Organic LETTERS

Letter

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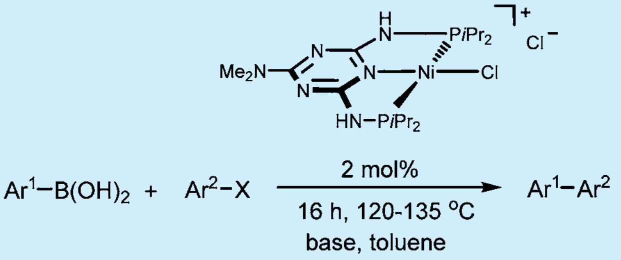
Air-Stable Triazine-Based Ni(II) PNP Pincer Complexes As Catalysts for the Suzuki–Miyaura Cross-Coupling

Matthias Mastalir,[†] Berthold Stöger,[‡] Ernst Pittenauer,[‡] Günter Allmaier,[‡] and Karl Kirchner*[,†]

[†]Institute of Applied Synthetic Chemistry, Vienna University of Technology, Getreidemarkt 9/163-AC, A-1060 Wien, Austria
[‡]Institute of Chemical Technologies and Analytics, Vienna University of Technology, Getreidemarkt 9/163-AC, A-1060 Wien, Austria

S Supporting Information

ABSTRACT: Air-stable, thermally robust, and well-defined cationic Ni(II) PNP pincer complexes based on the 2,4-diaminotriazine scaffold are described. These complexes are active catalysts for the Suzuki–Miyaura cross-coupling of a wide range of aryl, heteroaryl (including benzoxazole, thiazole, pyridine, pyrimidine, thiazole), primary and secondary alkyl halides, and pseudohalides with different organoboronate reagents giving excellent to good isolated yields. Neutral deprotonated complexes seem to play a key role in the catalytic process.



Since its discovery in 1979,[1] the Suzuki–Miyaura (SM) cross-coupling involving the coupling of an organoboron reagent and organic halides or pseudohalides has become one of the most important and prevalent methods for the construction of carbon–carbon bonds.[2−4] An advantage over other cross-coupling reactions is the wide accessibility of organoboronate reagents, which reveal a broad functional group tolerance, are markedly stable, and are generally environmentally benign. Accordingly, applications of SM couplings comprise a wide array of synthetic targets, ranging from manufacturing of materials and pharmaceuticals to the synthesis of building blocks and natural products.[2−4] Although palladium catalysts still dominate the field, the use of nickel catalysts has become increasingly important.[5−7] Nickel is more abundant, less toxic, and inexpensive as compared to palladium and thus preferable in terms of sustainability and economic viability. Moreover, nickel has a pronounced ability to cleave not only C-halide[8,9] but also C−O and C−N bonds such as in aryl ethers,[10]

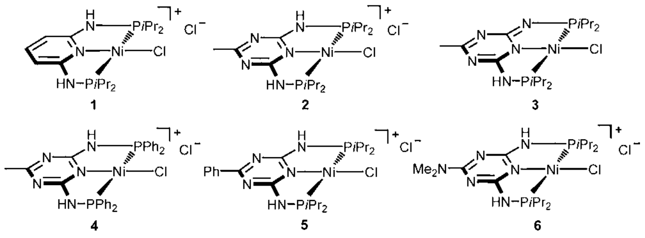


Figure 1. Ni(II) PNP pincer complexes **1**−**6**.

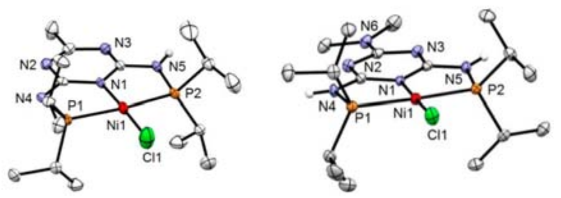
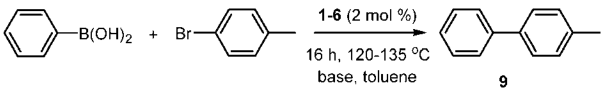


