influence of the hydroxyl group. The structure was furthermore confirmed by HR-MS, showing an $m/z$ value of 330.18908 (calc. $m/z$ 330.18618).

The initially targeted synthesis of $\mathbf{L_1}$ consisted of five steps, of which the route is depicted in Scheme 4. At first, it was reasoned that the synthesized phosphine would not be able to survive the harsh conditions required to cleave the methoxy group and it was therefore decided to protect the hydroxyl group as the tert-butyldimethylsilyl (TBDMS) ether as illustrated in Scheme 4. After lithiation and phosphorylation of the pyridine arm, this TBDMS group could be cleaved very mildly by using tetrabutylammonium fluoride (TBAF), providing $\mathbf{L_1}$, in analogy to reported synthetic protocols to e.g. bis(2-hydroxypyridyl)pyridine. Interestingly, this synthetic route did not lead to the proposed ligand, but it provided ligand $\mathbf{L_2}$. This system also has two potentially active side arms, but now the methylene spacer is more sterically protected.

Scheme 4. Initially targeted synthesis for the preparation of $\mathbf{L_1}$ led to formation of $\mathbf{L_2}$.
The ligand with the silyl moiety is very interesting as it allows to investigate the potential steric and electronic influences of this bulky group on both the ligand based proton-responsive reactivity and on the reactions occurring in the metal coordination sphere. D’ could be formed because an excess of ClSiMe₂Bu had to be used for the protection of C’. When an equimolar amount of chlorosilane was used compared to the bipyridine in the formation of C’, full conversion was never achieved. Removal of the remaining chlorosilane led to (partial) deprotection, recovering compound B’.

Spectroscopic data of L₂ indeed show that the TBDMS group has significant influence, as the ³¹P NMR spectrum displays a downfield shift for the phosphine at δ 47.6 (relative to L₁ at δ 37.5). Also, the normally distinct doublet in ¹H NMR that corresponds to the tert-butyl groups on the phosphine is now split into two doublets, indicating the inequivalence of the alkyl groups due to the addition chiral center. Furthermore, HR-MS data for the parent M⁺ ion (m/z of 445.28401; calc. m/z 445.2799) also confirmed the presence of L₂.

### 3.2.2 Coordination of L₁ and L₂ to ruthenium

Reaction of L₁ with RuCl(CO)(H)(PPh₃)₃ yielded an orange solid that was fully characterized and identified as RuCl(CO)(H)(L₁), complex 1 (Scheme 5). ³¹P NMR displays a singlet at 105.0 ppm and in the ¹H NMR spectrum a doublet is found at δ -14.87 (JₚH = 24 Hz) for the hydride. Furthermore, the CO ligand absorbs at 1916 cm⁻¹ in the IR region and HR-MS of m/z 461.0824 [M-Cl] (calc. 461.0932 [M-Cl]) was in agreement with the proposed structure. When L₂ was reacted with the Ru(II) precursor, a mixture of products was obtained, without any indication of the formation of the desired complex. Presumably the steric bulk of both the TBDMS group and the two tert-Bu-groups hinders the formation of the desired structure.

As a reference ligand that allows to investigate the involvement of the hydroxypyridine arm during catalysis, we also prepared methoxy-ether complex 2 (Scheme 5) in a similar fashion as complex 1, from ligand L₁Me and RuCl(CO)(H)(PPh₃)₃. For this complex, the ³¹P NMR spectrum shows a singlet at 105.9 ppm and a doublet at δ -14.93 (JₚH = 24 Hz) in the ¹H NMR spectrum for the hydride. All spectroscopic features are very similar to complex 1, but also to the known analogous Ru(II)PNN complex described by the group of Milstein. Single crystals of both complex 1 (slow diffusion of diethyl ether into a concentrated acetonitrile solution) and 2 (slow diffusion of pentane into a concentrated CH₂Cl₂ solution) were grown, which were
suitable for X-ray structure determination (Figure 4). The molecular structure of 1 reveals a distorted octahedral geometry around the ruthenium center, with the CO ligand trans to the central pyridine of the PNN system. The ligand is not completely planar, as the methylene bends out of the plane, which is common for this type of complexes. From this structure it became apparent that an acetonitrile molecule is coordinating to the metal center, in lieu of the chloride ligand which acts as a non-coordinating counter ion. Hence, it is named $\text{1MeCN}$. A hydrogen bond interaction is observed between the hydroxyl moiety and the non-coordinating chloride atom which is at a distance of 2.153 Å. For complex 2, the molecular structure also reveals a distorted octahedral geometry, with again the methylene group bending out of plane. Here, the chloride atom is coordinated to the ruthenium. The fact that this ligands binds only weakly to the metal center, as confirmed in complex $\text{1MeCN}$, is worthy knowledge for further reactivity as the chloride has to dissociate to create a vacant site for substrate binding.

When comparing the two structures, it is seen that for both complexes a different enantiomer was characterized by X-ray crystallography (hydride pointing backwards vs. forward). Coordination of the ligands to the metal center resulted in an racemic mixture, which is not visible in the applied spectroscopic methods and will not inflict problems in subsequent reactivity. The asymmetric unit cell shows that the solid state also contains both enantiomers as a racemate. In Table 1, selected bond lengths (Å), angles and torsion angles (º) are presented for complexes $\text{1MeCN}$ and 2, as well as for the comparable $\text{RuCl(CO)(H)(PNN)}$. All values are near-identical and IR spectroscopy also confirms the similarity, showing $\nu$(CO) bands at 1916, 1902 and 1906 cm$^{-1}$ for $\text{1MeCN}$, 2, and $\text{RuCl(CO)(H)(PNN)}$, respectively. In addition, complex 1 could be obtained as the neutral complex with the chloride ligand coordinated, when a work-up was performed without acetonitrile.
Table 1. Selected bond lengths (Å), angles and torsion angles (°) for complexes 1 and 2 and the analogous RuCl(CO)(H)PNN.

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<tr>
<th></th>
<th>Complex 1MeCN</th>
<th>Complex 2</th>
<th>RuCl(CO)(H)PNN&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
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<tr>
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<tr>
<td>N1-C2-C1-P1</td>
<td>(°)</td>
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</table>

In complex 2, the corresponding bond lengths are between Ru1-C21 and C21-O2, and bond angle between N1-Ru1-C21. In complex 1MeCN, the chloride ligand is replaced by an NCMe ligand, thus the bond length represents the Ru1-N3 bond and H1-Ru1-N3 bond angle.

3.2.3 Deprotonation/dearomatization of complexes 1 and 2

It was hypothesized that the hydroxy-pyridine moiety of the ligand would likely be deprotonated preferentially, and by weaker bases than the usual KO'Bu or KHMS that are used for the deprotonation of archetypical PNN pincer systems. However, addition of one equivalent of NEt<sub>3</sub> (pk<sub>a</sub> value in DMSO: 9)<sup>22</sup> to complex 1 did not provide the expected pyridone species, as concluded from <sup>1</sup>H NMR spectral data. The hydroxyl-group is apparently not acidic enough to be deprotonated by such a weak base. However, the slightly stronger base DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) (pk<sub>a</sub> value in DMSO: 12)<sup>22</sup> was able to realize selective deprotonation of the hydroxy-pyridine, generating complex 1' (Scheme 6) with an immediate color change from orange to brown-red. When one equivalent of KO'Bu or KHMS was added to complex 1, complex 1' was also obtained, indicating that the hydroxy-pyridine can be selectively deprotonated, with no intramolecular proton-transfer from the methylene spacer to the pyridine unit detected.

