ACS Catalysis

Research Article

pubs.acs.org/acscatalysis

Efficient Base-Free Hydrogenation of Amides to Alcohols and Amines Catalyzed by Well-Defined Pincer Imidazolyl−Ruthenium Complexes

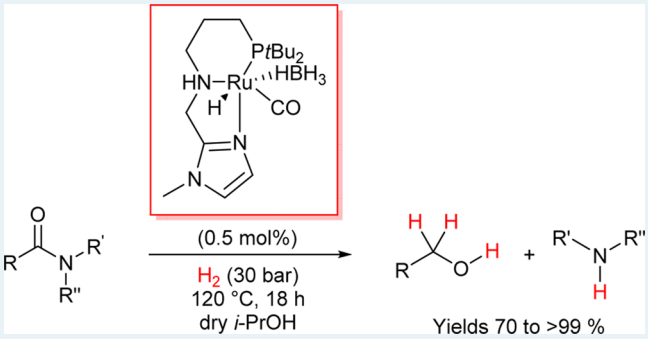
Jose R. Cabrero-Antonino,[†] Elisabetta Alberico,[†,‡] Hans-Joachim Drexler,[†] Wolfgang Baumann,[†] Kathrin Junge,[†] Henrik Junge,[†] and Matthias Beller*[,†]

[†]Leibniz-Institut für Katalyse e.V., Albert Einstein Strasse 29a, 18059 Rostock, Germany

[‡]Istituto di Chimica Biomolecolare, Consiglio Nazionale delle Ricerche, Tr. La Crucca 3, 07100 Sassari, Italy

Supporting Information

ABSTRACT: Novel homogeneous ruthenium catalysts bearing an imidazolylaminophosphino pincer ligand have been synthesized. The active catalyst allows for the hydrogenation of a range of amides under base-free conditions to afford the corresponding alcohols and amines in high yields.

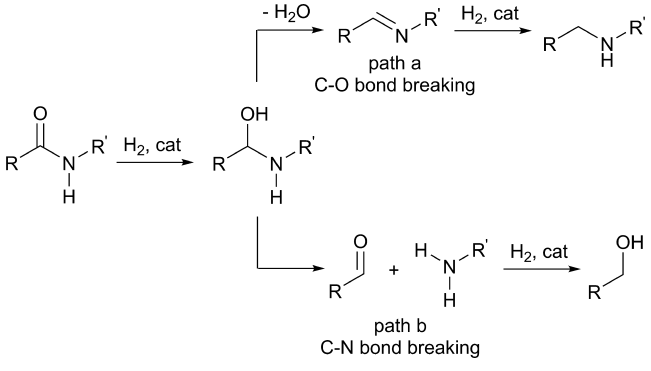


KEYWORDS: *amide hydrogenation, ruthenium, bifunctional catalysis, pincer complexes, homogeneous catalysis*

INTRODUCTION

Amines constitute an important class of compounds, which play a key role in numerous chemical processes. Today, they are commonly used on a bulk scale as building blocks for dyes, drugs, agrochemicals, polymers, and other materials. Among the methods amenable to the synthesis of amines,[1] catalytic reductions of nitroarenes and nitriles and reductive amination of carbonyl compounds prevail in industry. In addition, catalytic hydrogenation of amides using molecular hydrogen[2] offers an atomically economical and waste-free methodology (Scheme 1, path a) compared to the traditional reduction using metal hydrides,[2a] boranes,[3] or silanes.[4]

Scheme 1. Possible Reaction Pathways for the Reduction of Amides with Hydrogen



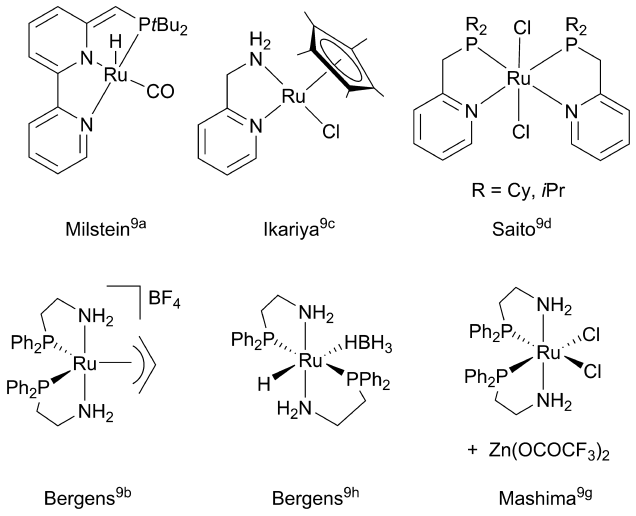
Unfortunately, because of the low electrophilicity of the carbonyl group, the reduction of amides with molecular hydrogen occurs in general at elevated pressures and very high temperatures, although recent improvements using heterogeneous catalysts have been achieved.[5] However, a drawback associated with the use of this latter catalysts is their incompatibility with aromatic groups and multiple C−C and C−X bonds that are likewise reduced. To overcome these problems, the development of more active molecularly defined catalysts is desirable. In this respect, the recent work on ruthenium complexes with 1,1,1-tris(diphenylphosphinomethyl)ethane (Triphos) as a ligand, which operate in the presence of an acid cocatalyst, is also noteworthy[6] yet has a rather limited scope and still requires temperatures of >200 °C.

Recently, different homogeneous catalysts that rely on metal−ligand cooperation (bifunctional catalysis)[7] have been disclosed for the reduction of amides under much milder conditions. Here, alternative reactivity is observed, and the initial reduction of the carboxylic group is followed by collapse of the intermediate hemiaminal to afford the corresponding alcohol and amine (Scheme 1, path b).[8] Notably, this transformation offers the possibility of accessing amines and alcohols from amides and might be used as a selective deprotection methodology. The structures of the known catalysts for amide hydrogenolysis are shown in Chart 1: with the exception of Milstein's and Bergen's BH_4-modified

Received: September 3, 2015
Revised: November 4, 2015
Published: November 12, 2015

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

Chart 1. Bifunctional Ruthenium Catalysts That Promote the Hydrogenation of Amides According to Path b in Scheme 1



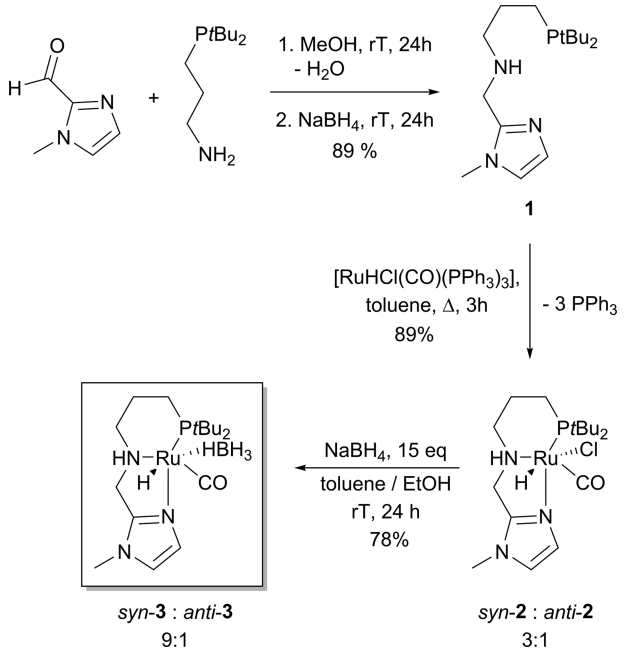
complexes, all catalysts require an excess of base to provide good activity.[9] In the past decade, pincer ligands that can engage in bifunctional catalysis have experienced widespread applications in catalysis.[10] So far, different sets of soft and hard donors have been combined, and the presence of hemilabile groups (NR_2 and Py) has been shown to be advantageous in ester[11] and amide reduction.[9a]