Figure 2. Structural views of [Ni(Triaz^{Me}-*i*Pr*)Cl]·$C_4H_8O_2$ (**3**·$C_4H_8O_2$) (left) and [Ni(Triaz^{NMe2}-*i*Pr)Cl]Cl (**6**) (right) showing 50% thermal ellipsoids (most H atoms omitted for clarity). Selected bond lengths (Å) and angles (deg): **3**: Ni1−Cl1 2.177(2), Ni1−P1 2.203(2), Ni1−P2 2.178(2), Ni1−N1 1.885(3), P1−Ni1−P2 167.4(1), Cl1−Ni1−N1 177.4(1). **6**: Ni1−Cl1 2.1491(8), Ni1−P1 2.1729(8), Ni1−P2 2.1670(8), Ni1−N1 1.868(2), Cl1−Ni1−N1 175.97(6), P1−Ni1−P2 170.31(3).

Table 1. Efficiency of Nickel Precatalysts 1−6 in Suzuki–Miyaura Cross-Couplings



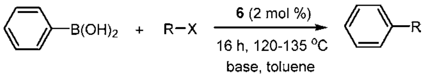
entry	precatalyst	base	yield[a] [%]
1	**1**	*t*-BuOK	12
2	**2**	*t*-BuOK	80
3	**2**	K_3PO_4	69
4	**3**	*t*-BuOK	81
5	**3**	K_3PO_4	72
6	**4**	*t*-BuOK	71
7	**4**	K_3PO_4	60
8	**5**	*t*-BuOK	78
9	**5**	K_3PO_4	52
10	**6**	*t*-BuOK	93
11	**6**	K_3PO_4	85

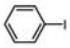
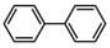
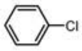
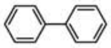
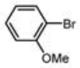
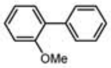
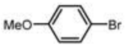
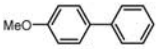
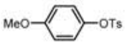
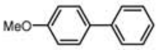
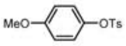
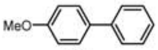
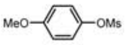
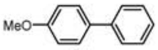
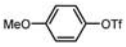
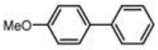
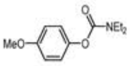
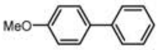
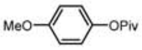
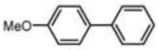
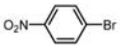
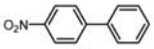
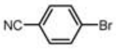
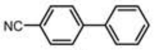
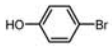
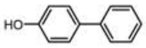
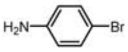
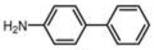
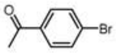
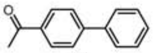
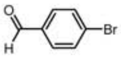
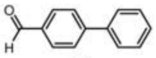
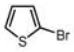
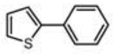
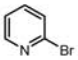
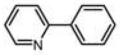
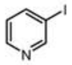
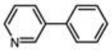
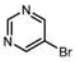
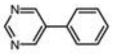
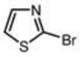
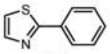
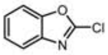
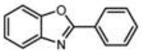
[a]Isolated yields after purification with silica column chromatography.

Received: May 13, 2016
Published: June 9, 2016

DOI: 10.1021/acs.orglett.6b01398
Org. Lett. 2016, 18, 3186−3189

Table 2. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Phenylboronic Acid with Aromatic Halides and Pseudohalides



entry	R-X	base	product	yield[a] [%]
1		*t*-BuOK	 **10**	92
2[b]		*t*-BuOK	 **10**	70
3		*t*-BuOK	 **11**	89
4		*t*-BuOK	 **12**	92
5		*t*-BuOK	 **12**	87
6		K_3PO_4	 **12**	81
7		K_3PO_4	 **12**	75
8		*t*-BuOK	 **12**	92
9		K_3PO_4	 **12**	84
10		K_3PO_4	 **12**	51
11		K_3PO_4	 **13**	80
12		K_3PO_4	 **14**	78
13		*t*-BuOK	 **15**	67
14		*t*-BuOK	 **16**	61
15		*t*-BuOK	 **17**	75
16		K_3PO_4	 **18**	44
17		*t*-BuOK	 **19**	73
18		*t*-BuOK	 **20**	72
19		*t*-BuOK	 **21**	85
20		*t*-BuOK	 **22**	82
21		*t*-BuOK	 **23**	77
22		*t*-BuOK	 **24**	83

[a] Isolated yields after purification with silica column chromatography. [b] At 135 °C for 24 h.

acetates,[11] pivalates, carbamates, sulfonates, sulfamates,[12] esters,[13] or amides[14] which renders these electrophiles to attractive coupling partners. With respect to the oxidation state of the Ni complexes for SM reactions both Ni(0) and Ni(II) compounds are utilized,[15] with the latter not being air and moisture sensitive and thermally stable; these are thus synthetically more easily accessible.