Scheme 6. Deprotonation of complex 1 to complex 1' by both weak and strong bases.
Conversion of 1 to 1' results in a small shift in the $^{31}$P NMR spectrum, to 102.5 ppm ($\Delta \delta = 2.5$ ppm). A larger shift was expected for the pyridone tautomer, as the trans pyridine formally becomes anionic, which therefore led us to the assumption that the complex is more akin to the pyridonate structure depicted in Scheme 7 (right), than to the neutral pyridone isomer (left). In the $^1$H NMR spectrum the hydride is found at $\delta$ -19.4 ($J_{PH} = 24$ Hz) and the two doublet of doublets at 3.94 and 3.42 ppm support the methylene spacer is not deprotonated.

Scheme 7. The equilibrium of complex 1' lies more to the pyridonate (right) instead of the assumed (pyridone) left species.

When one equivalent of DBU was combined with complex 2, no reaction took place, indicating that this relative weak base is only capable of deprotonating the hydroxy-pyridine arm of complex 1 (Scheme 8). Addition of the stronger bases KOtBu or KHMDS did result in deprotonation of the methylene arm of complex 2, which produced complex 2'. An immediate change of color was observed from orange to dark-green. The $^{31}$P NMR spectrum shows a singlet at 95.2 ppm, and in the $^1$H NMR spectrum, a signal for the methine proton arose at $\delta$ 3.36 ppm and a doublet ($J_{PH} = 26.1$ Hz) was observed at $\delta$ -21.3 for the hydride. These values are similar to the analogous RuPNN complex.

Scheme 8. Deprotonation of complex 2 does not occur in the presence of DBU. However, when treated with the stronger bases KOtBu or KHMDS, complex 2' was obtained.

3.2.4 Catalytic activity of 1 in the dehydrogenation of HCOOH

Hydrogen is potentially one of the major energy carriers for the future and formic acid has been demonstrated to provide an interesting storage-release system for the reversible storage of dihydrogen.\textsuperscript{23-25} Ruthenium pincer complexes that are analogous to complex 1 have been shown to be efficient catalysts for the reversible protonation of CO$_2$ to formic acid.\textsuperscript{26,27} As complex 1 is more easily deprotonated compared to many known complexes bearing proton-responsive ligands, we hypothesized that this could lead to enhanced catalytic activity in formic acid decomposition. Indeed, complex 1 was found to be a competent catalyst for the dehydrogenation of HCOOH, in the presence of only a small amount of base required to pre-
activate the system. When only one equivalent of formic acid was added to the \textit{in situ} generated complex \(1'\), a slight color change was observed from brown-red to orange-red, concomitant with the evolution of small bubbles of gas from the solution. Most likely, the bubbles represent both \(\text{CO}_2\) and \(\text{H}_2\), as \(1'\) is observed in the \(^{31}\text{P}\) NMR spectrum (together with decomposition products).

\textbf{Scheme 9.} Complex 1 in the stoichiometric dehydrogenation of HCOOH.

When a catalytic amount of 10 mol\% catalyst (in the presence of the same molar amount of base) was applied, the reaction progress could be monitored volumetrically (see the Experimental Section for a schematic representation of the set-up). With dioxane as solvent at 75 °C, dehydrogenation curves were obtained as depicted in Figure 5.

\textbf{Figure 5.} Formic acid dehydrogenation measured in volume produced gas (\(\text{H}_2 + \text{CO}_2\)) for three reactions in the presence of 10 mol\% of complex \(1'\).

The curves for this triplo-experiment are nearly linear and with a very similar slope, leading to turnover frequencies of 35, 33 and 29 h\(^{-1}\), for run 1, 2 and 3, respectively. The catalyst shows little sign of decomposition when all the formic acid has been converted, as these 3 runs were performed consecutively by directly adding new substrate after one run had finished. The produced gas was analyzed by a gas GC (Figure 6), which indicated that hydrogen and carbon dioxide are the only formed products. Carbon monoxide was not detected at all (detection limit = 10 ppm), meaning that clean dihydrogen can be formed under these conditions.
Figure 6. GC analysis of the formed products from the dehydrogenation of formic acid by complex 1. Left: detection of carbon dioxide; right: detection of dihydrogen.

Based on these data, the following mechanism is proposed for the cooperative dehydrogenation of formic acid with complex 1 (Scheme 10). Initially, HCOOH coordinates to deprotonated species $1'$. The protic hydrogen of formic acid binds via a hydrogen-bond to the ligand pyridonato group, which induces activation of the $\text{O-H}$, while the C=O fragment coordinates to the Ru center via the neutral oxygen. Different mechanisms are known for the dehydrogenation of formic acid, one of which involves $\beta$-H elimination. As there is likely no available vacant site on the metal (dissociation of a reprotonated pyridone group by Ru-N bond breaking is deemed less favorable but cannot be ruled out on the basis of these data), this route is deemed not preferred. Therefore, a rearrangement is necessary that involves a rotation around the O-H bond, to generate a species in which the formate hydrogen ($\text{HCOO}^-$) atom coordinates to the ruthenium, concomitant with proton-transfer to the pyridonato oxygen. This direct hydride-transfer or ligand-assisted direct hydride-transfer generates the release of carbon dioxide, which is accompanied by the formation of complex $1^{\text{HH}}$.

Scheme 10. Proposed mechanism for the cooperative dehydrogenation of formic acid with complex $1'$. 
In the final step the deprotonated species $1'$ is regenerated, concomitant with the release of $\text{H}_2$. Additional investigations should provide detailed information about the rate determining step, but because this system did not show the desired activity, these experiments were not executed.

### 3.2.5 Acceptorless dehydrogenative coupling of alcohols

Ruthenium pincer complexes have previously been successfully applied in the bifunctional activation of O-H bonds, a feature that can subsequently be used in dehydrogenative coupling reactions, e.g. to generate esters from alcohols with release of $\text{H}_2$. Complex 1 was explored as catalyst for this reaction, and benzyl alcohol was chosen as substrate. Addition of one equivalent of benzyl alcohol to the in situ generated complex $1'$ formed complex 3 (Scheme 11). Analysis of this yellow solution by NMR spectroscopy showed a singlet at $\delta$ 104.5 in the $^{31}\text{P}$ NMR spectrum and the $^1\text{H}$ NMR spectrum contained a triplet at -16.28 ppm for the hydride and a doublet at 3.35 ppm for the $-\text{OCH}_2\text{Ph}$. These combined observations in the NMR spectra and the color change are indicative for the formation of the alkoxy complex. Similar spectral features have been observed for the activation of benzyl alcohol with a ruthenium PNP complex.29

![Scheme 11](https://example.com/scheme11.png)

**Scheme 11.** Deprotonation and in situ addition of benzyl alcohol to complex 1 generates complex 3, in which the O-H bond of the substrate is activated over the metal-ligand system.

