A Structure-Activity Study of Nickel NNN Pincer Complexes for Alkyl-Alkyl Kumada and Suzuki-Miyaura Coupling Reactions

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Abstract: A new series of nickel NNN pincer complexes were synthesized and characterized. The main difference among these complexes is the substituents on the side arm amino group(s). No major structural difference was found except for the C-N-C angle of the various substituents and the "pseudo bite angle" of the complexes. Four new complexes were efficient for the alkyl-alkyl Kumada reaction of primary alkyl halides and among them, one complex was also efficient with secondary alkyl halides. The influence of the substituents on the catalytic performance of the nickel complexes in alkyl-alkyl Kumada and Suzuki-Miyaura cross-coupling reactions was systematically investigated. No correlation was found between the catalytic activity and the key structural parameters (C-N-C angle and "pseudo bite angle"), redox properties or Lewis acidity of the complexes.

Keywords: nickel • pincer ligands • cross-coupling • alkyl halides • structure-activity study

Supporting information for this article is given *via* a link at the end of the document.

Introduction

There is continuous interest in developing metal complexes of pincer ligands for catalytic applications due to their many desirable properties such as high stability, diversity, modularity, and ability to mediate unusual chemical transformations [1-9]. A common method to vary the properties of pincer ligands is to change either the central linker or the donor groups on the two side arms, or both. Such a change generally results in a dramatic difference in the electronic properties of the ligands [10-15]. A complimentary approach is to vary the substituents on the donor atoms without changing the donors themselves [16-18]. This approach is simple and straightforward from a synthetic point of view. It is especially appealing for the optimization of already active but not yet efficient catalysts because the changes in the stereoelectronic properties may be easy to identify and rationalize. Here we describe a structure-activity study of nickel NNN pincer complexes where only the substituents of two N donors on the side arms are systematically changed, leading to very different catalytic performances.

C-C cross-coupling of non-activated alkyl halides is challenging because alkyl electrophiles are less prone to oxidative addition and metal alkyl intermediates are susceptible to β-hydride elimination [19-21].

Moreover, alkyl halides suffer from many side reactions such as hydrodehalogenation, homocoupling or base-promoted HX elimination (X = halide) [22-23]. Despite these challenges, many efficient catalytic systems have been developed for the coupling of non-activated alkyl halides [24-26] with various base metal such as Fe [27-31], Co [32-35], Ni [36-40] and Cu [41-43]. However, the majority of these systems consists of a mixture of metal sources and ligands, making it difficult to identify the active catalysts and rationally improve them. These difficulties might be alleviated by using well-defined metal complexes as catalysts.

Our group previously reported a nickel pincer complex *Nickamine* ([(^{Me}N$_2$N)Ni−Cl], **1**, see Figure 1 for the ligand structure) as an efficient catalyst for a large number of cross-coupling reactions of non-activated alkyl halides [44-50]. A major limitation of **1** is its low efficiency for the coupling of sterically demanding substrates such as secondary alkyl halides.

Surprisingly, when one of the dimethylamino group in **1** was replaced by a pyrrolidino group, the resulting complex [(^{Pyr}N^{Me}NN)Ni−Cl] (**2**, see Figure 1 for the ligand structure), was able to catalyze the coupling of many

secondary alkyl halides in good yields [51]. This result indicated that a subtle change of the substituents of the side arm nitrogen atoms in this NNN pincer system could result in a significant change and improvement of the catalytic properties.

This inspired us to conduct a systematic study of the influence of various substituents on the catalytic performance of the Ni-NNN complexes in alkyl-alkyl Kumada and Suzuki-Miyaura cross-coupling reactions.

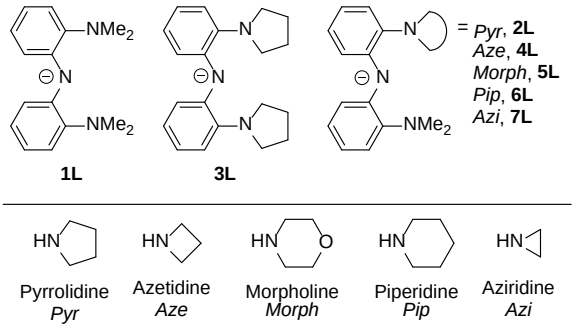


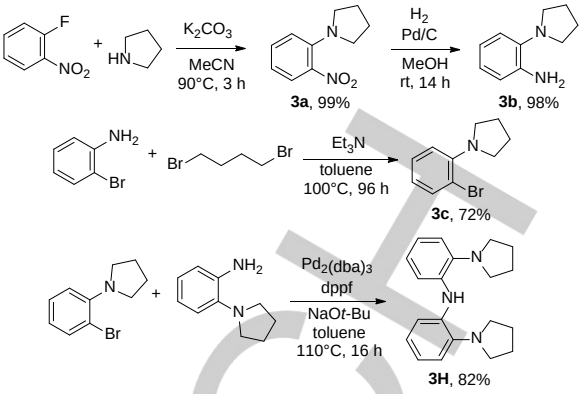
Figure 1. Structure of ligands **1L**-**7L**.

Results and Discussion

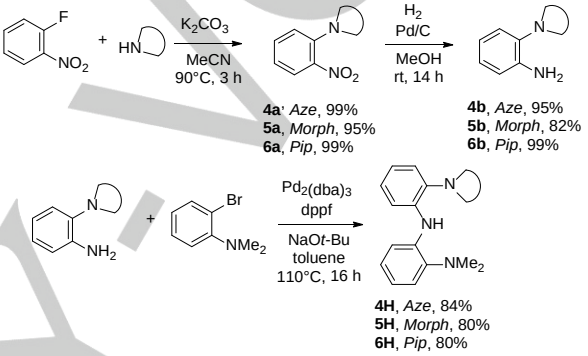
Synthesis and Characterization of New Nickel NNN Complexes.

Pro-ligands Synthesis. Five new NNN ligands **3L-7L** were prepared to compare with ligands **1L** and **2L** which are used in catalysts **1** and **2** (Figure 1). In the series of **1L-7L**, the ligand structure and donor atoms are maintained while the substituents on one or two of the side arm N donors are varied. The design of the five new ligands was inspired by the surprising activity of catalyst **2**. Like **2L**, each of ligands **4L-7L** contains a cyclic alkyl amine at one of the side arms. The cyclic amines were varied systematically from 3-membered ring to 6-membered ring. They were abbreviated as follow: *Pyr* for the pyrrolidine, *Aze* for the azetidine, *Morph* for the morpholine, *Pip* for the piperidine and *Azi* for the aziridine (Figure 1). Ligand **3L** contains two pyrrolidino side arms. The protonated forms of **3L-7L** were first synthesized similar to **1H** and **2H**. Scheme 1 shows the synthesis of **3H**, and Scheme 2 shows the synthesis of **4H-6H**. Synthesis of pro-ligand **7H** is shown in the supporting information (Scheme S1).

Scheme 1. Synthesis of Pro-Ligand **3H**.

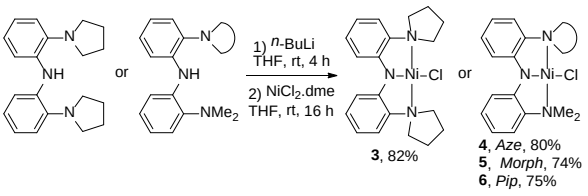


Scheme 2. Synthesis of the Pro-Ligands **4H**-**6H**.



Synthesis and Characterization of Nickel Chloride Complexes. Pro-ligands **3H-6H** were deprotonated with *n*-butyl lithium and then treated with $NiCl_2$·dme (dme = dimethoxyethane) to give the resulting Ni(II) chloride complexes in good yields (74-82 %; Scheme 3). The complexes are diamagnetic, suggesting a square planar structure. Pro-ligand **7H** was subjected to the same procedures to give the Ni(II) chloride complex **7** (Scheme S2, supporting information). Unfortunately, the purification of **7** was difficult and this compound seemed to decompose in solution over a short period of time. Therefore, no further studies were performed with this complex.

Scheme 3. Synthesis of Ni Pincer Complexes **3**-**6**.



The solid-state structures of complexes **3**-**6** were determined by X-ray crystallography (Figure 2).

Table 1. Comparison of Key Structural Parameters of Complexes **1**-**6**.

Entry	Complex	C-N-C Angle (°)	Ni-N(amide) Bond Length (Å)	Averaged Ni-N(amine) Bond Length (Å)	Ni-Cl Bond Length (Å)	"Pseudo Bite Angle" (°) [a]
1	**1**	108.9(2)	1.835(2)	1.958(2)	2.203(7)	105.97
2	**2**	104.7(4)	1.854(4)	1.966(4)	2.213(2)	101.24
3	**3**	103.5(1) and 104.6(1)	1.831(2)	1.970(2)	2.189(4)	95.59
4	**4**	91.6(4)	1.839(4)	1.950(4)	2.200(2)	98.76
5	**5i**	110.4(1)	1.838(2)	1.959(2)	2.222(6)	96.21
	5j	110.5(1)	1.838(2)	1.948(2)	2.209(6)	94.37
6	**6**	112.1(1)	1.841(2)	1.964(2)	2.211(5)	96.04

[a]) The larger angle of the two bite angles for each complex is used.