Following our previous work concerning the synthesis of bidentate imidazolyl phosphines and their successful application in the ruthenium-catalyzed hydrogenation of carboxylic acid derivatives,[12] we considered the synthesis of imidazole-based pincer ligands [P(NH)Im pincer motif]. 1-Methylimidazole, with a pK_{aH} of 7.0, has a basicity that is intermediate between that of the side arm nitrogen donors so far employed in NNP pincer ligands such as a pyridine (pyridine pK_{aH} = 5.2) and an amine moietiy NR_2 (fully saturated aliphatic amines have pK_{aH} values mostly within the range of 9−11).[13]

RESULTS AND DISCUSSION

The NNP pincer ligand, 3-(di-*tert*-butylphosphino)-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]propylamine **1** (Scheme 2), is easily assembled in a one-pot, two-step synthesis starting from commercially available 1-methyl-2-imidazolecarboxaldehyde and 3-(di-*tert*-butylphosphine)propylamine.[14] For the preparation of the corresponding ruthenium complex, [RuHCl(CO)(PPh_3)$_3$] was reacted with the ligand to afford (RuHCl(CO){3-(di-*tert*-butylphosphino)-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]propylamine}) **2** after displacement of PPh_3 in 89% yield, as a mixture of two isomers in a 3:1 ratio: each complex is characterized by a singlet in the $^{31}P\{^1H\}$ NMR spectrum at 78.11 ppm (major) and 74.19 ppm (minor), respectively. The signals of the hydride ligand in the ^1H NMR spectrum appear as doublets at −15.91 ppm (J_{HP} = 25.2 Hz) (major) and −16.25 ppm (J_{HP} = 23.0 Hz) (minor). The value of J_{HP} indicates that the hydride ligand is located, in both isomers, *cis* to the phosphorus donor, and their chemical shifts suggest that they must be *trans* to a donor of low *trans* influence.[15] Figure 1 illustrates the X-ray structure of the major isomer,[16] in which the ligand is coordinated to ruthenium in a meridional fashion with the CO ligand *trans* to the central aliphatic nitrogen. The metal hydride and the hydrogen on the nitrogen

Scheme 2. Synthesis of Pincer Ligand (1) and Its Ruthenium Complexes (2 and 3)



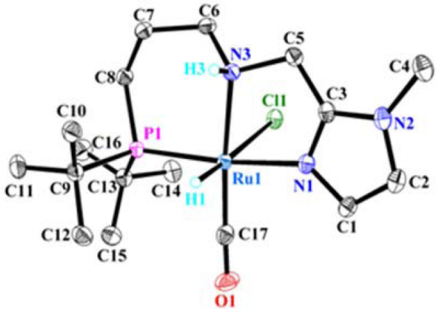


Figure 1. X-ray structure of *syn*-**2** with thermal ellipsoids drawn at the 30% probability level. Hydrogen atoms other than H1 and H3 have been omitted for the sake of clarity. Selected bond lengths (angstroms): Ru(1)−N(1), 2.1137(15); Ru(1)−N(3), 2.2219(16); Ru(1)−P(1), 2.2995(6); Ru(1)−Cl(1), 2.5741; Ru(1)−H(1), 1.52(2); Ru(1)−C(17), 1.809(2). Selected bond angles (degrees): N(1)−Ru(1)−N(3), 77.15(6); N(3)−Ru(1)−P(1), 94.14(4).

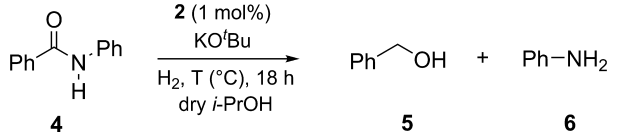
are located *syn* to the plane defined by the pincer ligand and ruthenium. Because a NOESY cross signal is present between the two hydrogens for the major isomer in solution, which is instead absent for the minor, the solid structure is assigned to the major isomer *syn*-**2**. Because of the similarity of the spectroscopic features of the two isomers, the minor must be the one in which the two hydrogens are oriented *anti* to each other, which is therefore denoted *anti*-**2**.

Preliminary catalytic tests to assess whether the new complex **2** is active in amide hydrogenation were run on the benchmark substrate benzanilide **4**. The reaction proceeded smoothly affording benzyl alcohol **5** and aniline **6** in quantitative yields using 1 mol % complex **2** in 2-propanol at 50 bar of H_2 and 150 °C in the presence of a slight excess of base (5 equiv to Ru) (entry 1, Table 1).

Indeed, 1 equiv of base was enough to secure quantitative yields of **5** and **6** (entry 2, Table 1), while no reaction took place in the absence of base (entry 3, Table 1). To our delight,

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

Table 1. Optimization of Reaction Conditions for the Hydrogenation of Benzanilide (4) with Ruthenium Complex 2



4 5 6

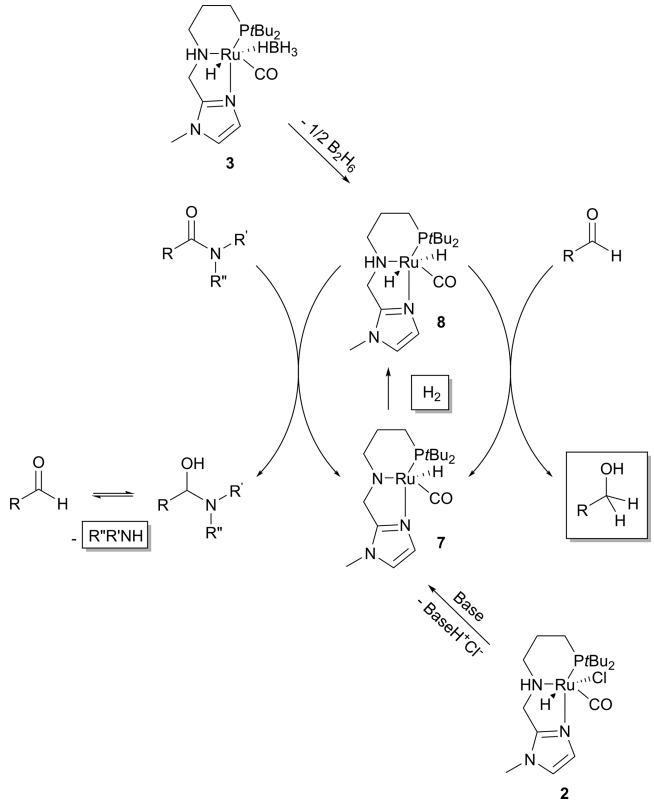
entry[a]	H_2 (bar)[b]	T (°C)	KO^{t}Bu (mol %)	conversion (%)[c]	5 (%)[c]	6 (%)[c]
1	50	150	5	100	>99	>99
2	50	150	1	100	>99	>99
3	50	150	–	–	–	–
4	30	120	1	100	>99	>99
5[d]	30	120	1	100	>99	>99
6	15	100	1	95	94	94
7	30	80	1	21	9	9