The application of both complexes 1 and 2 in the acceptorless catalytic dehydrogenative coupling of alcohols to esters was therefore initially studied using benzyl alcohol as substrate, following the procedure as described by Milstein and co-workers.11 We anticipated that this ligand scaffold may outperform the known PNP/N systems in these type of conversions, as the reactive pyridone C=O is closer to the metal center and the proton transfer process may be more facile. When complex 1 was used under the applied conditions (Table 2, entry 1), 90% conversion into the benzyl benzoate was obtained in 15 hours, without any formation of the aldehyde. When compared to the known RuH(CO)(Cl)(PNN) complex (entry 2), 1 seems slightly more active, as the PNN complex only reached 95% conversion after 24 hours. Entry 3 shows the result when the protected complex 2 is used, which resembles the known PNN complex because they both lack the hydroxyl functionality, but still contain a reactive methylene spacer. After 16 hours only 52% of the benzyl alcohol was converted into the product, which shows that it is less active then both the parent complex 1 as well as the known PNN complex. The importance of the generated vacant site on the metal center after deprotonation is presented in entry 4. Complex 1MeCN, obtained after work-up in acetonitrile,
contains a bound acetonitrile ligand (as is also deduced from the crystal structure, Figure 4), and this ligand appears to inhibit substrate coordination. Consequently, no conversion of the benzyl benzoate was observed. Comparison of the results in entry 1 and 5 shows that lowering the temperature to 70 ºC with complex 1 leads to 73% product after 28 hours, indicating that the dehydrogenative coupling also proceeds at reduced temperatures. However, entry 6 shows that the coupling of the alcohol does not succeed at room temperature for complex 1. Additionally, although complex 1 is also deprotonated smoothly by the weaker base DBU, no conversion was obtained after 20 hours at 117 ºC when this was used as base (entry 7). Alkali metals like potassium (from KO\textsubscript{t}Bu) may interact with the deprotonated and (partially) negatively charged pyridonate O\textsuperscript{-}, which could change the reactivity. It is this combination of complex and base that shows the best reactivity for this substrate (comparison of entry 1 and 7) and there may thus be a beneficial effect of the alkali metal counterion. Therefore, we also explored the combination of both a weak base and a potassium cation (entry 8). DBU and KPF\textsubscript{6} were applied on catalyst 1, but even under these circumstances only 3% of the ester was obtained. We believe a strong ion pair is formed between the pyridonate and the DBU salt, which is also observed for the proton-responsive METAMORPhos systems.\textsuperscript{30} This inhibits any further reactivity, leading to poor conversions. The combination of a base of equal strength (to DBU) and KPF\textsubscript{6} should give a decisive answer about this topic.

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Conditions: 1 mmol benzyl alcohol, 1 mol% catalyst, 1 mol% base, indicated temperature and reaction time in toluene (2 mL). Conversion and yield were determined by \textsuperscript{1}H NMR spectroscopy and GC analysis with p-xylene as internal standard. \textsuperscript{a} MeCN is coordinated, like in Figure 4. \textsuperscript{c} A combination of DBU/KPF\textsubscript{6} (ratio 1:1) was used.

Beside benzyl alcohol we also studied the dehydrogenative coupling of the aliphatic alcohol 1-butanol to form butyl butyrate, which is considered more challenging (the reactivity of alcohols toward dehydrogenation typically decreases in the order: aromatic secondary alcohol
Surprisingly, both complexes 1 and 2 gave full conversion of butanol to butyl butyrate after 15 hours at 117 °C (entry 1 and 2), thus outperforming the reaction with benzyl alcohol, which was supposed to be the easier substrate. Additionally, the known RuH(CO)(Cl)(PNN) complex (entry 3) produces almost full conversion (92%) of the ester only after 72 hours under the same conditions. For this PNN complex the conversion was indeed lower when 1-butanol was used compared to the more reactive benzyl alcohol. Lowering the temperature to 70 °C leads to an expected reduced conversion when complex 2 is used as catalyst (yield of 64% (entry 5). Remarkably, for complex 1 only 2% of the butyl butyrate was detected (entry 4), showing that more elevated temperatures are required when this catalyst is used for the conversion of this aliphatic substrate. We currently cannot explain the observed higher activity for butanol vs. benzyl alcohol. It might be that steric hindrance of the phenyl group of the corresponding bound alkoxide is more pronounced relative to the aliphatic chain of butanolate but this should be confirmed by further experiments.

Based on the above data and the well-known reactivity of the PNP and PNN pincer complexes, we propose a plausible catalytic cycle for the dehydrogenative coupling of alcohols by complex 1, as depicted in Scheme 12. Such mechanisms are known for the homo-coupling of alcohols by RuPNP and RuPNN complexes that utilize the reactive methylene spacer of the ligand backbone during the catalytic cycle. Here, the hydroxy-pyridine is proposed to be involved in the mechanism. Initially, activation of the alcohol O-H bond results in ligand side-arm rearomatization, to form the coordinatively saturated alkoxide complex 3. In the following step 1^HH is formed, presumably via dissociation of the reprotonated pyridone group by Ru-N bond breaking, which is accompanied by the formation of the aldehyde. Elimination of

Table 3. Dehydrogenative coupling of butanol to butyl butyrate catalyzed by complexes 1 and 2.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>T [°C]</th>
<th>t [h]</th>
<th>Conv. [%]</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>KO'Bu</td>
<td>117</td>
<td>15</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>KO'Bu</td>
<td>117</td>
<td>15</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>RuPNN</td>
<td>KOH</td>
<td>117</td>
<td>72</td>
<td>92.5</td>
<td>91.5</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>KO'Bu</td>
<td>70</td>
<td>17</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>KO'Bu</td>
<td>70</td>
<td>17</td>
<td>64</td>
<td>64</td>
</tr>
</tbody>
</table>

Conditions: 1 mmol butanol, 1 mol% catalyst, 1 mol% base, indicated temperature and reaction time in toluene (2 mL). Conversion and yield were determined by 1H NMR spectroscopy and GC analysis with p-xylene as internal standard.
dihydrogen then regenerates complex $1'$. The formed aldehyde can react with free alcohol in solution to form the hemi-acetal, which (upon reaction with complex $1'$) leads to aromatized complex $3'$. Dehydrogenation via β-H elimination eliminates the ester and generates the trans dihydride complex $1_{HH}$. A second equivalent of dihydrogen is then liberated to regenerate complex $1'$, which completes the catalytic cycle. Alternatively, inner-sphere formation of the hemiacetal by coupling of the bound alkoxide with alcohol from solution may proceed as well.

\[ \text{Scheme 12. Proposed catalytic cycle for the dehydrogenative coupling of alcohols to esters using complex 1.} \]