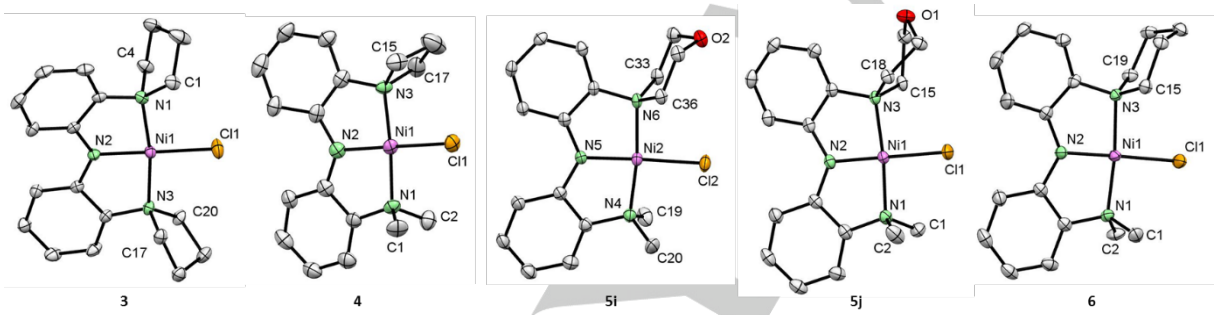


Figure 2. Crystal structure of complexes **3**-**6**. The two isomers of **5** are represented. Hydrogens atoms are omitted for clarity. The ellipsoids are displayed at a 50% probability.

The nickel centers in the four complexes all have a square planar coordination geometry. Two isomers were found for complex **5** due to the two different conformations adopted by the morpholino group. In **5i**, the morpholino group has a chair conformation, while in **5j**, it has a skew-boat conformation (Figure 2). The structural parameters for complexes **1**-**6** are very similar. The maximum difference is less than 0.033(7) Å and 0.023(4) Å for the corresponding Ni−Cl and Ni−N bond lengths, respectively (Table 1).

Likewise, the maximum difference of the bond angles around the nickel centers is less than 2°. The most important change in the structures of **1**-**6** is the C-N-C angle of the amino groups whose substituents are varied. The dimethyl amino group in **1** has a C-N-C angle of about 109°, close to that of an ideal tetrahedron. The C-N-C angles in the complexes with 6-membered rings, **5** and **6**, are about 110° and 112°, respectively, similar to those in **1**. The complexes with 5-membered ring(s), **2** and **3**, on the other hand, have a C-N-C angle of about 104°, indicating a significant contraction. The biggest contraction was found in the complex with a 4-membered ring, **4**, which has a C-N-C angle of only about 92°. This C-N-C angle is close to that of the free azetidine (92.2°) [52].

The "pseudo bite angle" between the amino groups and the nickel center as drawn in Figure 3 and Figure S1, supporting information, is measured from the crystal structures. Table 1 shows that the angle is largest in **1**, but varies only slightly among **2**-**6**.

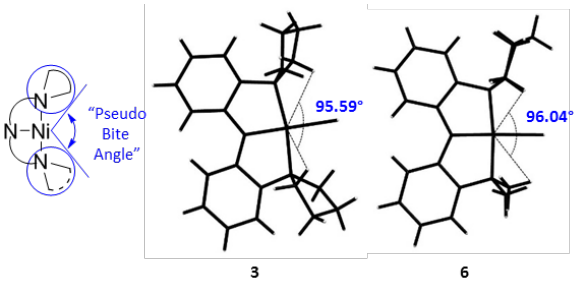


Figure 3. "Pseudo bite angle" for complexes **3** and **6**.

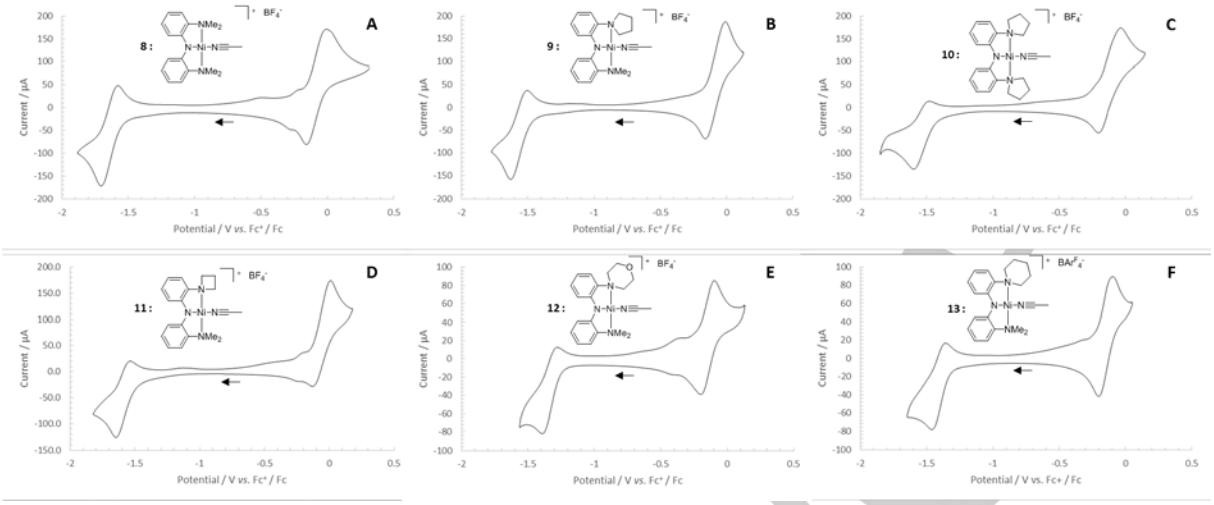
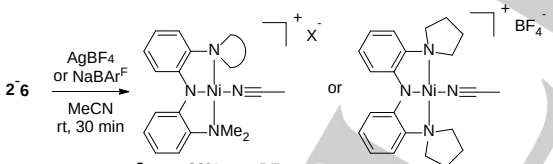


Figure 4. Cyclic voltammograms of complexes **8**-**13** (4 mM) recorded in CH_3CN solutions at a scan rate of 400 mV·s^{-1}; the potential is referenced to the ferrocene/ferrocenium couple. The arrows indicate the starting potential and the direction of each scan.

Synthesis and Properties of Nickel Acetonitrile Complexes. To study the electronic properties of the complexes (see below), nickel acetonitrile complexes **9**-**13** were synthesized by chloride abstraction from complexes **2**-**6**. The corresponding acetonitrile complex from **1** was previously reported (**8**) [53]. Complexes **9**-**12** were obtained by reaction of **2**-**6** with silver tetrafluroborate in CH_3CN, while complex **13** was obtained by reaction of **6** with sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($NaBAr^F{}_4$) (Scheme 4).

Scheme 4. Synthesis of the Acetonitrile Complexes **9**-**13**.



9, *Pyr*, 88% (X = BF_4)
11, *Aze*, 84% (X = BF_4)
12, *Morph*, 66% (X = BF_4)
13, *Pip*, 48% (X = $BAr^F{}_4$)
10, *(Pyr)*$_2$, 86%

Cyclic voltammetry was conducted on complexes **9**-**13** (Figure 4 and Table 2). All these complexes exhibit one reversible oxidation peak and one reduction peak which is either reversible (for **8** and **9**) or non-reversible (for **10**-**13**). The corresponding redox potentials are shown in Table 2. The values determined for **8** are in agreement with previous results [53]. From Table 2, the oxidation potentials of **8**-**12** are very close, and the maximum difference is only 90 mV. The peak separation between the cathodic and the anodic peaks is about 200 mV for each compound, so this small difference of redox potentials is well within the range of experimental uncertainty. The difference in the reduction potentials of **8**-**13** is more substantial, with the maximum difference of 300 mV. However, these potentials cannot be directly compared because of the complication in determining the true redox potentials of non-reversible electron transfer by cyclic voltammetry. Overall, the cyclic voltammogram data are indicative of similar electronic properties of this series of nickel complexes.

Table 2. Reductive and Oxidative Potential of the [($^{R}N^{R'}$NN)Ni-($NCCH_3$)]BR"$_4$ Complexes.

Entry	Complex	$E°'_{1/2\ red}$ (V) [a]	$E°'_{1/2\ ox}$ (V) [a]
1	**8**	-1.67 (rev)	-0.15 (rev)
2	**9**	-1.64 (rev)	-0.09 (rev)
3	**10**	-1.54 (non-rev)	-0.12 (rev)
4	**11**	-1.59 (non-rev)	-0.06 (rev)
5	**12**	-1.37 (non-rev)	-0.15 (rev)
6	**13**	-1.41 (non-rev)	-0.15 (rev)

[a]) rev = reversible, non-rev = non-reversible.

By determining how tightly a Lewis base such as CH_3CN is bound to a metal center, the Lewis acidity of the corresponding complex can be evaluated [54,55]. The stronger CH_3CN is coordinated to the Ni center, the more downfield will be the proton signal, which corresponds to a more Lewis acidic metal center. Thus, comparison of the shift in the ^1H NMR of the methyl group of coordinated CH_3CN allows the measurement of the relative Lewis

acidity of complexes **8**-**13**. (D_6)Acetone was chosen as the solvent in these NMR experiments because some complexes were poorly soluble in the commonly used $CDCl_3$ for this type of experiments. The results are shown in Table 3. According to Table 3, the Lewis acidity of these complexes have the order of **12** > **13** > **11** > **8** > **10** ≈ **9.** The complexes seem to have quite different Lewis acidity.

Table 3. The ^{1}H NMR Chemical Shift of Coordinated CH_3CN in **8**-**13**.

Entry	Complex	δ(H) for CH_3CN (ppm, in (D_6)Acetone)
1	**8**	2.53
2	**9**	2.31
3	**10**	2.32
4	**11**	2.70
5	**12**	2.90
6	**13**	2.83
7	-	2.05

Activity in Alkyl-Alkyl Kumada Coupling Reactions.