[a]Standard reaction conditions: benzanilide **4** (0.5 mmol, 100.62 mg), complex **2** (0.005 mmol, 1 mol %), KO^{t}Bu (1–5 mol %), dry 2-propanol (2 mL) under H_2. [b]Pressure of hydrogen at room temperature. [c]Conversion of **4** and yields of **5** and **6** were calculated by gas chromatography using hexadecane as an external standard. [d]The reaction was conducted with 0.5 mol % catalyst.

the catalyst was equally effective under milder conditions (30 bar of H_2 and 120 °C), even when the catalyst loading was reduced to 0.5 mol % (entries 4 and 5, Table 1). The reaction conditions could be mitigated further to 15 bar and 100 °C with only a minor erosion of yields (94%, entry 6, Table 1), but reducing the temperature to 80 °C led to detrimental results (9% yield, entry 7, Table 1).

These preliminary experiments suggest that the active catalytic species **7**, once formed by dehydrochlorination of catalyst precursor **2** (Scheme 3), might promote the reduction of amides even in the absence of base. Therefore, we prepared catalyst **3** in which the Cl ligand had been replaced by BH_4^- (Scheme 2), thus circumventing the need to use base to generate the active catalyst (Scheme 3).[17] Complex **3** was easily prepared in 78% isolated yield by treating **2** with an excess of $NaBH_4$. It was obtained as a white solid that can be handled in air, although it is sensitive to oxygen in solution and is better kept under argon if stored for a prolonged period of time. The complex was obtained as a mixture of two isomers in a a 90:10 ratio with singlet signals at 82.44 ppm (major) and 79.59 ppm (minor) in the $^{31}P\{^1H\}$ NMR spectrum. The coordinated hydrides appear as doublets in the ^1H NMR spectrum, at −13.00 ppm (major, J_{HP} = 22.7 Hz) and −13.56 ppm (minor, J_{HP} = 19.6 Hz), while the BH_4^- group gives rise to a broad four-proton resonance at −1.83 ppm. The chemical shift and the peak shape are indicative of an η^1-coordination mode, with a rapid exchange (on the NMR time scale) of the bridging and terminal hydrides.[18] On the basis of the similarity of the spectroscopic features between **2** and **3**, it is reasonable to assume that the same arrangement of ligands in the ruthenium coordination sphere is present in **3** as in **2**, with the pincer ligand arranged in a meridional fashion and the hydride and BH_4^- group disposed *trans* to each other in both isomers. Although the NOESY spectrum shows a through-space interaction between the hydride and the hydrogen on nitrogen in the major isomer for which the *syn* arrangement of the two might be then proposed, a cross peak in the same area could be observed for the hydride of the minor isomer, for which, however, the corresponding N*H* signal in the ^1H NMR

Scheme 3. Proposed Catalytic Cycle for Amide Reduction Promoted by Complexes 2 and 3



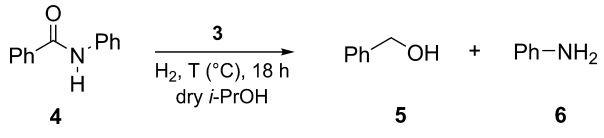
spectrum could not be identified because of overlapping. Therefore, we are unable to unequivocally assign the *syn* and *anti* configurations of **3**.

Reduction of benzanilide **4** in 2-propanol with 0.5 mol % **3** indeed afforded quantitative yields of benzyl alcohol **5** and aniline **6** under the conditions previously optimized for **2** [120 °C, 30 bar of H_2, 18 h, with no added base (entry 6, Table 2)]. The performance of catalyst **3** turned out to be affected by hydrogen pressure and temperature in the same way as **2** (Table 2). A striking difference in catalyst performance was observed in 2-propanol compared to that in other solvents, where either no reaction took place (entries 4–6, Table 3) or a 20% conversion was obtained at best with toluene (entry 7, Table 3). To test for transfer hydrogenation, a control experiment was performed in the absence of hydrogen gas at 120 °C using 0.5 mol % **3** (entry 14, Table 2). However, no reduction of benzanilide **4** was detected, excluding the possibility that 2-propanol might act as a hydrogen donor.

Next, several primary, secondary, and tertiary amides were tested in the presence of catalyst **3**. All substrates were reduced, affording excellent yields of the desired amine and/or alcohol under the optimized conditions [0.5 mol % **3**, 30 bar of H_2, 120 °C, in 2-propanol over 18 h (Table 4)]. For the less electrophilic amides, either a slightly higher catalyst loading, up to 2 mol %, more forcing conditions (50 bar of H_2 and 150 °C), or a combination of both allowed us to achieve very good yields. For example, reduction of benzyl-substituted (entry 3, Table 4) and fluoro- and chloro-substituted amides (entries 7–10 and 15, Table 4) proceeded smoothly. The possibility of effectively reducing heterocyclic amides, like 3-acetamidopyridine (entry 11, Table 4), three derivatives of nicotinic acid (entries 18–20, Table 4), including the primary amide

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47–54

Table 2. Optimization of Reaction Conditions for the Hydrogenation of Benzanilide 4 with Ruthenium Complex 3

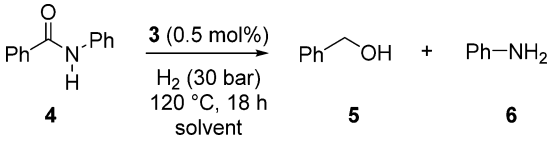


4 5 6

entry[a]	H_2 (bar)[b]	T (°C)	3 (mol %)	conversion (%)[c]	5 (%)[c]	6 (%)[c]
1	50	150	1	100	>99	>99
2	50	150	0.5	100	>99	>99
3	50	150	0.25	–	–	–
4	30	120	1	100	>99	>99
5[d]	30	120	1	100	99	99
6	**30**	**120**	**0.5**	**100**	**99**	**99**
7[d]	30	120	0.5	26	25	25
8	30	100	0.5	–	–	–
9	30	100	1	100	>99	>99
10	30	80	1	56	38	39
11	15	120	1	100	>99	>99
12	15	120	0.5	64	63	64
13	15	100	1	84	80	81
14[e]	–	120	0.5	–	–	–

[a]Standard reaction conditions: benzanilide **4** (0.5 mmol, 100.62 mg), complex **3** (0.005 mmol, 1 mol %), dry 2-propanol (2 mL) under H_2. [b]Pressure of hydrogen at room temperature. [c]Conversion of **4** and yields of **5** and **6** were calculated by gas chromatography using hexadecane as an external standard. [d]The reaction time was 3 h. [e]The reaction was conducted in a pressure tube without hydrogen.