### 3.2.6 Formation of amides from coupling of alcohols and amines

To further expand the application of complex 1 in dehydrogenative coupling reactions, the formation of amides (or imines, depending on the mechanism) between benzyl alcohol and benzyl amine was studied, which is typically more challenging than the homo-coupling of alcohols. The procedure followed is described by Milstein and co-workers, and the results
are displayed in Table 4. When complex 1 was used in combination with benzyl alcohol and benzyl amine, 26% conversion was obtained, but the main product was benzyl benzoate (entry 1). Conversely, when complex 2 was used as catalyst, only 3% conversion was observed after 17 hours, of which 72% was the corresponding amide (entry 2). Entry 3 shows the known active Ru(PNN) complex, that needs only 12 hours for 91% conversion, of which the main product is the desired amide. When the primary benzyl amine was replaced by the secondary methylbenzylamine, the same trend was observed. Entry 4 shows that complex 1 was quite unable to react with the amine, as 94% of the formed products turned out to be the ester. For complex 2, only 6% conversion was obtained, of which the ratio between the amide and ester was nearly equal (entry 5). The difference between the different reactive sites of the complexes is clearly demonstrated. Complex 2, which resembles active Ru(PNN) catalysts, is able to convert these substrates into the amide, although in very poor yields. Complex 1, proposedly utilizing the hydroxyl functionality, demonstrated poor ability in the alcohol—amide heterocoupling, as ester formation was predominant. It could be that the pyridonato/pyridone unit interacts more favorably with alcohols, leading to pre-organization of alcohol and alkoxide complex, which might enhance homo-coupling to form esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>R</th>
<th>T [°C]</th>
<th>t [h]</th>
<th>Conv. [%]</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>KO’Bu</td>
<td>H</td>
<td>117</td>
<td>40</td>
<td>26</td>
<td>62 (E)</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>KO’Bu</td>
<td>H</td>
<td>117</td>
<td>17</td>
<td>3</td>
<td>72 (A)</td>
</tr>
<tr>
<td>3</td>
<td>RuPNN^{33}</td>
<td>KO’Bu</td>
<td>H</td>
<td>120</td>
<td>12</td>
<td>91</td>
<td>86 (A)</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>KO’Bu</td>
<td>Me</td>
<td>117</td>
<td>40</td>
<td>78</td>
<td>94 (E)</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>KO’Bu</td>
<td>Me</td>
<td>117</td>
<td>17</td>
<td>6</td>
<td>51 (A)</td>
</tr>
</tbody>
</table>

Conditions: 1 mmol alcohol, 1 mmol amine, 1 mol% catalyst, 1 mol% base, indicated temperature and reaction time in toluene (2 mL). Conversion and yield were determined by $^1$H NMR spectroscopy and GC analysis with p-xylene as internal standard. A = amide, E = ester.

3.2.7 Computational investigations into dihydrogen formation

As can be seen in the above proposed catalytic cycles, the central complex formed is $^{1\text{HH}}$, concomitant with the release of CO$_2$ (formic acid dehydrogenation) or aldehyde/ester (dehydrogenative coupling of alcohols). To support these proposed mechanisms, DFT calculations (BP86, def2-TZVP, disp3) were performed and the obtained energy profile is displayed in Figure 7. Both the hydroxy-pyridine/pyridone feature and the phosphinomethyl arm are included, to support the hypothesis that the former is the more accessible. The aromatized trans dihydride complex $^{1\text{HH}}$ was used as reference point (0.0 kcal mol$^{-1}$). Starting from this complex, transition state $\text{TS}'$ (H$_2$ formation over the pyridone) is 5.0 kcal mol$^{-1}$
higher in free energy, while the barrier for TS” (H₂ formation over the phosphinomethyl) is 22.5 kcal mol⁻¹. However, proton shuttling via 'BuOH, obtained from protonation of KO'Bu, is most likely involved, which could lower the barrier significantly.³¹ Indeed, the barrier of TS’PS’ is lowered by 2.7 kcal mol⁻¹, but still lies 14.8 kcal mol⁻¹ higher in energy than TS’. Subsequent formation of intermediate Int’ is exergonic by 5.0 kcal mol⁻¹, and is therefore thermoneutral compared to 1HH. Species Int” lies slightly uphill in energy by 4.7 kcal mol⁻¹. Liberation of dihydrogen is found to be exergonic for both complexes, by roughly 4 kcal mol⁻¹. Overall, the formation of dihydrogen is exergonic by ~4.1 kcal mol⁻¹ for 1’ and slightly endergonic by 0.9 kcal mol⁻¹ for 1”, demonstrating that the pathway is both kinetically and thermodynamically favored via the hydroxy-pyridine species.

**Figure 7.** Potential energy diagram (DFT, BP86, def2-TZVP, disp3) for the formation of 1’, 1” and dihydrogen from 1HH; ΔG°₂₇₃K is in kcal mol⁻¹, with complex 1HH taken as reference point. One hydride ligand and the CO ligand were omitted for clarity in the depiction of TS’, TS”, TS’PS’, Int’ and Int”.

To assess the generality and to confirm the results obtained with the BP86 functional, we also performed calculations with the TPSS and B3LYP functionals, although without dispersion corrections. The calculated energies can be found in Table 5.
Table 5. Calculations in kcal mol⁻¹. The TPSS and B3LYP functional are not corrected by disp3.

<table>
<thead>
<tr>
<th></th>
<th>BP86</th>
<th>TPSS</th>
<th>B3LYP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1'</td>
<td>-4.1</td>
<td>-6.7</td>
<td>-9.8</td>
</tr>
<tr>
<td>1''</td>
<td>0.9</td>
<td>-2.0</td>
<td>-4.9</td>
</tr>
<tr>
<td>Int'</td>
<td>0.0</td>
<td>-2.0</td>
<td>-2.1</td>
</tr>
<tr>
<td>Int''</td>
<td>4.7</td>
<td>4.6</td>
<td>4.7</td>
</tr>
<tr>
<td>TS'</td>
<td>5.0</td>
<td>6.2</td>
<td>7.7</td>
</tr>
<tr>
<td>TS''</td>
<td>22.5</td>
<td>24.4</td>
<td>28.1</td>
</tr>
</tbody>
</table>

These calculations confirm our hypothesis that this bipy-PNN ligand scaffold benefits from the hydroxy-pyridine / pyridonate functionality as a more accessible cooperative site, as is also demonstrated by the dehydrogenation of formic acid and dehydrogenative coupling of alcohols. The reason for the poor catalytic activity in some catalytic transformations remains unknown. However, the performed calculations only concern the step of dihydrogen formation, whereas other, not-calculated, steps could be the challenging part of these conversions. Furthermore, competing, non-productive pathways could also be active, that do not lead to the desired products.