The catalytic activity of new nickel complexes **3**-**6** was examined using the coupling of (3-iodobutyl)benzene and (4-iodobutyl)benzene with *n*-butylMgCl (Tables 4-5 and Figures 5-6) as test reactions. The two substrates represent secondary and primary alkyl iodides, respectively. The previously optimized reaction conditions for complex **2** were chosen. Thus, the reactions were conducted using 3.5 mol % of catalyst in a 1:1.5 mixture of DMA/THF at -20 °C; 1.2 equivalent of Grignard reagent was slowly added over 2 h. Control experiments using $NiCl_2$·dme as catalyst or no catalyst were also conducted. The results using catalysts **1** and **2** were also listed for comparison.

Coupling of (3-iodobutyl)benzene with n-BuMgCl. With *Nickamine* (**1**) as catalyst, the coupling yield was only 5%, consistent with it being inefficient for the coupling of secondary alkyl halides (Table 4, Entry 1). The conversion was 59%, and a small amount of reduction and elimination products were also obtained. The main side product was (3-chlorobutyl)benzene (27%), presumably formed from I-Cl exchange. As previously reported, complex **2** was efficient for the coupling, giving a yield of 72% (Table 4, Entry 2). The conversion was complete, and the main side product was the reduction product (6%). Complexes **3** and **4** were also efficient for this reaction, with complete conversion and high yields (Table 4, Entries 3 and 4). Complexes **5** and **6** had modest efficiency (Table 4, Entries 5 and 6). While the conversion was complete, a significant amount of reduction and homocoupling products were also formed. $NiCl_2$·dme was not efficient as catalyst (Table 4, Entry 7). Without any catalyst, no coupling occurred (Table 4, Entry 8). About 21% of conversion was made, and the main reaction was the I-Cl exchange of (3-iodobutyl)benzene to give (3-chlorobutyl)benzene (16%). It is noted that no elimination product was observed without a nickel catalyst, suggesting that the elimination was metal-mediated. A graphical representation of the results in Table 4 is shown in Figure 4.

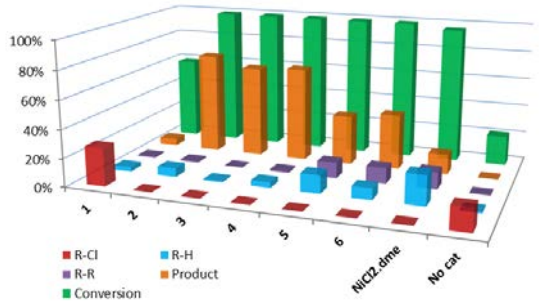
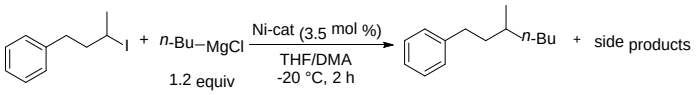


Figure 5. A graphical representation of the products distribution for the Kumada coupling with a secondary alkyl iodide. R-H = butylbenzene, R-R = (3,4-dimethylhexane-1,6-diyl)dibenzene, R-Cl = (3-chlorobutyl)benzene and Elim. = elimination products (but-3-en-1-ylbenzene and but-2-en-1-ylbenzene).

Coupling of (4-iodobutyl)benzene with n-BuMgCl. For the coupling of this primary alkyl iodide, complexes **1**-**4** all exhibited high efficiency (Table 5, Entries 1-4). Complexes **5** and **6** had slightly lower efficiency, with yields of 49% and 61%, respectively (Table 5, Entries 5 and 6). The conversion using these two catalysts was complete, but a significant amount of homocoupling was observed. $NiCl_2$·dme again had a very low efficiency (Table 5, Entry 7). Without any catalyst, the conversion was 38% and no product was formed (Table 5, Entry 8). The major side-product was (4-chlorobutyl)benzene (13%), formed via a I/Cl exchange of (4-iodobutyl)benzene with the Grignard reagent. A graphical representation of the results in Table 5 is shown in Figure 6.

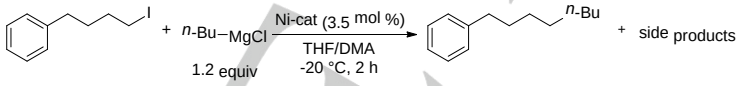
Table 4. Conversion and Product Distribution for the Kumada Coupling of (3-Iodobutyl)benzene with *n*-BuMgCl. [a] [b]



Entry	Ni-cat	Conv. (%)	Yield (%)	R-H (%) [c]	R-R (%) [d]	R-Cl (%) [e]	Elim (%) [f]
1	**1**	59	5	3	1	27	2
2	**2**	> 99	72	6	1	0	3
3	**3**	> 99	65	1	0	0	0
4	**4**	> 99	67	4	1	0	3
5	**5**	> 99	35	13	11	0	5
6	**6**	> 99	39	8	11	0	5
7	$NiCl_2$·dme	96	14	21	12	0	15
8	-	21	0	1	0	16	1

[a] *n*-BuMgCl (1.2 equiv, 0.24 mmol) was diluted in THF (1 mL) and added dropwise via a syringe pump (2 h) to a DMA/THF solution (0.3 and 0.2 mL) of catalyst (3.5 mol %) and alkyl iodide (0.2 mmol) at -20 °C under N_2. The reaction time was 30 min. [b] Conversions and yields were determined by GC-MS relative to the alkyl halide. [c] R-H = butylbenzene. [d] R-R = (3,4-dimethylhexane-1,6-diyl)dibenzene. [e] R-Cl = (3-chlorobutyl)benzene. [f] Elim. = elimination products (but-3-en-1-ylbenzene and but-2-en-1-ylbenzene).

Table 5. Conversion and Product Distribution for the Kumada Coupling of (4-Iodobutyl)benzene with *n*-BuMgCl. [a] [b]



Entry	Ni-cat	Conv. (%)	Yield (%)	R-H (%) [c]	R-R (%) [d]	R-Cl (%) [e]	Elim (%) [f]
1	**1**	> 99	78	1	1	4	0
2	**2**	> 99	70	1	1	8	0
3	**3**	> 99	76	1	6	1	0
4	**4**	89	70	1	6	2	0
5	**5**	> 99	49	8	17	0	3
6	**6**	> 99	61	2	13	5	0
7	$NiCl_2$·dme	98	22	10	1	10	15
8	-	38	0	0	0	13	0

[a] Same conditions as in Table 4. [b] Conversions and yields were determined by GC-MS relative to the alkyl halide. [c] R-H = butylbenzene. [d] R-R = 1,8-diphenyloctane. [e] R-Cl = (4-chlorobutyl)benzene. [f] Elim. = elimination products (but-3-en-1-ylbenzene and but-2-en-1-ylbenzene).

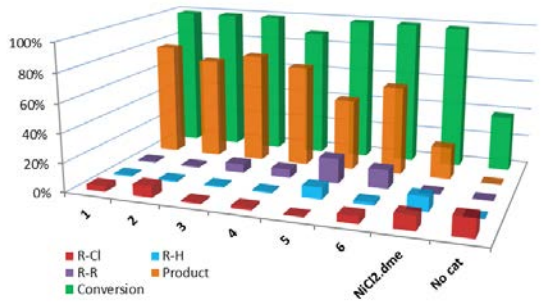


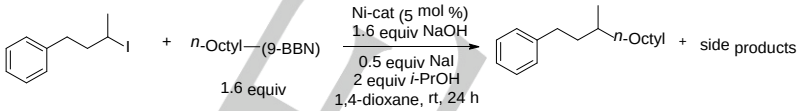
Figure 6. A graphical representation of the products distribution for the Kumada coupling with a primary alkyl iodide. R-H = butylbenzene, R-R = 1,8-diphenyloctane, R-Cl = (4-chlorobutyl)benzene and Elim. = elimination products (but-3-en-1-ylbenzene and but-2-en-1-ylbenzene).

Activity in Alkyl-Alkyl Suzuki-Miyaura Coupling Reactions. The reactions of (3-iodobutyl)benzene and (4-iodobutyl)benzene with 9-octyl-9-borabicyclo[3.3.1]nonane (abbreviated *n*-octyl-(9-BBN)) were used as the test reactions (Tables 6-7). The previously developed conditions for complexes **1** and **2** were applied: 5 mol % of catalyst, 1.6 equivalent of sodium hydroxide, 0.5 equivalent of sodium iodide, 2 equivalent of isopropanol, 1,4-dioxane as solvent and stirring at room temperature for 24 h.

Coupling of (3-iodobutyl)benzene with n-octyl-(9-BBN). For this reaction, only complex **2** was efficient (Table 6, Entry 2). Complexes **1** and **4** have low conversion and yields (Table 6, Entries 1 and 4). The conversion using complexes **3**, **5**, and **6** was modest, so were the yields (30-40%; Table 6, Entries 3, 5 and 6). $NiCl_2$.dme gave low conversion and no coupling yields (Table 6, Entry 7). Without a nickel catalyst, the conversion was about 22% and no coupling product was made (Table 6, Entry 8). None of the new catalysts showed better efficiency than **2** for the Suzuki-Miyaura coupling with non-activated secondary alkyl iodides.

Coupling of (4-iodobutyl)benzene with n-octyl-(9-BBN). For this reaction, complex **1** has a modest efficiency while complex **2** is quite efficient (Table 7, Entries 1 and 2). Complexes **3**-**6** exhibited similar and quite low efficiency (Table 7, Entries 3-6). The problem seemed to be related to the low conversion. No product was obtained using $NiCl_2$·dme as catalyst or without a nickel catalyst (Table 7, Entries 7-8). Under these conditions, nearly no conversion was made.