Table 3. Influence of Solvent on the Hydrogenation of Benzanilide 4 with Ruthenium Complex 3



4 5 6

entry[a]	solvent	conversion (%)[b]	5 (%)[b]	6 (%)[b]
1	*i*-PrOH	100	>99	>99
2	*i*-PrOH/H_2O (10:1)	3	2	2
3	EtOH	8	7	6
4	MeOH	–	–	–
5	THF	–	–	–
6	1,4-dioxane	–	–	–
7	toluene	20	19	19

[a]Standard reaction conditions: benzanilide **4** (0.5 mmol, 100.62 mg), complex **3** (0.0025 mmol, 0.5 mol %), dry solvent (2 mL), H_2 (30 bar) at 120 °C over 18 h. Pressure of hydrogen at room temperature. [b]Conversion of **4** and yields of **5** and **6** were calculated by gas chromatography using hexadecane as an external standard.

nicotinamide, and *N*-acetyl-1,2,3,4-tetrahydroquinoline, giving 1,2,3,4-tetrahydroquinoline in quantitative yield (entry 16, Table 4), is worth mentioning. In addition, aliphatic tertiary amides such as *N*,*N*-dimethyloctanamide could be hydrogenated as well in excellent yield (entry 17, Table 4).

To date, the hydrogenolysis of primary amides has been scarcely investigated,[9] and no general catalyst for such transformations exists. Although **3** alone failed to catalyze the reduction of less reactive benzamide and octanamide, addition of 10 mol % KO^{t}Bu at 150 °C under 50 bar of H_2 gave satisfactory yields of the desired products. The positive influence of base is in agreement with the recent work by Bergens et al.[9f,h] and can be ascribed to the increased nucleophilicity of the coordinated hydride in the ruthenium dihydride that has been further deprotonated at the ligand aliphatic nitrogen. As shown in Table 5, various primary and secondary amides underwent successful hydrogenolysis.

More specifically, *N*-methyl- and *N*-cyclohexylbenzamide were hydrogenated in very good yields (entries 1 and 2, respectively, Table 5). Primary amides such as benzamide and *p*-dimethylamino- and *p*-methoxybenzamide afforded moderate to good yields of the corresponding benzyl alcohols (entries 3−5, respectively, Table 5), which were clearly dependent on the electrophilicity of the carbonyl group. Although in moderate yield, the primary amide 2-furamide was reduced, as well (entry 6, Table 5). Last but not least, octanamide, an aliphatic poorly reactive primary amide, could be reduced to octanol in good yield (61%, entry 7, Table 5).

CONCLUSIONS

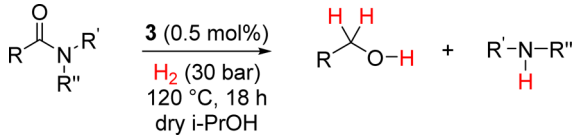
In conclusion, we have synthesized two novel ruthenium pincer complexes bearing an imidazolylaminophosphino ligand. The BH_4-substituted derivative **3** constitutes an efficient catalyst for the hydrogenolysis of different substituted amides to the corresponding alcohols and amines without base under relatively mild conditions. Less reactive aliphatic and aromatic primary amides have been successfully reduced with such a system for the first time. Interestingly, the novel catalyst possesses a modular structure by virtue of which its electronic and steric properties can be easily modified. In this respect, the preparation of a small library of new complexes is underway in our group.

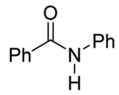
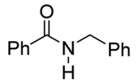
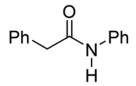
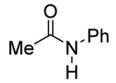
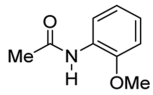
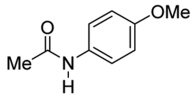
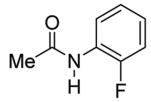
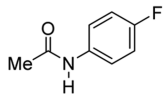
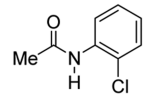
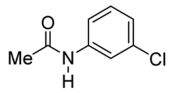
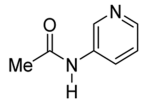
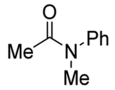
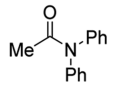
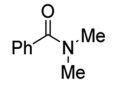
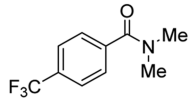
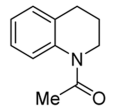
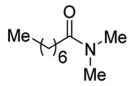
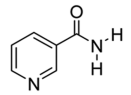
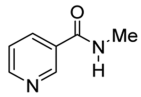
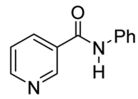
EXPERIMENTAL SECTION

Synthesis of 3-(Di-*tert*-butylphosphino)-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]propylamine (1). A solution of 3-(di-*tert*-butylphosphino)propylamine (500 mg, 2.46 mmol, 1 equiv) in 10 mL of methanol was added dropwise to a solution of 1-methyl-1*H*-imidazole-2-carbaldehyde (271 mg, 2.46 mmol, 1 equiv) in 10 mL of methanol. The resulting solution was stirred at room temperature for 24 h. It was then cooled to 0 °C with a water/ice bath and sodium borohydride (139 mg, 3.70 mmol, 1.5 equiv) added in one portion. The resulting solution was stirred at room temperature for 24 h. The solvent was then removed under reduced pressure and the oily residue partitioned between 20 mL of dichloromethane and 20 mL of distilled water. The organic phase was separated and the aqueous phase further extracted with dichloromethane (2 × 10 mL). The collected organic phases were dried over sodium sulfate and then filtered through a short pad of basic alumina. The solvent was removed under reduced pressure to leave 3-(di-*tert*-butylphosphino)-*N*-[(1-methyl-1*H*-imidazol-2-yl)-methyl]propylamine **1** as a very faint yellow liquid. The compound was 89% pure according to ^{31}P NMR (89% yield) and was used as such for the next step: ^{1}H{^{31}P} NMR (400 MHz, DCM-d_2) δ 6.89−6.85 (m, 2H, C$\underline{H}_{Im}$), 3.82 (s, 2H, Im-C$\underline{H}_2$), 3.68 (s, 3H, NC$\underline{H}_3$), 2.73 (t, J = 7.0 Hz, 2H, HN(C$\underline{H}_2$)), 1.71−1.61 (m, 2H, C$\underline{H}_2$), 1.54 (b, 1H, N$\underline{H}$), 1.41−1.36 (m, 2H, (C$\underline{H}_2$)P), 1.09 (s, 18H, C(C$\underline{H}_3$)$_3$); ^{1}H NMR (400 MHz, DCM-d_2) δ 1.14 (d, J_{HP} = 10.7 Hz, 18H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (101 MHz, DCM-d_2) δ 147.30 (s, $\underline{C}_{Im}$), 127.11 (s, $\underline{C}H_{Im}$), 121.41 (s, $\underline{C}H_{Im}$), 51.34 (d, J_{CP} = 13.8 HN(C$\underline{H}_2$)), 46.28 (s, Im-C$\underline{H}_2$), 32.95 (s, NC$\underline{H}_3$), 31.41 (d, J_{CP} = 21.2 Hz, $\underline{C}$(CH$_3$)$_3$), 31.24 (d, J_{CP} = 25.2 Hz, $\underline{C}H_2$), 29.78 (d, J_{CP} = 13.6 Hz,