3.3 Conclusions

Novel bipyridine PNN(O) pincer ligands L1, L2 and L1Me were prepared, EW bearing two different cooperative sites. Coordination of L1 and L1Me to ruthenium has led to Ru(Cl)(CO)(H)(L) complexes 1 and 2, respectively, which were crystallographically characterized. Deprotonation of complex 1, which was expected to react with weak bases, could indeed be carried out using DBU, KHMDS and KOtBu, whereas complex 2 was only deprotonated by the stronger bases KHMDS and KOtBu. Application of complex 1 in the dehydrogenation of formic acid resulted in rather poor turnover frequencies of 30 h⁻¹, but did produce clean, CO-free dihydrogen. It also showed to be a robust catalyst, as it did not decompose after several runs. Using the dearomatization-reprotonation strategy of complex 1 in the dehydrogenative coupling of alcohols into esters, resulted in 90% conversion for benzyl alcohol and full conversion for 1-butanol. The more challenging dehydrogenative coupling of benzyl alcohol and benzyl amine into benzyl benzamide led to small amounts of amide, as the main product proved to be the ester. In spite of the performed calculations, which indicate that this ligand system should have enhanced reactivity compared to the parent pincers, the reason why the catalytic activity is not higher, especially in the formic acid dehydrogenation, remains unknown. However, the calculations we have performed only concern the step that involves the formation of dihydrogen. Whereas the results indicate that this step is indeed lower in activation energy, it implies that another step of the catalytic cycle is higher in energy, or that a competing, non-productive pathway is active. For example, coordination of the substrate or activation of the O-H bond could be challenging steps, but those stages have not been calculated.
3.4 Experimental Section

General procedures

Solvents were either distilled over suitable drying agents or dried using an MBraun SPS (Solvent Purification System). All experiments were carried out under an inert gas atmosphere using standard Schlenk techniques. All chemicals were commercially available and used without further purification, unless described otherwise. The $^{1}$H, $^{13}$C{($^{31}$P}), $^{31}$P{($^{1}$H)} and $^{13}$C{($^{1}$H)} NMR spectra were recorded at room temperature on a Bruker AV400 (at 400, 162, and 100 MHz, respectively) and on a Bruker DRX500 (at 500, 202, and 126 MHz, respectively) and calibrated to the residual proton and carbon signals of the solvent. High resolution mass spectra were recorded on a JEOL AccuTOF GC v 4g, JMS-T100GCV mass spectrometer (FD) and on a JEOL AccuTOF LC, JMS-T100LP mass spectrometer (CSI). IR spectra were recorded with a Bruker Alpha-p FT-IR spectrometer operated in the ATR mode. GC analysis for esters and amides was performed on a Thermo Scientific Trace GC Ultra equipped with a Restek RTX-200 column (30 m x 0.25 mm x 0.5 μm). Temperature program: Initial temperature 50 °C, hold for 4 min, heat to 130 °C with 30 °C/min, hold for 2 min, heat to 250 °C with 50 °C/min, hold for 9 min. Inlet temperature 200 °C, split ratio of 60, 1 mL/min carrier flow, FID temperature 250 °C.

Syntheses and characterization

2-methyl-6-(tributylstannyl)pyridine. This synthesis was based on a literature procedure. 2-Bromo-6-methylpyridine (7.56 g, 43.9 mmol) was dissolved in THF (20 mL) and cooled to -78 °C. A 2.5M solution of n-BuLi in hexanes (17.6 mL, 43.9 mmol) was added over the course of 20 minutes and stirred for 3 more hours at -78°C. Tributyltin chloride (14.3 g, 43.9 mmol) was added, and the mixture was allowed to warm up to room temperature overnight. The reaction was quenched with saturated NH$_4$Cl solution (40 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with water and brine (both 50 mL), dried over Na$_2$SO$_4$ and concentrated in vacuo to give a yellow oil (16.58 g, quantitative). $^{1}$H NMR (300 MHz, chloroform-$d$, ppm): δ 7.89 (t, $J_{HH}$ = 7.5 Hz, 1H, pyH), 7.20 (d, $J_{HH}$ = 7.5 Hz, 1H, pyH), 6.98 (dd, $J_{HH}$ = 7.9, 1.1 Hz, 1H, pyH), 2.57 (s, 3H, Me), 1.64 - 1.54 (m, 6H, SnBu), 1.36 (h, $J_{HH}$ = 7.2 Hz, 6H, SnBu), 1.18 - 1.07 (m, 6H, SnBu), 0.91 (t, $J_{HH}$ = 7.3 Hz, 9H, SnBu). $^{31}$C NMR (75 MHz, chloroform-$d$-ppm): δ 173.04 (s, 1C, pyC), 158.57 (s, 1C, pyC), 133.23 (s, 1C, pyCH), 129.33 (s, 1C, pyCH), 121.45 (s, 1C, pyCH), 29.13 (s, 3C, CH$_3$), 27.37 (s, 3C, CH$_3$), 24.93 (s, 1C, Me), 13.72 (s, 3C, CH$_3$), 9.85 (s, 3C, CH$_3$). HRMS (FD+) (C$_{18}$H$_{33}$NSn): m/z: calc 383.16380 (M)$^{+}$, found: 383.17925 [M]$^{+}$.

Compound A, 6-methoxy-6'-methyl-2,2'-bipyridine. This synthesis was based on a literature procedure. 2-Methoxy-6-bromopyridine (8.2 g, 43.4 mmol), Pd(PPh$_3$)$_4$ (0.5 g, 0.434 mmol), LiCl (3.8 g, 96.8 mmol) and 2-methyl-6-(tributylstannyl)pyridine (16.58 g, 43.4 mmol) were dissolved in toluene (50 mL) and stirred at reflux overnight. The solution was cooled down to room temperature and the organic layer was extracted thrice with a 6M HCl solution (3 x 50 mL). The combined aqueous layers were neutralized with a saturated solution of NH$_4$OH and then extracted with DCM (3 x 75 mL). The organic layer was washed with water and brine (both 50 mL), dried over Na$_2$SO$_4$ and finally concentrated in vacuo to yield a yellow oil (8.68 g, quantitative). $^{1}$H NMR (300 MHz, chloroform-$d$, ppm): δ 8.22 (d, $J_{HH}$ = 7.9 Hz, 1H, pyH), 8.06 (dd, $J_{HH}$ = 7.4, 0.8 Hz, 1H, pyH), 7.71 (td, $J_{HH}$ = 7.9, 1.8 Hz, 1H, pyH), 7.23 - 7.44 (m, 2H, pyH), 6.78 (dd, $J_{HH}$ = 8.2, 0.8 Hz, 1H, pyH), 4.07 (s, 3H, OMe), 2.65 (s, 3H, Me). $^{31}$C NMR (75 MHz, chloroform-$d$-ppm): δ 163.41 (s, 1C, pyC), 157.56 (s, 1C, pyC), 155.36 (s, 1C, pyC), 153.73 (s, 1C, pyC), 139.14 (s, 1C, pyCH), 136.71 (s, 1C, pyCH), 122.94 (s, 1C, pyCH), 117.84 (s, 1C, pyCH), 113.66 (s, 1C, pyCH),
110.80 (s, 1C, pyCH), 52.95 (s, 1C, OMe), 24.54 (s, 1C, Me). HRMS (FD+) \((\text{C}_{29}\text{H}_{30}\text{N}_{3}\text{O})\): \(m/z\): calc 200.0946 (M)+, found: 200.0936 (M)+.