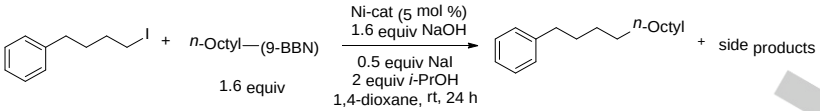
Table 6. Conversion and Product Distribution for the Szuki-Miyaura Coupling of (3-Iodobutyl)benzene with *n*-Octyl-(9-BBN). [a] [b]



Entry	Ni-cat	Conv. (%)	Yield (%)	R-H (%) [c]	Elim (%) [d]
1	**1**	23	9	8	2
2	**2**	96	89	6	0
3	**3**	75	42	6	3
4	**4**	38	8	5	2
5	**5**	59	36	6	6
6	**6**	61	30	7	2
7	$NiCl_2$·dme	31	0	6	4
8	-	22	0	2	2

[a]) NaOH (1.6 equiv), catalyst (5 mol %), NaI (0.5 equiv), *i*-PrOH (2 equiv), alkyl iodide (0.2 mmol) and alkyl-(9-BBN) (1.6 equiv) in 1,4-dioxane (1 mL), at room temperature and under N_2. The reaction time was 24 h. [b]) Conversions and yields were determined by GC-MS relative to the alkyl halide. [c]) R-H = butylbenzene. [d]) Elim. = elimination products (but-3-en-1-ylbenzene and but-2-en-1-ylbenzene).

Table 7. Conversion and Product Distribution for the Szuki-Miyaura Coupling of (4-Iodobutyl)benzene with *n*-Octyl-(9-BBN). [a] [b]



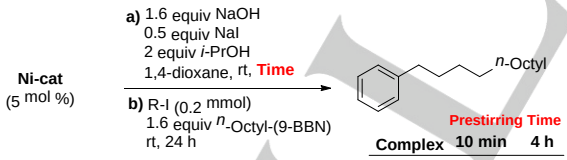
Entry	Ni-cat	Conv. (%)	Yield (%)	R-H (%) [c]	Elim (%) [d]
1	**1**	76	53	5	0
2	**2**	73	70	4	0
3	**3**	36	27	2	1
4	**4**	27	25	0	1
5	**5**	37	15	3	7
6	**6**	27	23	3	2
7	$NiCl_2$·dme	12	0	4	0
8	-	3	0	0	0

[a]) Same conditions as in Table 6. [b]) Conversions and yields were determined by GC-MS relative to the alkyl halide. [c]) R-H = butylbenzene. [d]) Elim. = elimination products (but-3-en-1-ylbenzene).

Stability of Nickel Complexes under Suzuki-Miyaura Coupling Conditions.

Complexes **3**-**6** exhibited in general lower activity in the Suzuki-Miyaura coupling reactions than in the Kumada coupling reactions. A test was made to probe whether they decomposed during the Suzuki-Miyaura coupling reactions (Scheme 5).

Scheme 5. Stability Tests for the Suzuki-Miyaura Cross-Coupling Reaction.



Complex	Prestirring Time 10 min	4 h
1	**48%**	**0%**
2	**69%**	**0%**
3	**< 1%**	**0%**
4	**< 1%**	**0%**
5	**0%**	**0%**
6	**16%**	**0%**

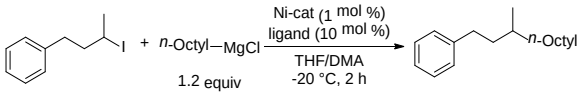
Thus, complexes **1**-**6** were subjected to the basic reaction conditions without the substrates. After the pre-mixing, the two substrates (alkyl halide and boron reagent) were added and the reaction was stirred at room temperature for 24 h. When the pre-mixing time was 10 min, coupling yields were similar to those obtained under conventional coupling conditions were obtained for complexes **1** and **2**, suggesting that these two complexes were stable during the pre-mixing period. For complexes **3**-**6**, however, the coupling yields after 10 min of pre-mixing were much lower than those obtained under conventional coupling conditions. This result suggests that a large portion of complexes **3**-**6** were decomposed during the pre-mixing period. When the pre-mixing time was extended to 4 h, even complexes **1** and **2** seemed to decompose, leading to negligible coupling yields.

Hemilability Tests.

Previously we used an "inhibition" test to probe the potential hemilability of the pincer ligand in complexes **2**.[51] An analogous test was made for complexes **3**-**6** for the Kumada coupling reaction between (3-iodobutyl)benzene and *n*-octylmagnesium chloride. With 3.5 mol % of catalyst and 10 equivalent of an exogenous ligand (2,4-lutidine, pyridine, and PPh_3; relative to the catalyst), no noticeable changes in the product yield were observed. However, with a lower catalyst loading (1 mol %), inhibition of the coupling for certain complexes was observed (Table 8). The addition of 10 equivalent (relative to the catalyst) of an external ligand (2,4-lutidine or pyridine) to the reaction mixture decreased significantly the yields for complexes **2** and **4**-**6**. Addition of 10 equivalent of PPh_3 had no effect on the catalysis of **4** and **6** while yield decreased for **2** and **5**. It was reported that for some nickel complexes with bidentate NN ligands, PPh_3 binds less strongly than pyridine and 2,4-lutidine [56]. Thus, complexes **2** and **5** seem more "hemilabile" than

complexes **4** and **6**. For complex **3**, no inhibition was observed with 10 mol % of an external ligand.

Table 8. Effect of the Addition of Exogenous Ligands on Kumada Coupling. [a]) [b])



Entry	Ligand	Yield **2** (%)	Yield **3** (%)	Yield **4** (%)	Yield **5** (%)	Yield **6** (%)
1	-	70	64	29	18	24
2	2,4-Lutidine	22	65	18	3	5
3	Pyridine	24	64	14	5	7
4	PPh_3	36	82	32	13	20

[a]) Same conditions as in Table 4 with 10 mol % of the exogenous ligand. [b]) Yields determined by GC-MS relative to the alkyl halide.

Discussion.

The synthesis of complexes **3**-**6** allows us to conduct a structure-activity study of this series of nickel pincer complexes in Kumada and Suzuki-Miyaura coupling reactions of alkyl halides. The new complexes **3**-**6** exhibited lower efficiency for the Suzuki-Miyaura coupling than for the Kumada coupling.

The pre-mixing experiments shown in Scheme 5 suggest that complexes **3**-**6** are not stable under the conditions of Suzuki-Miyaura, possibly due to reactions with NaOH. Complexes **1** and **2** are more stable under these conditions. But in the absence of substrates, they seem to be unstable as well over a longer period of pre-mixing. It is possible that when the substrates are present, the stability of the complexes **1**-**6** is higher than when the substrates are absent. Nevertheless, the low yields of **3**-**6** in Suzuki-Miyaura reactions might be attributed to their lower stability under the reaction conditions.

For alkyl-alkyl Kumada coupling of a primary alkyl iodide, complexes **3**-**6** all exhibited good to excellent efficienc. For the coupling of a secondary alkyl iodide, complexes **3** and **4** were efficient, complexes **5** and **6** gave low coupling yields. For complexes **1**-**6**, there is a substantial difference in their catalytic activity in the Kumada coupling reactions. We attempted to correlate their activity with four different parameters: the Lewis acidity represented by the ^{1}H NMR chemical shift of the methyl group of [Ni]-NCMe complexes; the electronic property represented by the oxidation potential of the [Ni]-NCMe complexes; the C-N-C angle of the substituents of the side arm amino groups; the "pseudo bite angles".

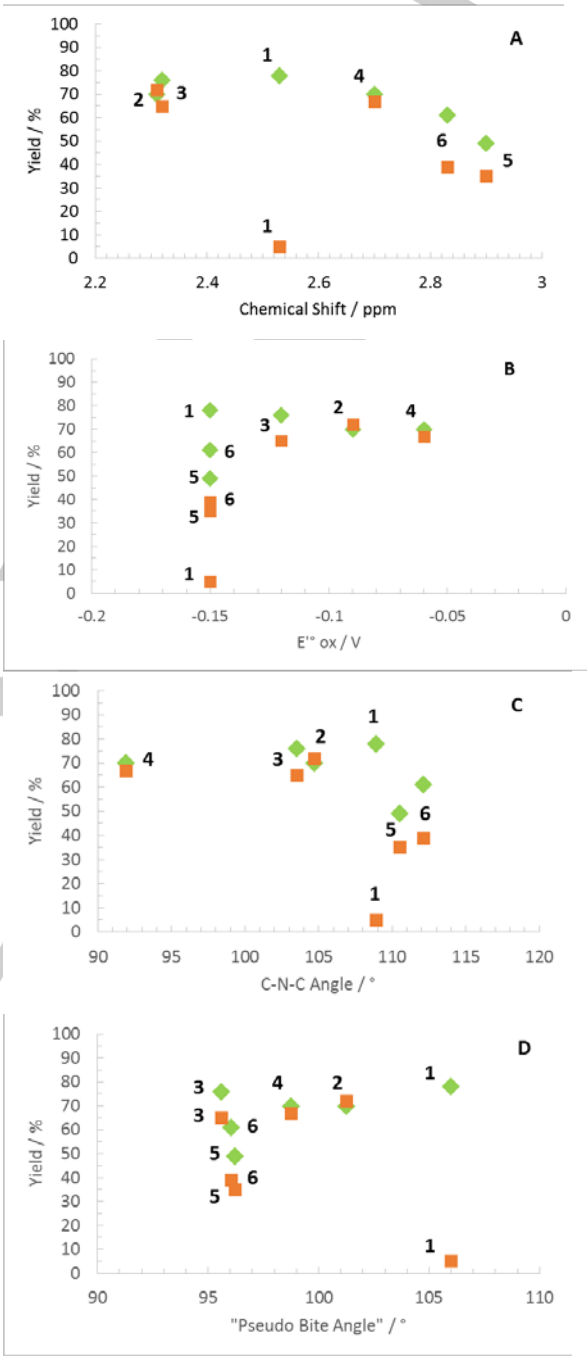


Figure 7. Correlation plots between electronic properties (Lewis acidity, **A**; and oxidative potential, **B**) or structural parameters (C-N-C angle of the varying amino group, **C**; and "pseudo bite angle", **D**) and product yields for the Kumada reactions catalyzed by **1**-**6** (coupling of primary alkyl iodide ♦ and secondary alkyl iodide ■).