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

Table 4. Hydrogenation of Amides Catalyzed by Complex 3 without Added Base



Run[a]	Amide	Conv. (%)[b]	Alcohol (%)[b]	Amine (%)[b]
1		100	>99	>99
2		75	70	67
3[c]		100	93	94
4		100	>99	>99
5		100	>99	>99
6		100	98	98
7[d]		100	>99	>99
8[e]		93	93	89
9[d]		100	98	97
10[f]		100	99	98
11		100	97	96
12		96	83	83
13		100	96	96
14		100	96	n.d.
15[e]		100	>99	n.d.
16		100	99	99
17		92	90	n.d.
18[c]		100	95	n.d.
19[g]		93	82	n.d.
20		100	99	99

[a]Reaction conditions: amide (0.5 mmol), complex(**3** (0.0025 mmol, 0.5 mol %, 1.10 mg), dry 2-propanol (2 mL), H_2 (30 bar) at 120 °C over 18 h. Pressure of hydrogen at room temperature in all cases. [b]Conversion and yields were calculated by gas chromatography using hexadecane as an external standard. [c]The reaction was conducted using 2 mol % catalyst under 50 bar of H_2 at 150 °C. [d]The reaction was conducted using 1 mol % catalyst. [e]The reaction was conducted using 1 mol % catalyst under 50 bar of H_2 at 150 °C. [f]The reaction was conducted using 2 mol % catalyst. [g]The reaction was conducted using 0.5 mol % catalyst under 50 bar of H_2 at 150 °C (n.d., not detected).

C($\underline{C}H_3$)$_3$), 19.02 (d, J_{CP} = 21.0 Hz, ($\underline{C}H_2$)P); $^{31}P\{^1H\}$ NMR (162 MHz, DCM-d_2) δ 28.71 (s).

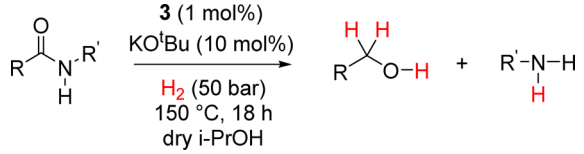
Synthesis of {Ru(H) (Cl) (CO)(3-(di-*tert*-butylphosphino)-*N*-((1-methyl-1*H*-imidazol-2-yl)methyl)-propylamine)} (2). To a suspension of {Ru(H) (Cl) (CO) (PPh_3)$_3$} (1.39 g, 1.46 mmol, 1 equiv) in toluene (10 mL) was added 3-(di-*tert*-butylphosphino)-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]propylamine **1** (478 mg, 1.61 mmol, 1.1 equiv). The suspension was refluxed for 3 h. During this time, the reaction mixture turned into a suspension of a white solid in a yellow solution. After being cooled, the suspension was filtered with the aid of a sintered glass frit, and the solid was rinsed several times with diethyl ether. The product was obtained as an off-white solid (601 mg, 89% yield). The complex was obtained as a mixture of two isomers, *syn*-**2** (74%) and *anti*-**2** (26%).

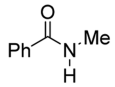
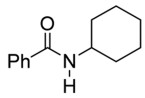
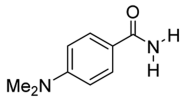
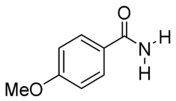
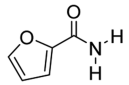
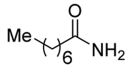
NMR spectra were recorded in DCM-d_2. However, in this solvent, the complex is not indefinitely stable as the hydride is slowly replaced by chloride.

syn-**2**. Yield 74%; $^1H\{^{31}P\}$ NMR (400 MHz, DCM-d_2) δ 7.15 (t, J = 1.2 Hz, 1H, =NC$\underline{H}_{Im}$=), 6.90 (bs, 1H, MeNC$\underline{H}_{Im}$=), 4.23 (dd, J = 14.7, 5.2 Hz, 1H, Im-C$\underline{H}_2$), 4.05 (bt, 1H, N$\underline{H}$), 3.60 (s, 3H, NC$\underline{H}_3$), 3.58 (dd, J = 14.7, 11.2 Hz, 1H, Im-C$\underline{H}_2$), 3.31 (ddd, J = 11.7, 5.6, 3.5 Hz, 1H, HN(C$\underline{H}_2$)), 2.66−2.48 (m, 1H, HN(C$\underline{H}_2$)), 2.24−2.15 (m, 1H, C$\underline{H}_2$), 2.06

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

Table 5. Hydrogenation of Primary and Secondary Amides Catalyzed by Complex 3 in the Presence of Added Base



Run[a]	Amide	Conv.(%)[b]	Alcohol (%)[b]	Amine (%)[b]
1		100	92	n.d.
2		83	80	80
3		65	54	n.d.
4		47	42	n.d.
5		35	28	n.d.
6		25	19	n.d.
7		65	61	n.d.

[a]Reaction conditions: amide (0.5 mmol), complex **3** (0.005 mmol, 1.0 mol %, 2.21 mg), KO^{t}Bu (0.05 mmol, 10 mol %, 2.8 mg), dry 2-propanol (2 mL), H_2 (50 bar) at 150 °C, 18 h. Pressure of hydrogen at room temperature. [b]Conversion and yields were calculated by gas chromatography using hexadecane as an external standard (n.d., not detected).

(ddd, J = 14.9, 5.7, 1.8 Hz, 1H, (C$\underline{H}_2$)P), 1.96 (m, 1H, C$\underline{H}_2$), 1.44 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.36 (m, 1H, (C$\underline{H}_2$)P, overlapped by C(C$\underline{H}_3$)$_3$ signals), 1.25 (s, 9H, C(C$\underline{H}_3$)$_3$), −15.91 (s, 1H, Ru$\underline{H}$); ^{1}H NMR (400 MHz, DCM-d_2) δ 1.44 (d, J_{HP} = 12.6 Hz, 9H, C(C$\underline{H}_3$)$_3$), 1.25 (d, J_{HP} = 12.3 Hz, 9H, C(C$\underline{H}_3$)$_3$), −15.91 (d, J_{HP} = 25.2 Hz, 1H, Ru$\underline{H}$); ^{13}C NMR (101 MHz, DCM-d_2) δ 208.17 (d, J_{CP} = 17.8 Hz, $\underline{C}$O), 145.22 (s, $\underline{C}_{Im}$), 128.55 (s, =N$\underline{C}$H$_{Im}$=), 122.34 (s, MeN$\underline{C}$H$_{Im}$=), 55.63 (s, HN(C$\underline{H}_2$)), 51.27 (s, Im-C$\underline{H}_2$), 38.44 (d, J_{CP} = 15.0 Hz, $\underline{C}$(CH$_3$)$_3$), 35.75 (d, J_{CP} = 27.0 Hz, $\underline{C}$(CH$_3$)$_3$), 34.54 (s, NC$\underline{H}_3$), 30.38 (bs, C(C$\underline{H}_3$)$_3$), 30.22 (d, J_{CP} = 4.1 Hz, C(C$\underline{H}_3$)$_3$), 26.64 (d, J_{CP} = 3.4 Hz, C$\underline{H}_2$), 20.33 (d, J_{CP} = 15.9 Hz, (C$\underline{H}_2$)P); ^{31}P{^{1}H} NMR (162 MHz, DCM-d_2) δ 78.11 (s).