**Ligand L1Me.** 6-methoxy-6'-methyl-2,2'-bipyridine (1 g, 4.99 mmol) was dissolved in diethyl ether (20 mL) and then cooled to -78 °C. \(\text{n-BuLi} (2.5\text{M solution in hexanes}) (2\text{ mL}, 5.01\text{ mmol}) was added over the course of 20 minutes and the reaction was stirred for an additional hour at -78 °C. CIPB\(\text{Bu}_3\) (0.902 g, 5 m mol) was added and the reaction mixture was allowed to warm up to room temperature overnight. The mixture was stirred for an additional 6 days and its progress was checked by \(\text{\textsuperscript{31}P NMR}\) every day. Degassed water (20 mL) was added and the diethyl ether layer was poured over a fritted 

These diethyl ether layers were also poured over \(\text{Na}_2\text{SO}_4\) and combined together. The solvent was evaporated in vacuo to yield a white powder, which was washed twice in pentane (4 and 2 mL). \(\text{\textsuperscript{1}H NMR}\) (300 MHz, acetone-\(\text{d}_6\), ppm): \(\delta\) 8.23 (d, \(J_H = 7.9\text{ Hz}, 1\text{H, pyH}), 8.12\) (d, \(J_H = 7.4\text{ Hz}, 1\text{H, pyH}), 7.80\) (td, \(J_H = 7.8, 4.3\text{ Hz}, 2\text{H, pyH}), 7.44\) (d, \(J_H = 7.8\text{ Hz}, 1\text{H, pyH}), 7.41\) (d, \(J_H = 8.2\text{ Hz}, 1\text{H, pyH}), 4.03\) (s, 3H, methoxy), 3.16 (d, \(J_P = 2.7\text{ Hz}, 2\text{H, CH}_2\)). 1.19 (d, \(J_P = 10.7\text{ Hz}, 18\text{H, P}^\text{Bu}_3\). \(\text{\textsuperscript{31}P NMR}\) (121 MHz, acetone-\(\text{d}_6\), ppm): \(\delta\) 36.4. \(\text{\textsuperscript{13}C NMR}\) (75 MHz, CD\(\text{Cl}_3\), ppm): \(\delta\) 163.58 (s, 1C, pyC), 158.55 (s, 1C, pyC), 146.96 (s, 1C, pyC), 142.15 (s, 1C, pyC), 139.65 (s, 1C, pyC), 136.89 (s, 1C, pyCH), 129.99 (s, \(J_H = 7.4\text{ Hz}, 1\text{C, pyCH}), 123.21\) (s, 1C, pyCH), 113.32 (s, 1C, pyCH), 110.70 (s, 1C, pyCH), 52.75 (s, 1C, OMe), 31.55 \(d,J = 25.5\text{ Hz}, 1\text{C, CH}_2\), 31.50 \(d,J = 23.2\text{ Hz}, 2\text{C, P}^\text{Bu}_3\), 29.07 (d, \(J = 13.7\text{ Hz}, 6\text{C, P}^\text{Bu}_3\). HRMS (FD+) \((\text{C}_{29}\text{H}_{30}\text{N}_{3}\text{O})\): \(m/z\): calcd 344.18610; found, 344.19566 (M)+. 

**Ligand L1.** This synthesis is a modified literature procedure.\(^3\) \(\text{Ligand L1Me}\) (1.055 g, 3.065 mmol) was dissolved in 33% HBr in glacial acetic acid (25 mL) and stirred at reflux overnight. The reflux cooler was connected to a gas trap filled with NaOH (1M). The solution was cooled to room temperature, and neutralized with a degassed saturated aqueous solution of NaHCO\(_3\). The mixture was extracted with dichloromethane (3 \(\times\) 20 mL). The DCM layers were poured over \(\text{Na}_2\text{SO}_4\) and evaporated in vacuo to yield a dark red oil, which was washed with a degassed saturated solution of NaHCO\(_3\). The product was obtained as a purple solid (1.012 g, 69%). 

\(\text{Compound B'}.\) Compound A (9.3 g, 43.4 mmol) was dissolved in 33% HBr in glacial acetic acid (30 mL) and stirred at reflux overnight. The reflux cooler was connected to a gas trap filled with 1M NaOH. The solution was cooled down to room temperature, and neutralized with a saturated aqueous solution of NaHCO\(_3\). The mixture was extracted with DCM (3 \(\times\) 70 mL) and the combined organic layers were washed with water and brine (both 50 mL). The solution was dried over \(\text{Na}_2\text{SO}_4\) and concentrated in vacuo to yield a dark red oil (4.35 g, 54%). \(\text{\textsuperscript{1}H NMR}\) (300 MHz, chloroform-\(d\), ppm): \(\delta\) 11.37 (s, 1H, OH), 7.72 (t, \(J = 7.7\text{ Hz}, 1\text{H, pyH}), 7.64\) (d, \(J = 7.8\text{ Hz}, 1\text{H, pyH}), 7.53\) (dd, \(J = 9.1, 7.0\text{ Hz}, 1\text{H, pyH}), 7.23\) (d, \(J = 7.5\text{ Hz}, 1\text{H, pyH}), 6.85\) (dd, \(J = 7.0, 0.9\text{ Hz}, 1\text{H, pyH}), 6.67\) (dd, \(J = 9.1, 0.9\text{ Hz}, 1\text{H, pyH}), 2.62\) (s, 3H, methyl). \(\text{\textsuperscript{31}C NMR}\) (75 MHz, chloroform-\(d\), ppm): \(\delta\) 163.35 (s, 1C, pyC), 154.56 (s, 1C, pyC), 153.76 (s, 1C, pyC), 147.07 (s, 1C, pyC), 146.96 (s, 1C, pyC), 142.15 (s, 1C, pyC), 137.76 (s, 1C, pyCH), 128.21 (s, 1C, pyCH), 125.21 (s, \(J_{CH} = 8.3\text{ Hz}, 1\text{C, pyCH}), 120.39\) (s, 1C, pyCH), 104.27 (s, 1C, pyCH), 31.62 (d, \(J_{PC} = 22.2\text{ Hz}, 1\text{C, CH}_2\), 30.92 (d, \(J_{PC} = 24.3\text{ Hz}, 2\text{C, P}^\text{Bu}_3\), 28.98 (d, \(J_{PC} = 13.6\text{ Hz}, 6\text{C, P}^\text{Bu}_3\). HR-MS (FD+) \((\text{C}_{29}\text{H}_{30}\text{N}_{3}\text{O})\): \(m/z\): calcd 344.2017 (M)+, found: 344.19566 (M)+.
(s, 1C, pyC), 141.06 (s, 1C, pyCH), 137.55 (s, 1C, pyCH), 124.30 (s, 1C, pyCH), 121.43 (s, 1C, pyCH), 116.79 (s, 1C, pyCH), 103.27 (s, 1C, pyCH), 24.23 (s, 1C, CH3).