Figure 7 shows that there is no obvious correlation between the activity and these parameters for the coupling of both a primary and a secondary alkyl iodide.

Thus, two empirical parameters of the electronic properties of the catalysts, redox potential and Lewis acidity, are not good descriptors of the catalytic activity of these structurally similar complexes. The structural differences, represented by the C-N-C angles of the side arm amino groups and the “pesudo bite angles“, also have no direct translation to the activity.

This result is probably not surprising because the efficiency of a catalyst in a multiple-step reaction depends on many factors such as stability, reaction barriers, mechanism, etc. Considering the previous and current studies of this nickel pincer system, we hypothesize the following reasons for the observed trend in catalytic activity. For Kumada coupling of primary alkyl halides, most Ni-NNN complexes should be electronically rich enough to activate the alkyl halide by a single-electron-transfer [57], so complexes **1**-**6** all have good to excellent efficiency, with a modest difference in yields for certain reactions. For Kumada coupling of secondary alkyl halides, the main problem is the access of the nickel center by the substrate. For a rigid [Ni]-NNN complex such as **1**, the access is blocked; if one of the amino groups is "hemilabile" like in **2**, then the alkyl halide can be activated. Complexes **2**, **4**-**6** all showed a certain level of hemilability according to the test in Table 8, so they should be active for the coupling of secondary alkyl halides. This was indeed observed. No inhibition was found for complex **3**. However, this does not mean that **3** is not "hemilabile". There are two "hemilabile" pyrolidino groups in **3**, so when one arm dissociates and binds to an exogenous ligand, the other arm can also dissociate and allow the access of the secondary alkyl halide. The detailed difference in the efficiency of active catalysts is not easily explained due to the complexity mentioned above.

Conclusion

In summary, a series of nickel NNN pincer complexes with difference only in the substituents of the side arm amino groups were synthesized and characterized. A structure-activity study of these complexes in alkyl-alkyl Kumada and Suzuki-Miyaura coupling reactions was conducted. The catalytic activity shows no obvious correlation with the redox potential, Lewis acidity, or a key structural parameter (C-N-C angle) of the complexes. The study underlines the complexity of catalyst design even on a well-defined metal-ligand system.

Subtle changes of the substituents of the side arm amino groups of this pincer NNN ligand framework resulted in a significant difference in catalytic activity. Through this work, four new nickel pincer complexes (complexes **3**-**6**) with good to excellent efficiency in alkyl-alkyl Kumada coupling of primary alkyl halides were prepared. Among these four, one (complex **3**) was also efficient for the coupling of secondary alkyl halides.

Acknowledgements

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Author Contribution Statement

Thomas Di Franco performed the majority of synthesis, characterization, and catalysis tests; Marko Stojanovic contributed to the synthesis and characterization of complexes **3** and **5**; Sébastien C. Keller contributed to the synthesis of **5** and preliminary catalysis tests of **3** and **5**; Rosario Scopelliti performed the X-ray crystallographic analysis; Xile Hu designed and directed the project. Thomas Di Franco and Xile Hu wrote the paper.

Supplementary Data

^{1}H and ^{13}C NMR spectra, X-ray crystal details, tables giving additional experimental details and crystallographic data can be found in the supporting information. This is available free of charge *via* the internet at http://onlinelibrary.wiley.com.

Experimental Part

Chemicals and Reagents.

All manipulations were carried out under an inert $N_{2(g)}$ atmosphere using standard Schlenk or glovebox techniques. Solvents were purified using a two-column solid-state purification system (Innovative Technology, NJ, USA) and transferred to the glovebox without exposure to

air. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc., and were degassed and stored over activated 3 Å molecular sieves. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources and used without further purification. Liquid compounds were degassed by standard freeze-pump-thaw procedures prior to use. The following chemicals were prepared according to literature procedures: *Nickamine* (complex **1**) [58], complex **2** [51], 2-bromo-*N*,*N*-dimethylaniline [58], (4-iodobutyl)benzene [59] and (3-iodobutyl)benzene [60].

Physical Methods.

The ^{1}H and ^{13}C NMR spectra were recorded at 293 K on a Bruker Avance 400 spectrometer. ^{1}H NMR chemical shifts were referenced to residual solvent as determined relative to Me_4Si (δ = 0 ppm). The $^{13}C\{^{1}H\}$ chemical shifts were reported in ppm relative to the carbon resonance of $CDCl_3$ (77.0 ppm). GC-MS measurements were conducted on a Perkin-Elmer Clarus 600 GC equipped with Clarus 600T MS. HRESI-MS measurements were conducted at the EPFL ISIC Mass Spectrometry Service with a Micro Mass QTOF Ultima spectrometer. Cyclic voltammetric measurements were recorded in a glovebox by a CHI760E electrochemical workstation that was connected to a glassy carbon working electrode (surface area = 0.07 cm^2), a platinum wire auxiliary electrode, and an $Ag/AgNO_3$ (0.01 M) reference electrode filled with acetonitrile and [*n*-Bu_4] [PF_6] (0.1 M). All potentials were referenced to Fc/Fc^+ as internal standard. The temperature of reactions below room temperature was regulated by a Julabo FT-902 chiller. Elemental analyses were performed on a Carlo Erba EA 1110 CHN instrument at EPFL. X-ray diffraction studies were carried out in the EPFL Crystallographic Facility. Data collections were performed at low temperature by two four-circle kappa diffractometers equipped with CCD detectors and a marresearch marmx system equipped S3 with mar345 imaging plate scanner. Data were reduced and corrected for absorption only in the case of crystals measured by means of CCD detectors [61]. Solution, refinement and geometrical calculations for all crystal structures were performed by SHELXTL [62].

Experimental Details

Synthesis of 1-(2-nitrophenyl)pyrrolidine (3a). 1-Fluoro-2-nitrobenzene (1 equiv, 43 mmol, 4.5 mL) was dissolved with K_2CO_3 (0.6 equiv, 26 mmol, 3.59 g) in 40 mL of acetonitrile. Pyrrolidine (1 equiv, 43 mmol, 3.06 g) was added under stirring to the resulting mixture. The reaction was then heated under reflux during 3 h. 40 mL of water were added to the reaction mixture and the product was extracted with DCM (3 × 50 mL). The organic phase was washed with brine (2 × 50 mL) and with distilled water (50 mL). The organic phase was then dried over Na_2SO_4, filtered and the solvent was evaporated under vacuum to give the product as orange oil. Yield: 8.26 g (99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.73 (*d*, *J* = 8.2 Hz, 1H), 7.36 (*t*, *J* = 8.2 Hz, 1H), 6.90 (*d*, *J* = 8.6 Hz, 1H), 6.70 (*t*, *J* = 7.6 Hz, 1H), 3.21 (*t*, *J* = 6.4 Hz, 4H), 1.98 (*t*, *J* = 6.5 Hz, 4H). ^{13}C-NMR (101 MHz, $CDCl_3$): 142.9, 137.2, 133.1, 126.9, 116.0, 115.6, 50.5, 25.9. HRMS (ESI) for ($[M+H]^+$: $C_{10}H_{13}N_2O_2^+$), calculated: 193.0977, found: 193.0979.

Synthesis of 1-(2-nitrophenyl)azetidine (4a). It was synthesized in a procedure similar to the one described for **3a** except that azetidine (15.8 mmol, 1.67 mL) was used instead of pyrrolidine. Yield: 2.79 g (99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.80 (*d*, *J* = 8.4 Hz, 1H), 7.38 (*dd*, *J* = 8.4, 7.1 Hz, 1H), 6.72 (*dd*, *J* = 8.4, 7.1 Hz, 1H), 6.60 (*d*, *J* = 8.4 Hz, 1H), 3.98 (*t*, *J* = 7.6 Hz, 4H), 2.38 (*quint.*, *J* = 7.5 Hz, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 145.9, 135.7, 133.5, 126.6, 116.5, 115.7, 53.7, 16.4. HRMS (ESI) for ($[M+H]^+$: $C_9H_{11}N_2O_2^+$), calculated: 179.0820, found: 179.0825.

Synthesis of 4-(2-nitrophenyl)morpholine (5a). It was synthesized in a procedure similar to the one described for **3a** except that morpholine (1.74 g, 20 mmol) was used instead of pyrrolidine. Yield: 3.96 g (95%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.77 (*dd*, *J* = 8.1, 1.6 Hz, 1H), 7.50 (*ddd*, *J* = 8.4, 7.4, 1.6 Hz, 1H), 7.15 (*dd*, *J* = 8.3, 1.1 Hz, 1H), 7.12-7.01 (*m*, 1H), 3.92-3.76 (*m*, 4H), 3.14-2.97 (*m*, 4H). ^{13}C-NMR (101 MHz, $CDCl_3$): 146.0, 143.9, 133.7, 126.0, 122.4, 121.1, 67.0, 52.2. HRMS (ESI) for ($[M+H]^+$: $C_{10}H_{13}N_2O_3^+$), calculated: 209.0926, found: 209.0932.