*anti-**2***. Yield 26%; ^{1}H{^{31}P} NMR (400 MHz, DCM-d_2) δ 7.15 (m, 1H, =NC$\underline{H}_{Im}$=, overlapped by the same signal from the major isomer), 6.89 (bs, 1H, C$\underline{H}_{Im}$), 3.92 (d, J = 13.9 Hz, 1H, C$\underline{H}_2$), 3.59 (s, 3H, NC$\underline{H}_3$), 2.99−2.80 (m, 1H, C$\underline{H}_2$), 1.81−1.66 (m, 1H, C$\underline{H}_2$), 1.34 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.31 (s, 9H, C(C$\underline{H}_3$)$_3$), −16.25 (bs, 1H, Ru$\underline{H}$); ^{1}H NMR (400 MHz, DCM-d_2) δ 1.34 (d, J_{HP} = 11.3 Hz, 9H, C(C$\underline{H}_3$)$_3$), 1.31 (d, J_{HP} = 12.2 Hz, 9H, C(C$\underline{H}_3$)$_3$), −16.25 (bd, J_{HP} = 23.0 Hz, 1H, Ru$\underline{H}$); ^{31}P{^{1}H} NMR (162 MHz, DCM-d_2) δ 74.19 (s); IR ATR $\bar{\nu}$ 1890 cm^{-1} (s, ν CO); ESI-HRMS (positive) calcd for $C_{17}H_{32}ClN_3OPRu$ $[M - H]^+$ m/z 462.10108, found m/z 462.10123.

Synthesis of {Ru(H) (BH$_4$) (CO)(3-(di-*tert*-butylphosphino)-*N*-((1-methyl-1*H*-imidazol-2-yl)methyl)-propylamine)} (3). To a solution of {Ru(H) (Cl) (CO)(3-(di-*tert*-butylphosphino)-*N*-((1-methyl-1*H*-imidazol-2-yl)-methyl)propylamine)} **2** (360 mg, 0.78 mmol, 1 equiv) in ethanol/toluene 1/1 (30 mL) was added sodium borohydride (441 mg, 11.66 mmol, 15 equiv). The flask was immersed in a preheated oil bath (set temperature of 90 °C) and the mixture refluxed for 30 min. After this time, the solution was stirred at room temperature for 24 h. The solvents were removed under reduced pressure, and the residue was partitioned between 35 mL of water and 35 mL of dichloromethane. The organic phase was separeted and the aqueous phase further extracted with dichloromethane (2 × 15 mL). The collected organic phases were dried over sodium sulfate. The solution was filtered with the aid of a sintered glass frit. The solvent was removed under reduced pressure. The solid was then washed with diethyl ether until the surnatant solution was no longer yellowish and became colorless. The solvent was removed under reduced pressure to leave an off-white solid. The isolated yield was 78% (270 mg). The complex was obtained as a mixture of two isomers in a a 90:10 ratio.

3 proved to be poorly soluble in various solvents. Solubility in tetrahydrofuran allows for a good signal-to-noise ratio. However, in this solvent, the complex is not indefinitely stable and slowly decomposes.

Major Isomer. ^{1}H{^{31}P} NMR (400 MHz, THF-d_8) δ 7.02 (d, J = 1.5 Hz, 1H, =NC$\underline{H}_{Im}$=), 6.93 (d, J = 1.5 Hz, 1H, MeNC$\underline{H}_{Im}$=), 4.69 (bt, 1H, N$\underline{H}$), 4.30 (dd, J = 14.5, 5.0 Hz, 1H, Im-C$\underline{H}_2$), 3.61 (s, 3H, NC$\underline{H}_3$), 3.46 (dd, J = 14.5, 11.2 Hz, 1H, Im-C$\underline{H}_2$), 3.31 (ddt, J = 10.6, 8.1, 4.1 Hz, 1H, HN(C$\underline{H}_2$)), 2.47 (bq, J = 11.5 Hz, 1H, HN(C$\underline{H}_2$)), 2.17−2.06 (m, 1H, C$\underline{H}_2$), 2.01 (ddd, J = 14.8, 5.5, 1.9 Hz, 1H, (C$\underline{H}_2$)P), 1.86 (ddd, J = 14.9, 13.1, 11.3 Hz, 1H, C$\underline{H}_2$), 1.43 (dd, J = 12.1, 10.3 Hz, 1H, (C$\underline{H}_2$)P), 1.37 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.28 (s, 9H, C(C$\underline{H}_3$)$_3$), −1.83 (unresolved q, J = 102.7 Hz, 4H, B$\underline{H}_4$), −13.00 (s, 1H, Ru$\underline{H}$); ^{1}H NMR (400 MHz, THF-d_8) δ 1.37 (d, J_{HP} = 12.4 Hz, 9H, C(C$\underline{H}_3$)$_3$), 1.28 (d, J_{HP} = 12.2 Hz, 9H, C(C$\underline{H}_3$)$_3$), −13.00 (d, J_{HP} = 22.7 Hz, 1H, Ru$\underline{H}$); ^{13}C NMR (101 MHz, THF-d_8) δ 208.32 (d, J_{CP} = 18.0 Hz, $\underline{C}$O), 145.92 (s, $\underline{C}_{Im}$), 129.33 (s, =N$\underline{C}$H$_{Im}$=), 121.91 (s, MeN$\underline{C}$H$_{Im}$=), 55.77 (s, HN($\underline{C}$H$_2$)), 51.62 (s, Im-C$\underline{H}_2$), 38.40 (d, J_{CP} = 16.5 Hz, $\underline{C}$(CH$_3$)$_3$), 35.83 (d, J_{CP} = 25.4 Hz, $\underline{C}$(CH$_3$)$_3$), 33.83 (s, NC$\underline{H}_3$), 30.59 (s, C(C$\underline{H}_3$)$_3$), 30.15 (d, J_{CP} = 4.4 Hz, C(C$\underline{H}_3$)$_3$), 27.00 (d, J_{CP} = 3.4 Hz, C$\underline{H}_2$), 20.82 (d, J_{CP} = 3.4 Hz, (C$\underline{H}_2$)P); ^{31}P{^{1}H} NMR (162 MHz, THF-d_8) δ 82.44 (s); ^{11}B{^{1}H} NMR (96 MHz, THF-d_8) δ −26.55 (bs).