**Compound C’**. This synthesis is carried out by using a modified literature procedure.34 A mixture of compound B’ (1.58 g, 8.5 mmol), DMAP (0.104 g, 0.85 mmol), imidazole (1.45 g, 21.3 mmol), and tert-butyldimethylsilyl chloride (1.28 g, 8.5 mmol) was dissolved in DMF (20 mL) and stirred overnight at room temperature. The reaction mixture was poured into 80 mL of distilled water and then washed with diethyl ether (3 × 50 mL). The ether layers were combined, washed with water (50 mL) and brine (50 mL) and dried over Na2SO4. All volatiles were removed in vacuo. The obtained yellow oil was poured over a silica plug and washed with diethyl ether to afford 6-((tert-butyldimethylsilyl)oxy)-6’-methyl-2,2’-bipyridine in 72% (1.83 g) yield as a pale yellow oil that crystallized over time. 1H NMR (400 MHz, CDCl3, ppm): δ 8.11 (d, J = 7.8 Hz, 1H), 8.05 (d, J = 7.5 Hz, 1H), 7.70 (t, J = 7.8 Hz, 2H), 7.15 (d, J = 7.6 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 2.64 (s, 3H), 1.03 (s, 9H), 0.43 (s, 6H).

**Compound D’**. This product is prepared via a modified literature procedure.34 LDA was prepared by dissolving diisopropylamine (2.56 mL, 18.3 mmol) in 50 mL dry THF under argon atmosphere and the flask was placed in an ice bath. To this mixture, n-BuLi was added while stirring. After 15 minutes, a solution of compound C’ (1.83 g, 6.1 mmol) in 20 mL THF was added to the LDA solution at 0 °C. After stirring for 3 hours at 0 °C, ditert-butylphosphine chloride (1.16 mL, 6.1 mmol) was added slowly and the mixture was allowed to warm up to room temperature overnight. The mixture was diluted with 50 mL diethyl ether and washed with three portions of degassed water. The organic layer was dried over Na2SO4 and all volatiles were removed in vacuo. The crude solid was directly used in the synthesis of L2.

**Ligand L2**. This product is prepared via a modified literature procedure.34 Compound D’ was dissolved in 50 mL THF. Tetrabutylammonium fluoride trihydride (1.59 g, 6.1 mmol) was added and the solution was stirred overnight at room temperature. The reaction mixture was diluted with 50 mL diethyl ether and washed with three portions of degassed water. The organic layer was dried over Na2SO4 and all volatiles were removed in vacuo. The solid residue was suspended in hexane. The suspension was poured over a silica plug and was rinsed with additional hexane. The product was flushed off with dichloromethane and it was then concentrated under reduced pressure. Ligand L2 was obtained in 19% yield as a white powder. 1H NMR (300 MHz, chloroform-d, ppm): δ 10.35 (s, 1H), 7.68 – 5.74 (m, 2H), 7.47 (dd, J = 9.2, 6.9 Hz, 1H), 7.36 (dd, J = 7.1, 1.4 Hz, 1H), 6.84 – 6.71 (m, 1H), 6.64 (dd, J = 9.1, 0.9 Hz, 1H), 3.10 (d, J = 3.1 Hz, 1H), 1.28 (d, J = 10.7 Hz, 9H), 1.17 (d, J = 11.8 Hz, 9H), 0.72 (s, 9H), 0.33 (s, 3H), 0.31 (d, J = 2.0 Hz, 3H). 31P NMR (162 MHz, chloroform-d, ppm): δ 47.6. 31C NMR (75 MHz, chloroform-d, ppm): δ 164.11 (s), 162.62 (s), 146.59 (s), 141.92 (s), 140.46 (s), 136.91 (s), 127.34 (s), 121.97 (s), 116.15 (s), 102.74 (s), 35.23 (d, J = 31.1 Hz), 33.70 (d, J = 31.6 Hz), 31.57 (d, J = 8.8 Hz), 31.38 (d, J = 9.5 Hz), 30.52 (s), 27.37 (s), 18.89 (d, J = 5.8 Hz), -3.03 (d, J = 14.7 Hz), -4.27 (d, J = 1.4 Hz). HRMS (CSI+) (C35H40N2OPSi): m/z calcd, 445.28040; found, 445.28401.
Complex 1, Ru(Cl)(CO)(H)(L1). RuCl(Cl)(CO)(H)(PPh3)3 (342.7 mg, 0.36 mmol) and L1 (118.8 mg, 0.36 mmol) were dissolved in 10 mL THF. The solution was heated to 50 °C and stirred overnight. The reddish-orange mixture was allowed to cool down to room temperature and was filtered. The solid was washed with cold Et2O (3 x 5 mL) and an orange solid was obtained (120.1 mg, 67%). 1H NMR (500 MHz, acetonitrile-d3, ppm): δ 13.23 (s, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.99 (t, J = 7.9 Hz, 1H), 7.88 (t, J = 7.9 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.2 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 3.85 (dd, J = 17.3, 11.2 Hz, 1H), 3.71 (dd, J = 17.6, 7.9 Hz, 1H), 1.44 (d, J = 13.6 Hz, 9H), 1.23 (d, J = 13.6 Hz, 9H), -2.16 (s, 3H), -1.487 (d, J = 24.1 Hz, 1H). 31P NMR (202 MHz, acetonitrile-d3, ppm): δ 105.0 (s).

Complex 2, Ru(Cl)(CO)(H)(L1Me). This complex was synthesized in the same manner as complex 1 from L1Me (152.5 mg, 0.334 mmol) and RuCl(Cl)(CO)(H)(PPh3)3 (318.2 mg, 0.334 mmol), and was obtained as an orange red powder (155.0 mg, 91%). 1H NMR (400 MHz, acetonitrile-d3, ppm): δ 8.17 (d, J = 8.1 Hz, 1H), 8.12 (t, J = 8.1 Hz, 1H), 8.04 (t, J = 8.1 Hz, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 8.6 Hz, 1H), 4.16 (s, 3H), 3.87 (dd, J = 17.4, 11.3 Hz, 1H), 3.73 (dd, J = 17.3, 7.9 Hz, 1H), 1.42 (d, J = 13.7 Hz, 9H), 1.22 (d, J = 13.7 Hz, 9H), -14.93 (d, J = 24.3 Hz, 1H). 31P NMR (162 MHz, acetonitrile-d3, ppm): δ 105.9 (s). 31C NMR (126 MHz, CD3CN, ppm): δ 208.71 (d, J = 15.5 Hz), 164.83 (s), 161.75 (s), 155.52 (d, J = 32.3 Hz), 139.51 (s), 136.98 (s), 128.84 (s), 122.64 (d, J = 9.0 Hz), 119.68 (s), 115.21 (s), 107.53 (s), 56.81 (s), 37.53 - 37.13 (m), 36.33 (d, J = 24.7 Hz), 29.79 (d, J = 4.3 Hz), 28.74 (d, J = 3.4 Hz). HR-MS (CSI) (C20H18ClN2O3P)Ru: m/z calcld, 496.06204, 461.0932 [M-Cl]; found, 461.0824 [M-Cl]. IR (ATR, cm⁻¹): 1995 (m), 1916 (s), 1598 (m), 1566 (m).