Synthesis of 1-(2-nitrophenyl)piperidine (6a). It was synthesized in a procedure similar to the one described for **3a** except that piperidine (2.82 g, 20 mmol) was used instead of pyrrolidine. Yield: 4.31 g (99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.74 (*d*, *J* = 8.1 Hz, 1H), 7.43 (*t*, *J* = 7.8 Hz, 1H), 7.11 (*d*, *J* = 8.3 Hz, 1H), 6.95 (*t*, *J* = 7.7 Hz, 1H),

3.10-2.92 (*m*, 4H), 1.78-1.66 (*m*, 4H), 1.66- 1.46 (*m*, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 147.2, 142.8, 133.4, 126.1, 121.0, 120.7, 53.1, 26.1, 24.2. HRMS (ESI) for ([M+H]$^+$: $C_{11}H_{15}N_2O_2^+$), calculated: 207.1134, found: 207.1132.

Synthesis of 2-(pyrrolidin-1-yl)aniline (3b). 1-(2-Nitrophenyl)pyrrolidine **3b** (8.0 g, 42 mmol) was dissolved in 40 mL of methanol and 400 mg of Pd/C (5 %/weight of Pd) was added. The reaction flask was degassed and flushed with hydrogen twice. It was then stirred for 14 h under hydrogen (2 bar) at room temperature. The Pd catalyst was filtered off on silica, and the solvent was removed under reduced pressure. The pure compound was obtained as dark yellow oil. Yield: 6.66 g (98%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.00 (*dd*, *J* = 8.2, 1.3 Hz, 1H), 6.96-6.81 (*m*, 1H), 6.74 (*ddd*, *J* = 7.9, 6.1, 1.5 Hz, 2H), 3.86 (*s*, 2H), 3.14-2.93 (*m*, 4H), 2.00-1.83 (*m*, 4H). ^{13}C-NMR (101 MHz, $CDCl_3$): 141.4, 137.8, 123.5, 118.8, 118.7, 115.5, 51.0, 24.2. HRMS (ESI) for ([M+H]$^+$: $C_{10}H_{15}N_2^+$), calculated: 163.1235, found: 163.1240.

Synthesis of 2-(azetidin-1-yl)aniline (4b). It was synthesized in a procedure similar to the one described for **3b** except that 1-(2-nitrophenyl)azetidine (2.78 g, 15.6 mmol) was used instead of 1-(2-nitrophenyl)pyrrolidine. Yield: 2.19 g (95%). ^{1}H-NMR (400 MHz, $CDCl_3$): 6.84-6.75 (*m*, 2H), 6.70-6.60 (*m*, 2H), 3.84 (*t*, *J* = 7.1 Hz, 4H), 3.51 (*s*, 2H), 2.37-2.16 (*m*, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 139.9, 137.4, 121.4, 119.2, 116.0, 114.4, 53.4, 17.6. HRMS (ESI) for ([M+H]$^+$: $C_9H_{13}N_2^+$), calculated: 149.1079, found: 149.1085.

Synthesis of 2-morpholinoaniline (5b). It was synthesized in a procedure similar to the one described for **3b** except that 4-(2-nitrophenyl)morpholine (3.94 g, 18.9 mmol) was used instead of 1-(2-nitrophenyl)pyrrolidine. Yield: 2.75 g (82%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.01 (*d*, *J* = 7.7 Hz, 1H), 6.96 (*t*, *J* = 7.6 Hz, 1H), 6.76 (*t*, *J* = 8.4 Hz, 2H), 4.09-3.91 (*m*, 2H), 3.91-3.79 (*m*, 4H), 3.01-2.84 (*m*, 4H). ^{13}C-NMR (101 MHz, $CDCl_3$): 141.6, 139.1, 125.0, 120.0, 118.8, 115.4, 67.8, 51.6. HRMS (ESI) for ([M+H]$^+$: $C_{10}H_{15}N_2O^+$), calculated: 179.1184, found: 179.1193.

Synthesis of 2-(piperidin-1-yl)aniline (6b). It was synthesized in a procedure similar to the one described for **3b** except that 1-(2-nitrophenyl)piperidine (4.31 g, 21 mmol) was used instead of 1-(2-nitrophenyl)pyrrolidine. Yield: 3.65 g (99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.00 (*d*, *J* = 8.0 Hz, 1H), 6.92 (*t*, *J* = 7.5 Hz, 1H), 6.75 (*t*, *J* = 7.1 Hz, 2H), 3.98 (*s*, 2H), 2.84 (*s*, 4H), 1.71 (*quint.*, *J* = 5.3 Hz, 4H), 1.58 (*s*, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 141.7, 140.9, 124.3, 119.9, 118.6, 115.1, 52.8, 27.0, 24.5. HRMS (ESI) for ([M+H]$^+$: $C_{11}H_{17}N_2^+$), calculated: 177.1392, found: 177.1395.

Synthesis of 1-(2-bromophenyl)pyrrolidine (3c). 1,4-Dibromobutane (1 equiv., 17.4 mmol, 2.1 mL) and *N*,*N*-diisopropylethylamine (2.4 equiv., 41.9 mmol, 7.3 mL) were added to a solution of 2-bromoaniline (1 equiv., 17.4 mmol, 3.01 g) in toluene (20 mL). The reaction was heated at 100°C for 96 h. The product was then purified by column chromatography (on SiO_2, Hexane) to afford the pure compound **3c** as yellow oil. Yield: 2.86 g (72%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.51 (*d*, *J* = 7.9 Hz, 1H), 7.20 (*t*, *J* = 7.4 Hz, 1H), 6.93 (*d*, *J* = 8.1 Hz, 1H), 6.74 (*t*, *J* = 7.5 Hz, 1H), 3.36 (*t*, *J* = 6.2 Hz, 4H), 1.95 (*t*, *J* = 6.3 Hz, 4H). ^{13}C-NMR (101 MHz, $CDCl_3$): 148.9, 134.7, 127.9, 121.4, 118.0, 114.0, 51.4, 25.2. HRMS (ESI) for ([M+H]$^+$: $C_{10}H_{13}BrN^+$), calculated: 226.0231, found: 226.0233.

Synthesis of N^1-(2-(azetidin-1-yl)phenyl)-N^2,N^2-dimethylbenzene-1,2-diamine (4H). A 100 mL reaction vessel was charged with $Pd_2(dba)_3$ (0.02 equiv., 0.27 mmol, 0.25 g), bis(diphenylphosphino)-ferrocene (dppf) (0.04 equiv., 0.54 mmol, 0.30 g), NaO*t*-Bu (1.3 equiv., 17.6 mmol, 1.69 g) and toluene (50 mL) under a N_2 atmosphere. 2-Bromo-*N*,*N*-dimethylaniline (1.1 equiv., 14.9 mmol, 2.98 g) and 2-(azetidin-1-yl)aniline **4b** (13.5 mmol, 2.0 g) were added to the reaction mixture. The resulting brown solution was vigorously stirred for 16 h at 110 °C. The solution was then cooled to room temperature and filtered through Celite. Removal of the solvent yielded a black liquid which was then dissolved in dichloromethane and filtered through silica. The solvent was evaporated and the crude product was purified by column chromatography (on SiO_2, Hexane/Ethyl Acetate 9:1) to afford the pure compound **4H** as a brown oil. Yield: 2.54 g (84%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.30-7.21 (*m*, 1H), 7.13 (*d*, *J* = 7.7 Hz, 1H), 7.05 (*t*, *J* = 7.6 Hz, 1H), 6.98 (*quint.*, *J* = 9.1, 8.4 Hz, 2H), 6.82 (*dt*, *J* = 22.8, 7.4 Hz, 2H), 6.66 (*d*, *J* = 7.9 Hz, 1H), 6.26 (*s*, 1H), 3.85 (*t*, *J* = 7.1 Hz, 4H), 2.73 (*s*, 6H), 2.31-2.14 (*m*, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 146.2, 141.1, 140.3, 130.4, 124.5, 123.7, 123.6, 119.6, 119.5, 118.3, 114.1, 112.7, 53.9, 44.3, 17.6. HRMS

(ESI) for ([M+H]$^+$: $C_{17}H_{22}N_3^+$), calculated: 268.1814, found: 268.1812.

Synthesis of bis(2-(pyrrolidin-1-yl)phenyl)amine (3H). It was synthesized in a procedure similar to the one described for **4H** except that 1-(2-bromophenyl)pyrrolidine **3c** (1 equiv., 27 mmol, 6.24 g) was used instead of 2-bromo-*N*,*N*-dimethylaniline and 2-(pyrrolidin-1-yl)aniline **3b** (1.2 equiv., 32.4 mmol, 5.26 g) was used instead of 2-(azetidin-1-yl)aniline. Yield: 6.81 g (82%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.22 (*d*, *J* = 7.9 Hz, 2H), 7.05 (*d*, *J* = 7.6 Hz, 2H), 6.93 (*t*, *J* = 7.3 Hz, 2H), 6.87 (*t*, *J* = 7.5 Hz, 2H), 6.68 (*s*, 1H), 3.09 (*t*, *J* = 6.0 Hz, 8H), 1.90 (*quint.*, *J* = 3.2 Hz, 8H). ^{13}C-NMR (101 MHz, $CDCl_3$): 140.8, 137.3, 122.6, 120.6, 118.4, 117.3, 51.3, 24.7. HRMS (ESI) for ([M+H]$^+$: $C_{20}H_{26}N_3^+$), calculated: 308.2127, found: 308.2124.