Minor Isomer. ^{1}H{^{31}P} NMR (400 MHz, THF-d_8) δ 7.04 (d, J = 1.4 Hz, 1H, C$\underline{H}_{Im}$), 6.94 (d, J = 1.4 Hz, 1H, C$\underline{H}_{Im}$), 4.11 (dd, J = 14.3, 10.8 Hz, 1H, C$\underline{H}_2$), 3.91 (dd, J = 14.4, 5.8 Hz, 1H, C$\underline{H}_2$), 3.77 (d, J = 8.7 Hz, 1H, C$\underline{H}_2$), 2.99−2.93 (bm, 1H, C$\underline{H}_2$), 1.34 (s, 9H, C(C$\underline{H}_3$)$_3$), −1.83 (unresolved q, J = 102.7 Hz, 4H, B$\underline{H}_4$) −13.52 (s, 1H, Ru$\underline{H}$); ^{1}H NMR (400 MHz, THF-d_8) δ −13.52 (d, J_{HP} = 19.6 Hz, 1H, Ru$\underline{H}$); ^{31}P{^{1}H} NMR (162 MHz, THF-d_8) δ 79.59 (s); ^{11}B{^{1}H} NMR (96 MHz, THF-d_8) δ −31.51 (bs); IR ATR $\bar{\nu}$ [cm^{-1}] 2344 (ν BH$_t$), 1905 (s, ν CO, BH$_b$); ESI-HRMS (positive) calcd for $C_{17}H_{33}N_3OPRu$ [M-BH$_4$]$^+$ m/z 428.14039, found m/z 428.14056.

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

General Procedure for the Hydrogenation of Amides with Ruthenium Complexes without Added Base. A 4 mL glass vial containing a stirring bar was sequentially charged with the corresponding amide (0.5 mmol) and the corresponding amount of ruthenium complex **2** or **3** (0.25−2 mol %). Afterward, the reaction vial was capped with a septum equipped with a disposable syringe needle and set in the alloy plate and the vial was purged with three cycles of vacuum and argon, and an argon atmosphere was established. Then, dry 2-propanol (2 mL) was added under argon, and the vials were then placed into a 300 mL autoclave. Once sealed, the autoclave was purged three times with 30 bar of hydrogen, then pressurized to the desired hydrogen pressure (15, 30, or 50 bar), and placed into an aluminum block that was preheated to the desired temperature (80−150 °C). After the desired reaction time (3−18 h), the autoclave was cooled in an ice bath and the remaining gas was carefully released. Finally, *n*-hexadecane (50 mg) was added as an external standard, and the reaction mixture was diluted with ethyl acetate and analyzed by gas chromatography.

General Procedure for the Hydrogenation of Amides with Ruthenium Complexes and Base. A 4 mL glass vial containing a stirring bar was sequentially charged with the corresponding amide (0.5 mmol) and the corresponding amount of ruthenium complex **2** or **3** (0.25−2 mol %). Afterward, the reaction vial was capped with a septum equipped with a disposable syringe needle and set in the alloy plate and the vial was purged with three cycles of vacuum and argon, and an argon atmosphere was established. Then, dry 2-propanol (1 mL) and the corresponding amount of KO^{t}Bu (1−10 mol %) previously dissolved in dry 2-propanol (1 mL) were sequentially added under argon and the vials were then placed into a 300 mL autoclave. Once sealed, the autoclave was purged three times with 30 bar of hydrogen, then pressurized to the desired hydrogen pressure (15, 30, or 50 bar), and placed into an aluminum block that was preheated to the desired temperature (80−150 °C). After the corresponding reaction time of 3−18 h, the autoclave was cooled in an ice bath and the remaining gas was carefully released. Finally, *n*-hexadecane (50 mg) was added as an external standard, and the reaction mixture was diluted with ethyl acetate and analyzed by gas chromatography.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b01955.

General information concerning synthesis and hydrogenation reactions, NMR and IR spectra of **1**−**3**, and crystal data of *syn*-**2** (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: matthias.beller@catalysis.de. Fax: (+49) 381-1281-5000.

Author Contributions

J.R.C.-A. and E.A. contributed equally to this work.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the ACS Pharmaceutical Roundtable for financial support and its members, especially Dr. Fabrice Gallou, for fruitful scientific discussions. In addition, support by the state of Mecklenburg-Vorpommern and the BMBF is acknowledged. J.R.C.-A. thanks the Ramon Areces Foundation for a postdoctoral fellowship.

■ REFERENCES

(1) (a) Eller, K.; Henkes, E.; Rossbacher, R.; Hoke, H. *Ullman's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2000, Amines, Aliphatic. DOI: 10.1002/14356007.a02_001. (b) Lawerence, S. A., Ed. *Amines: Synthesis, Properties and Applications*; Cambridge University Press: Cambridge, U.K., 2006.

(2) (a) Dodds, D.; Cole-Hamilton, D. J. In *Sustainable Catalysis: Challenges and Practices for the Pharmaceutical and Fine Chemical Industries*; Dunn, P. J., Hii, K. K., Krische, M. J., Williams, M. T., Eds.; John Wiley and Sons, Inc.: Hoboken, NJ, 2013; pp 1−36. (b) Smith, A. M.; Whyman, R. *Chem. Rev.* **2014**, *114*, 5477−5510.

(3) Lampland, N. L.; Hovey, M.; Mukherjee, D.; Sadow, A. D. *ACS Catal.* **2015**, *5*, 4219−4226.

(4) Selected recent examples: (a) Zhou, S.; Junge, K.; Addis, D.; Das, S.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 9507−9510. (b) Das, S.; Addis, D.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 1770−1771. (c) Das, S.; Addis, D.; Junge, K.; Beller, M. *Chem. - Eur. J.* **2011**, *17*, 12186−12192. (d) Das, S.; Wendt, B.; Möller, K.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1662−1666. (e) Park, S.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 640−653. (f) Cheng, C.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 11304−11307. (g) Reeves, J. T.; Tan, Z.; Marsini, M. A.; Han, Z. S.; Xu, Y.; Reeves, D. C.; Lee, H.; Lu, B. Z.; Senanayake, C. H. *Adv. Synth. Catal.* **2013**, *355*, 47−52. (h) Dombray, T.; Helleu, C.; Darcel, C.; Sortais, J.-B. *Adv. Synth. Catal.* **2013**, *355*, 3358−3362. For a recent example of organocatalytic promoted hydrosilylation of amides to amines, see: (i) Blondiaux, E.; Cantat, T. *Chem. Commun.* **2014**, *50*, 9349−9352.

(5) (a) Hirosawa, C.; Wakasa, N.; Fuchikami, T. *Tetrahedron Lett.* **1996**, *37*, 6749−6752. (b) Beamson, G.; Papworth, A. J.; Philipps, C.; Smith, A. M.; Whyman, R. *J. Catal.* **2010**, *269*, 93−102. (c) Beamson, G.; Papworth, A. J.; Philipps, C.; Smith, A. M.; Whyman, R. *J. Catal.* **2011**, *278*, 228−238. (d) Stein, M.; Breit, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 2231−2234. (e) Burch, R.; Paun, C.; Cao, X.-M.; Crawford, P.; Goodrich, P.; Hardacre, C.; Hu, P.; McLaughlin, L.; Sá, J.; Thompson, J. M. *J. Catal.* **2011**, *283*, 89−97. (f) Coetzee, J.; Manyar, H. G.; Hardacre, C.; Cole-Hamilton, D. J. *ChemCatChem* **2013**, *5*, 2843−2847.