Complex 1', Ru(CO)(H)(L1*). In an NMR tube, complex 1 (5.5 mg, 0.011 mmol) and KO(Bu)1 (1.2 mg, 0.011 mmol) were charged in 0.7 mL THF-d8, and the tube was shaken thoroughly. A red solution was obtained immediately and NMR was measured. 1H NMR (500 MHz, THF-d8, ppm): δ 7.70 (br s, 1H), 7.50 (br s, 1H), 7.22 (d, J = 7.4 Hz, 1H), 7.16 (d, J = 7.4 Hz, 1H), 6.54 (d, J = 7.8 Hz, 1H), 6.46 (d, J = 6.8 Hz, 1H), 3.94 (dd, J = 15.3, 8.0 Hz, 1H), 3.42 (dd, J = 14.3, 7.0 Hz, 1H), 1.80 (d, J = 13.1 Hz, 9H), 1.67 (d, J = 13.1 Hz, 9H), -19.37 (d, J = 23.7 Hz, 1H). 31P NMR (202 MHz, THF-d8): δ 102.5 (s).

Complex 2', Ru(CO)(H)(L1Me*). In an NMR tube, complex 2 (10.0 mg, 0.02 mmol) and KO(Bu)1 (2.2 mg, 0.02 mmol) were charged in 0.7 mL THF-d8, and the tube was shaken thoroughly. A black green mixture was obtained immediately and NMR was measured. 1H NMR (500 MHz, THF-d8, ppm): δ 7.80 (t, J = 8.0 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 6.28 (d, J = 8.8 Hz, 1H), 6.24 (d, J = 8.3 Hz, 1H), 6.06 (d, J = 6.8 Hz, 1H), 3.36 (s, 1H), 1.31 (d, J = 12.4 Hz, 18%), -21.32 (d, J = 6.1 Hz, 1H). 31P NMR (202 MHz, THF-d8, ppm): δ 95.2 (s). 31C NMR (126 MHz, THF-d8, ppm): δ 206.81 (d, J = 17.2 Hz), 168.81 (d, J = 18.3 Hz), 160.81 (s), 140.05 (s), 138.76 (s), 135.03 (s), 128.85 (s), 127.80 (d, J = 7.9 Hz), 116.75 (d, J = 17.2 Hz), 113.94 (s), 99.91 (s), 65.62 (d, J = 50.6 Hz), 36.01 (d, J = 24.5 Hz), 29.86 (d, J = 4.3 Hz).
**Complex 3, Ru(CO)(H)L1(OBz).** In an NMR tube, complex 1 (11.2 mg, 0.023 mmol) and KOtBu (2.5 mg, 0.023 mmol) were charged in 0.7 mL toluene-d8, the tube was shaken thoroughly and cooled to -32 ºC. To the brown red solution was added benzyl alcohol (2.5 µL, 0.023 mmol) and the solution turned yellow immediately. NMR was measured. 1H NMR (400 MHz, toluene-d8, ppm): δ 8.20 (br s, 1H), 7.58 – 6.83 (m, 6H), 6.76 (d, J = 11.5 Hz, 1H), 6.69 (br s, 1H), 6.57 (br s, 1H), 6.42 (d, J = 8.6 Hz, 1H), 6.09 (br s, 1H), 3.54 (br s, 2H), 3.35 (d, J = 10.6 Hz, 2H), 1.23 (d, J = 13.6 Hz, 18H), -16.28 (t, J = 21.0 Hz, 1H). 31P NMR (162 MHz, toluene-d8, ppm): δ 104.5 (s).

**General procedure for formic acid dehydrogenation experiments**

To a Schlenk equipped with a condenser and containing a magnetic stirrer, 10 mol% of complex 1 and 10 mol% of KOtBu, 1 mL of dioxane was added. The reaction mixture was heated to 75 ºC and stirred for 10 minutes. Formic acid was added (10 µL) and the evolved gas was collected via the experimental set-up depicted in Scheme 13. Evolved gases were analyzed with a G·A·S Compact GC (Rt-MSieve 5A 20 m x 0.32 mm + Rt-Q-bond 2 m x 0.32 mm). The amounts of mol converted were determined from the volumes of gas collected using equation 1a and 1b.

**Scheme 13.** Schematic representation of experimental set-up utilized in the catalytic dehydrogenation of formic acid.

\[
V_{H_2} = \frac{RT}{p} + b - \frac{a}{RT} = 24.49 \frac{L}{mol}
\]  \[1a\]

R = 8.3145 m³·Pa·mol⁻¹·K⁻¹
T = 298.15 K
p = 101325 Pa
b = 26.7·10⁻⁶ m³·mol⁻¹
a = 2.49·10⁻¹⁰ Pa·m³·mol⁻²

\[
V_{CO_2} = \frac{RT}{p} + b - \frac{a}{RT} = 24.42 \frac{L}{mol}
\]  \[1b\]

R = 8.3145 m³·Pa·mol⁻¹·K⁻¹
T = 298.15 K
p = 101325 Pa
b = 42.7·10⁻⁶ m³·mol⁻¹
a = 36.5·10⁻¹⁰ Pa·m³·mol⁻²
**General procedure for catalytic alcohol dehydrogenative esterification**

To a Schlenk containing a magnetic stirrer, 1 mol% of catalyst, and 1 mol% of base were added the distilled alcohol (1 mmol) as substrate, 10 μL p-xylene as internal standard, and 2 mL toluene. The mixture was stirred at 117 °C in an open system, unless stated otherwise. Aliquots were taken from the mixture during the reaction, which were subsequently filtered over a plug of silica and analyzed by GC and 1H NMR spectroscopy.

**General procedure for synthesis of amides from alcohols and amines**

To a Schlenk containing a magnetic stirrer, 1 mol% of catalyst, and 1 mol% of base were added the distilled alcohol (1 mmol) and amine (1 mmol) as substrate, 10 μL p-xylene as internal standard, and 2 mL toluene. The mixture was stirred at 117 °C in an open system, unless stated otherwise. Aliquots were taken from the mixture during the reaction, which were subsequently filtered over a plug of silica and analyzed by GC and 1H NMR spectroscopy.

**X-ray crystallography**

X-ray intensities were measured on a Bruker D8 Quest Eco diffractometer equipped with a Triumph monochromator (λ = 0.71073 Å) and a CMOS Photon 50 detector at a temperature of 150(2) K. Intensity data were integrated with the Bruker APEX2 software. Absorption correction and scaling was performed with SADABS. The structures were solved with the program SHELXL. Least-squares refinement was performed with SHELXL-2013 against F² of all reflections. Non-hydrogen atoms were refined with anisotropic displacement parameters. The H atoms were placed at calculated positions using the instructions AFIX 13, AFIX 43 or AFIX 137 with isotropic displacement parameters having values 1.2 or 1.5 times Ueq of the attached C atoms. N-H hydrogen atoms were refined freely with isotropic displacement parameters.

**Computational details**

Geometry optimizations were carried out with the Turbomole program package, coupled to the PQS Baker optimizer via the BOpt package. We used the BP86 functional in combination with the def2-TZVP basis set. Grimme’s dispersion corrections (version 3, disp3) were used to include Van der Waals interactions. For both the TPSS and B3LYP functional, geometry optimizations were carried out, but without the inclusion of dispersion corrections. All minima (no imaginary frequencies) and transition states (one imaginary frequency) were characterized by calculating the Hessian matrix. ZPE and gas-phase thermal corrections (273 K) were calculated from these analyses.

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**3.5 References**


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