Synthesis of N^1,N^1-dimethyl-N^2-(2-morpholinophenyl)benzene-1,2-diamine (5H). It was synthesized in a procedure similar to the one described for **4H** except that 2-morpholinoaniline **5b** (2.75 g, 15.4 mmol) was used instead of 2-(azetidin-1-yl)aniline. Yield: 3.67 g (80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.63 (*s*, 1H), 7.52-7.37 (*m*, 2H), 7.17-6.97 (*m*, 4H), 6.96-6.82 (*m*, 2H), 3.96-3.77 (*m*, 4H), 3.06-2.91 (*m*, 4H), 2.72 (*s*, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$): 142.9, 141.4, 137.7, 137.6, 124.6, 124.1, 120.1, 120.0, 119.9, 119.8, 115.6, 114.2, 67.9, 52.0, 44.3. HRMS (ESI) for ([M+H]$^+$: $C_{18}H_{23}N_3O^+$), calculated: 298.1919, found: 298.1921.

Synthesis of N^1,N^1-dimethyl-N^2-(2-(piperidin-1-yl)phenyl)benzene-1,2-diamine (6H). It was synthesized in a procedure similar to the one described for **4H** except that 2-(piperidin-1-yl)aniline **6b** (1.72 g, 10 mmol) was used instead of 2-(azetidin-1-yl)aniline. Yield: 2.37 g (80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.69 (*s*, 1H), 7.52-7.41 (*m*, 2H), 7.16-6.96 (*m*, 4H), 6.87 (*t*, *J* = 7.4 Hz, 2H), 2.86 (*s*, 4H), 2.73 (*s*, 6H), 1.79-1.69 (*m*, 4H), 1.63-1.56 (*m*, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 143.0, 143.0, 137.8, 137.7, 124.0, 123.9, 120.2, 119.7, 119.6, 114.8, 114.3, 53.2, 44.1, 27.0, 24.6. HRMS (ESI) for ([M+H]$^+$: $C_{20}H_{25}N_3^+$), calculated: 296.2121, found: 296.2126.

Synthesis of bis(2-(pyrrolidin-1-yl)phenyl)amine nickel(II) chloride (3). *n*-BuLi (1 equiv, 1.6 M in hexane, 10.5 mmol, 6.6 mL) was slowly added to a THF solution (80 mL) of the bis(2-(pyrrolidin-1-yl)phenyl)amine **3H** (3.22 g, 10.5 mmol) at room temperature. The reaction mixture was stirred for 2 h at room temperature, and then $NiCl_2$·dme (1 equiv, 10.5 mmol, 2.31 g, dme = dimethoxyethane) was added at room temperature. The resulting solution was stirred for 5 h and then evaporated under vacuum. The residue was extracted with toluene, filtered through a PTFE filter (0.22 µm pore size) and concentrated to ca. 5 mL. Addition of pentane (20 mL) afforded a brown precipitate which was filtered, washed with additional pentane and dried under vacuum. Yield: 3.45 g (82%). Diffusion of pentane into a toluene solution of **3** at room temperature afforded brown crystals suitable for X-ray analysis. CCDC-1482732 contain(s) the supplementary crystallographic data for this work. These data can be obtained free of charge from *The Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.32 (*d*, *J* = 9.1 Hz, 2H), 6.93 (*t*, *J* = 8.4 Hz, 2H), 6.67 (*d*, *J* = 9.1 Hz, 2H), 6.37 (*t*, *J* = 8.1 Hz, 2H), 4.51-4.30 (*m*, 4H), 3.24-3.10 (*m*, 4H), 1.91 (*t*, *J* = 7.0 Hz, 8H). ^{13}C-NMR (101 MHz, $CDCl_3$): 150.4, 147.5, 127.3, 121.5, 116.0, 113.6, 61.9, 24.7. Anal. calc. for $C_{20}H_{24}ClN_3Ni$ (400.58): C 59.97, H 6.04, N 10.49; found: C 60.05, H 6.06, N 10.34.

Synthesis of N^1-(2-(azetidin-1-yl)phenyl)-N^2,N^2-dimethylbenzene-1,2-diamine nickel(II) chloride (4). It was synthesized in a procedure similar to the one described for **3** except that N^1-(2-(azetidin-1-yl)phenyl)-N^2,N^2-dimethylbenzene-1,2-diamine **4H** (1.53 g, 5.7 mmol) was used instead of bis(2-(pyrrolidin-1-yl)phenyl)amine. Yield: 1.64 g (80%). Single crystals suitable for X-ray crystallography were obtained by diffusion of pentane into a toluene solution of **4** at room temperature. CCDC-1482731 contain(s) the supplementary crystallographic data for this work. These data can be obtained free of charge from *The Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.47-7.30 (*m*, 3H), 7.08-6.89 (*m*, 3H), 6.57 (*t*, *J* = 7.5 Hz, 1H), 6.47 (*t*, *J* = 7.4 Hz, 1H), 5.08 (*quint.*, *J* = 9.7 Hz, 2H), 3.64 (*q*, *J* = 9.8 Hz, 2H), 2.91 (*s*, 6H), 2.43 (*tt*, *J* = 17.4, 7.6 Hz, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 149.4, 148.1, 147.6, 146.7, 128.3, 128.1, 120.9, 120.3, 116.7, 116.0, 114.0, 113.7, 64.8, 51.3, 18.0. Anal. calc. for $C_{17}H_{20}ClN_3Ni$ (360.51): C 56.64, H 5.59, N 11.66; found: C 56.66, H 5.57, N 11.57.

Synthesis of N^1,N^1-dimethyl-N^2-(2-morpholinophenyl)benzene-1,2-diamine nickel(II)

chloride (5). It was synthesized in a procedure similar to the one described for **3** except that N^1,N^1-dimethyl-N^2-(2-morpholinophenyl)benzene-1,2-diamine **5H** (2.58 g, 8.7 mmol) was used instead of bis(2-(pyrrolidin-1-yl)phenyl)amine. Yield: 2.51 g (74%). Single crystals suitable for X-ray crystallography were obtained by diffusion of pentane into a toluene solution of **5** at room temperature. CCDC-1482733 contain(s) the supplementary crystallographic data for this work. These data can be obtained free of charge from *The Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36 (*d*, *J* = 7.7 Hz, 1H), 7.23 (*dd*, *J* = 12.8, 8.1 Hz, 2H), 7.07-6.90 (*m*, 3H), 6.42 (*dt*, *J* = 21.8, 6.8 Hz, 2H), 4.44 (*s*, 2H), 4.11 (*s*, 2H), 3.94 (*s*, 2H), 3.22 (*d*, *J* = 11.8 Hz, 2H), 2.91 (*s*, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$): 147.1, 147.0, 146.9, 145.8, 128.0, 127.7, 121.7, 120.1, 117.0, 116.1, 115.2, 113.9, 63.3, 54.9, 51.6. Anal. calc. for $C_{18}H_{22}ClN_3NiO$ (390.54): C 55.36, H 5.68, N 10.76; found: C 55.35, H 5.64, N 10.68.

Synthesis of N^1,N^1-dimethyl-N^2-(2-(piperidin-1-yl)phenyl)benzene-1,2-diamine nickel(II) chloride (6). It was synthesized in a procedure similar to the one described for **3** except that N^1,N^1-dimethyl-N^2-(2-(piperidin-1-yl)phenyl)benzene-1,2-diamine **6H** (1 g, 3.4 mmol) was used instead of bis(2-(pyrrolidin-1-yl)phenyl)amine. Yield: 0.99 g (75%). Single crystals suitable for X-ray crystallography were obtained by diffusion of pentane into a toluene solution of **6** at room temperature. CCDC-1482734 contain(s) the supplementary crystallographic data for this work. These data can be obtained free of charge from *The Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39 (*t*, *J* = 7.3 Hz, 2H), 7.32 (*d*, *J* = 8.3 Hz, 1H), 6.96 (*t*, *J* = 8.1 Hz, 3H), 6.40 (*dt*, *J* = 28.8, 7.6 Hz, 2H), 4.39-4.21 (*m*, 2H), 3.47 (*d*, *J* = 13.1 Hz, 2H), 2.90 (*s*, 6H), 1.91 (*q*, *J* = 10.1, 7.5 Hz, 2H), 1.83-1.67 (*m*, 2H), 1.60 (*d*, *J* = 14.1 Hz, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$): 147.9, 147.2, 147.0, 146.6, 128.0, 127.4, 123.4, 120.1, 116.4, 115.4, 114.7, 114.0, 55.8, 51.6, 22.3, 22.3. Anal. calc. for $C_{19}H_{24}ClN_3Ni$ (388.57): C 58.73, H 6.23, N 10.81; found: C 58.68, H 6.26, N 10.72.

Synthesis of [(^{Me}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (8). A solution of silver tetrafluoroborate $AgBF_4$ (1 equiv, 0.4 mmol, 78 mg) in CH_3CN (2 mL) was added to a solution of **1** (0.4 mmol, 139 mg) in CH_3CN (2 mL). The resulting green solution was stirred for 30 min and then the white precipitate of AgCl was isolated by filtration. The filtrate was evaporated and the solid was washed with toluene (1 mL) and pentane (2 mL), then dried under vacuum to afford a green solid. Recrystallized at room temperature from a 1:5 MeCN/Et_2O mixture. Yield: 159 mg (90%). ^{1}H-NMR (400 MHz, (D_6)Acetone): 7.47 (*d*, *J* = 8.3 Hz, 2H), 7.35 (*d*, *J* = 7.9 Hz, 2H), 7.08 (*t*, *J* = 7.6 Hz, 2H), 6.59 (*t*, *J* = 7.5 Hz, 2H), 3.06 (*s*, 12H), 2.53 (*s*, 3H, C*H*$_3$CN). ^{13}C-NMR (101 MHz, (D_6)Acetone): 147.9, 146.3, 129.6, 121.6, 117.8, 115.3, 51.3. Anal. calc. for $C_{18}H_{23}N_4NiBF_4$ (440.91): C 49.03, H 5.26, N 12.71; found: C 48.97, H 5.34, N 12.26.