(6) (a) Núñez Magro, A. A.; Eastham, G. R.; Cole-Hamilton, D. J. *Chem. Commun.* **2007**, 3154−3156. (b) Dodds, D. L.; Coetzee, J.; Klankermayer, J.; Brosinski, S.; Leitner, W.; Cole-Hamilton, D. J. *Chem. Commun.* **2012**, *48*, 12249−12262. (c) Coetzee, J.; Dodds, D. L.; Klankermayer, J.; Brosinski, S.; Leitner, W.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *Chem. - Eur. J.* **2013**, *19*, 11039−11050. (d) vom Stein, T.; Meuresch, M.; Limper, D.; Schmitz, M.; Hölscher, M.; Coetzee, J.; Cole-Hamilton, D. J.; Klankermayer, J.; Leitner, W. *J. Am. Chem. Soc.* **2014**, *136*, 13217−13225.

(7) (a) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931−7944. (b) Gunanathan, C.; Milstein, D. *Acc. Chem. Res.* **2011**, *44*, 588−602. (c) Schneider, S.; Meiners, J.; Askevold, B. *Eur. J. Inorg. Chem.* **2012**, *2012*, 412−429.

(8) Cantillo, D. *Eur. J. Inorg. Chem.* **2011**, *2011*, 3008−3013.

(9) (a) Balaraman, E.; Gnanaprakasam, B.; Shimon, L. J. W.; Milstein, D. *J. Am. Chem. Soc.* **2010**, *132*, 16756−16758. (b) John, J. M.; Bergens, S. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 10377−10380. (c) Ito, M.; Ootsuka, T.; Watari, R.; Shiibashi, A.; Himizu, A.; Ikariya, T. *J. Am. Chem. Soc.* **2011**, *133*, 4240−4242. (d) Miura, T.; Held, I. E.; Oishi, S.; Naruto, M.; Saito, S. *Tetrahedron Lett.* **2013**, *54*, 2674−2678. (e) Barrios-Francisco, R.; Balaraman, E.; Diskin-Posner, Y.; Leitus, G.; Shimon, L. J. W.; Milstein, D. *Organometallics* **2013**, *32*, 2973−2982. (f) John, J. M.; Takebayashi, S.; Dabral, N.; Miskolzie, M.;

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54

Bergens, S. H. *J. Am. Chem. Soc.* **2013**, *135*, 8578−8584. (g) Kita, Y.; Higuchi, T.; Mashima, K. *Chem. Commun.* **2014**, *50*, 11211−11213. (h) John, J. M.; Loorthuraja, R.; Antoniuk, E.; Bergens, S. H. *Catal. Sci. Technol.* **2015**, *5*, 1181−1186.

(10) (a) Gunanathan, C.; Milstein, D. *Chem. Rev.* **2014**, *114*, 12024−12087. (b) Younus, H. A.; Su, W.; Ahmad, N.; Chen, S.; Verpoort, F. *Adv. Synth. Catal.* **2015**, *357*, 283−330.

(11) Representative applications: (a) Zhang, J.; Leitus, G.; Ben-David, Y.; Milstein, D. *Angew. Chem., Int. Ed.* **2006**, *45*, 1113−1115. (b) Spasyuk, D.; Smith, S.; Gusev, D. G. *Angew. Chem., Int. Ed.* **2012**, *51*, 2772−2775. (c) Fogler, E.; Garg, J. A.; Hu, P.; Leitus, G.; Shimon, L. J. W.; Milstein, D. *Chem. - Eur. J.* **2014**, *20*, 15727−15731. (d) Spasyuk, D.; Vicent, C.; Gusev, D. G. *J. Am. Chem. Soc.* **2015**, *137*, 3743−3746. (e) Fuentes, J. A.; Smith, S. M.; Scharbert, M. T.; Carpenter, I.; Cordes, D. B.; Slawin, A. M. Z.; Clarke, M. L. *Chem. - Eur. J.* **2015**, *21*, 10851−10860. References to further transformations catalyzed by PNN−Ru complexes can be found in ref 10.

(12) (a) Junge, K.; Wendt, B.; Westerhaus, F. A.; Spannenberg, A.; Jiao, H.; Beller, M. *Chem. - Eur. J.* **2012**, *18*, 9011−9018. (b) Werkmeister, S.; Junge, K.; Wendt, B.; Spannenberg, A.; Jiao, H.; Bornschein, C.; Beller, M. *Chem. - Eur. J.* **2014**, *20*, 4227−4231.

(13) Joule, J. A., Mills, K., Eds. *Heterocyclic chemistry*, 5th ed.; John Wiley and Sons, Inc.: Chichester, U.K., 2010.

(14) The related pincer imine ligand derived from the condensation of 1-methyl-2-imidazolecarboxaldehyde and 2-(diphenylphosphino) ethylamine and its Ni(II) complex have been reported. The latter has been applied as a catalyst in the oligomerization of ethylene: Boudier, A.; Breuil, P.-A. R.; Magna, L.; Olivier-Bourbigou, H.; Braunstein, P. *J. Organomet. Chem.* **2012**, *718*, 31−37.

(15) (a) Buckingham, A. D.; Stephens, P. J. *J. Chem. Soc.* **1964**, 2747−2759. (b) Appleton, T. G.; Clark, H. C.; Manzer, L. E. *Coord. Chem. Rev.* **1973**, *10*, 335−422.

(16) Crystal data for *syn*-**2**: $C_{17}H_{33}N_3OPRu$, M = 462.95, monoclinic space group $P2_1/c$ (No. 14), a = 13.505(3) Å, b = 12.224(2) Å, c = 15.157(3) Å, β = 105.990(3)°, V = 2271.9(9) Å^3, T = 150.(2) K, Z = 4, ρ_{calcd} = 1.353 g cm^{-3}, μ(Mo Kα) = 0.887 mm^{-1}, 31730 total data, Θ_{max} = 26.00°, 4468 independent reflections (R_{int} = 0.0348), R = 0.0227 for 3948 unique data with $I > 2\sigma(I)$ and 232 refined parameters. The final R_1 values were 0.0260 (all data). The final $wR(F^2)$ values were 0.0612 (all data). The goodness of fit on F^2 was 1.055. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication CCDC-1404520 for *syn*-**2**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB21EZ, UK (fax: int. code +(1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk).

(17) (a) Ohkuma, T.; Koizumi, M.; Muñiz, K.; Hilt, G.; Kabuto, C.; Noyori, R. *J. Am. Chem. Soc.* **2002**, *124*, 6508−6509. (b) Sandoval, C. A.; Yamaguchi, Y.; Ohkuma, T.; Kato, K.; Noyori, R. *Magn. Reson. Chem.* **2006**, *44*, 66−75.

(18) (a) Marks, T. J.; Kolb, J. R. *Chem. Rev.* **1977**, *77*, 263−293. (b) Besora, M.; Lledós, A. *Struct. Bonding (Berlin)* **2008**, *130*, 149−202.

DOI: 10.1021/acscatal.5b01955
ACS Catal. 2016, 6, 47−54