Synthesis of [(^{Pyr}N^{Me}NN)Ni(NCCH$_3$)]BF$_4$ (9). It was synthesized in a procedure similar to the one described for [(^{Me}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (**8**) except that complex **2** (0.4 mmol, 150 mg) was used instead of complex **1**. Green crystals recrystallized at room temperature from a 1:5 MeCN/Et_2O mixture. Yield: 164 mg (88%). ^{1}H-NMR (400 MHz, (D_6)Acetone): 7.48-7.38 (*m*, 2H), 7.34 (*d*, *J* = 8.0 Hz, 1H), 7.02 (*d*, *J* = 7.9 Hz, 3H), 6.58 (*t*, *J* = 7.6 Hz, 1H), 6.52 (*t*, *J* = 7.5 Hz, 1H), 4.39 (*dt*, *J* = 11.5, 6.1 Hz, 2H), 3.44-3.32 (*m*, 2H), 3.06 (*s*, 6H), 2.31 (*s*, 3H, C*H*$_3$CN), 2.25-2.11 (*m*, 4H). ^{13}C-NMR (101 MHz, (D_6)Acetone): 149.5, 147.9, 147.5, 146.2, 129.6, 129.4, 128.7, 122.4, 121.4, 117.7, 115.1, 114.7, 62.9, 51.2, 25.5. Anal. calc. for $C_{20}H_{25}N_4NiBF_4$ (466.95): C 51.44, H 5.40, N 12.00; found: C 51.40, H 5.44, N 12.09.

Synthesis of [(^{Pyr}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (10). It was synthesized in a procedure similar to the one described for [(^{Me}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (**8**) except that complex **3** (0.4 mmol, 160 mg) was used instead of complex **1**. Green crystals recrystallized at room temperature from a 1:5 MeCN/Et_2O mixture. Yield: 170 mg (86%). ^{1}H-NMR (400 MHz, (D_6)Acetone): 7.45-7.30 (*m*, 2H), 7.01 (*d*, *J* = 6.8 Hz, 4H), 6.51 (*m*, 2H), 4.47-4.34 (*m*, 4H), 3.43-3.33 (*m*, 4H), 2.32 (*s*, 3H, C*H*$_3$CN), 2.18 (*m*, 8H). ^{13}C-NMR (101 MHz, (D_6)Acetone): 149.4, 147.5, 128.4, 122.1, 117.6, 114.3, 62.8, 25.3. Anal. calc. for $C_{22}H_{27}N_4NiBF_4$ (492.98): C 53.60, H 5.52, N 11.37; found: C 53.65, H 5.54, N 11.45.

Synthesis of [(^{Aze}N^{Me}NN)Ni(NCCH$_3$)]BF$_4$ (11). It was synthesized in a procedure similar to the one described for [(^{Me}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (**8**) except that complex **4** (0.4 mmol, 144 mg) was used instead of complex **1**. Green crystals recrystallized at room temperature from a 1:5

MeCN/Et_2O mixture. Yield: 152 mg (84%). ^{1}H-NMR (400 MHz, (D_6)Acetone): 7.74-7.58 (*m*, 1H), 7.45-7.28 (*m*, 3H), 7.10-6.97 (*m*, 2H), 6.67 (*t*, *J* = 7.4 Hz, 1H), 6.57 (*t*, *J* = 7.3 Hz, 1H), 5.00 (*q*, *J* = 10.1 Hz, 2H), 4.00 (*q*, *J* = 10.0 Hz, 2H), 3.07 (*s*, 6H), 2.70 (*s*, 3H, C*H*$_3$CN), 2.43 (*d*, *J* = 9.4 Hz, 2H). ^{13}C-NMR (101 MHz, (D_6)Acetone): 148.5, 148.4, 148.0, 146.2, 129.5, 129.3, 122.2, 121.5, 118.3, 117.6, 114.9, 114.6, 64.9, 51.2, 17.7. Anal. calc. for $C_{19}H_{23}N_4NiBF_4$ (452.92): C 50.39, H 5.12, N 12.37; found: C 50.36, H 5.16, N 12.44.

Synthesis of [(^{Morph}N^{Me}NN)Ni(NCCH$_3$)]BF$_4$ (12). It was synthesized in a procedure similar to the one described for [(^{Me}N$_2$N)Ni(NCCH$_3$)]BF$_4$ (**8**) except that complex **5** (0.4 mmol, 160 mg) was used instead of complex **1**. Blue crystals recrystallized at room temperature from a 1:5 MeCN/Et_2O mixture. Yield: 127 mg (66%). ^{1}H-NMR (400 MHz, (D_6)Acetone): 7.43 (*dd*, *J* = 12.2, 8.2 Hz, 2H), 7.23-7.11 (*m*, 2H), 7.11-7.00 (*m*, 2H), 6.88 (*dt*, *J* = 12.8, 7.3 Hz, 2H), 4.13 (*d*, *J* = 9.0 Hz, 2H), 3.96-3.71 (*m*, 6H), 2.90 (*s*, 3H, C*H*$_3$CN), 2.73 (*s*, 6H). ^{13}C-NMR (101 MHz, (D_6)Acetone): 144.5, 143.9, 141.9, 140.6, 127.0, 126.5, 123.6, 123.1, 120.1, 119.3, 119.0, 114.3, 63.8, 53.2, 47.6. Anal. calc. for $C_{20}H_{25}N_4NiOBF_4$ (482.94): C 49.74, H 5.22, N 11.60; found: C 49.86, H 5.26, N 11.51.

Synthesis of [(^{Pip}N^{Me}NN)Ni(NCCH$_3$)]BAr$^F_4$ (13). A solution of sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate NaBAr$^F_4$ (1 equiv, 0.4 mmol, 354 mg) in CH_3CN (2 mL) was added to a solution of **6** (0.4 mmol, 155 mg) in CH_3CN (2 mL). The resulting green solution was stirred for 30 min and then filtred through PTFE filter (0.22 µm pore size). The filtrate was evaporated and the solid was washed with cold pentane (2 mL), then dried under vacuum to afford a green solid, which was directly used for NMR and electrochemical measurements in solution.Yield: 241 mg (48%). ^{1}H NMR (400 MHz, Acetone-d_6): 7.82 (s, 8H), 7.70 (s, 4H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.31-7.25 (m, 2H), 7.15 (dd, *J* = 13.0, 6.4 Hz, 4H), 4.16 (d, *J* = 34.6 Hz, 4H), 3.54 (s, 6H), 2.83 (s, 3H, C*H*$_3$CN), 2.70 (m, 6H). ^{13}C NMR (101 MHz, Acetone-d_6): 163.1, 162.6, 162.1, 161.7, 135.4, 130.3, 130.0, 130.0, 129.7, 129.4, 129.3, 128.8, 128.6, 126.5, 123.8, 121.3, 121.1, 118.3, 56.7, 50.5, 23.7, 22.5.

General procedure for the alkyl-alkyl Kumada reactions. A 2 M solution of alkyl-MgCl (commercially available, 1.2 equiv, 0.6 mmol) was diluted to 1 mL with THF. The solution was then slowly added by a syringe pump over 2 h to a solution containing the catalyst (3.5 mol %, 0.007 mmol), 0.3 mL of DMA, 0.2 mL of THF and the halide (0.2 mmol) at -20°C. After the addition, the solution was stirred for 30 min at -20°C. It was then quenched by the addition of 5 mL water. The organic phase in the resulting solution mixture was extracted with 20 mL of ether, and subjected to GC-MS analysis. 60 µL of decane (0.31 mmol) were used as an internal standard.

General procedure for the alkyl-alkyl Suzuki-Miyaura reactions. To a solution of sodium hydroxide (1.6 equiv, 0.32 mmol, 13 mg), catalyst (5 mol %, 0.01 mmol), sodium iodide (0.5 equiv, 0.1 mmol, 15 mg), isopropanol (2 equiv, 0.4 mmol, 30 µL) in 1 mL of dry 1,4-dioxane, were added alkyl halide (0.2 mmol) and the 9-octyl-9-borabicyclo[3.3.1]nonane (1.6 equiv, 0.32 mmol, 0.64 mL of a 0.5 M stock solution in 1,4-dioxane) under a N_2 atmosphere. The reaction mixture was stirred at room temperature for 24 h. The solution was diluted in ether (20 mL) and subjected to GC-MS analysis. 60 µL of decane (0.31 mmol) were used as an internal standard.

Inhibition experiments for Kumada coupling. Following the general procedure used for the alkyl-alkyl Kumada reactions, the inhibition experiments were conducted with 1 mol % of catalyst (0.002 mmol) and 10 mol % of extra ligand (10 equivalent relative to catalyst, 0.02 mmol) in the starting reaction mixture. Amount of 10 mol % of extra ligand were: 2.3 µL of 2,4-lutidine, 1.6 µL of pyridine and 5.2 mg of PPh_3.

Stability experiments for Suzuki-Miyaura cross-coupling reactions. Following the general procedure used for the alkyl-alkyl Suzuki-Miyaura reactions, the reaction mixtures were stirred at room temperature for a defined pre-stirring time before the simultaneous addition of (4-iodobutyl)benzene and 9-octyl-9-borabicyclo[3.3.1]nonane (*n*-octyl-(9-BBN)). Reaction mixture was then stirred for 24 h at room temperature.

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