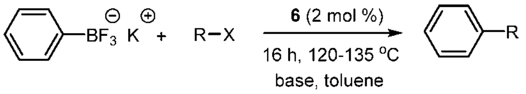
Here, we report air-stable and well-defined Ni(II) PNP pincer complexes based on the triazine scaffold as catalysts for the SM cross-coupling of several sp^2 and sp^3 halides and pseudohalides with different organoboronate reagents. This type of ligands was recently successfully applied by Kempe and co-workers[16] for the synthesis of stable cobalt complexes which turned out to be active catalysts for the hydrogenation of C═O bonds and the alkylation of aromatic amines by alcohols. It has to be noted that pincer complexes have been rarely used for nickel catalyzed SM reactions.[17]

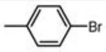
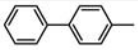
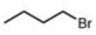
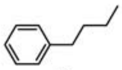
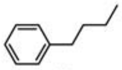
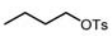
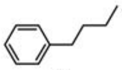
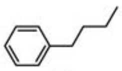
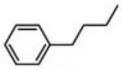
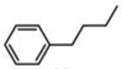
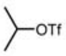
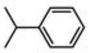
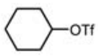
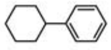
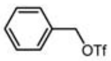
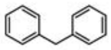
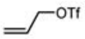
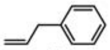
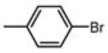
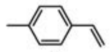
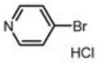
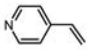
We prepared the air-stable cationic Ni(II) complexes **1**, **2**, **4**–**6** by treatment of $NiCl_2 \cdot 6H_2O$ with the respective PNP ligands in 94–96% isolated yields (Figure 1).[18] The deprotonated complex **3** was obtained by reacting **2** with 1 equiv of *t*-BuOK toluene in 62% isolated yield. This complex was prepared since deprotonated species appear to play a key role in Kempe's cobalt catalyzed reactions.[16] The solid state structures of **3** and **6** were determined by single-crystal X-ray diffraction. Structural views are depicted in Figure 2 with selected bond distances given in the caption.

The reaction of 4-bromotoluene and phenyl boronic acid in toluene at 120–135 °C for 16 h was investigated to identify the most efficient catalyst for the SM coupling in the presence of the bases *t*-BuOK and K_3PO_4 (Table 1). All complexes are poorly soluble in toluene at room temperature, but readily dissolve at elevated temperatures in the presence of a base. Complexes **2**, **3**, and **6** turned out to the best catalyst with 80%, 81%, and 93% isolated yields in the presence of *t*-BuOK (Table 1, entries 2, 4, and 10), while the pyridine-based complex **1** was the least active one. The yields with K_3PO_4 as a base are generally slightly lower under the same reaction conditions. Interestingly, the deprotonated complex **3** compared to complex **2** showed similar reactivity, suggesting that a deprotonated complex may play a key role in the catalytic process.[16] In contrast to all other complexes, this species is air and moisture sensitive.

In the following, precatalyst **6** is used for this study in combination with the bases *t*-BuOK and K_3PO_4. To explore the scope of this catalyst we evaluated first the coupling of various

Table 3. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Aromatic and Aliphatic Bromides, Tosylates, and Triflates with Potassium Phenyltrifluoroborate

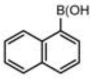
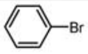
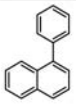
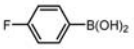
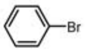
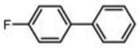
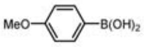
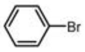
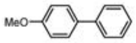
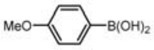
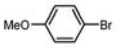
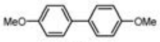
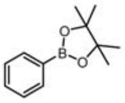
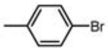
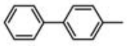
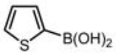
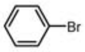
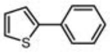
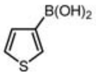
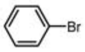
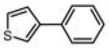


entry	R-X	base	product	yield[a] [%]
1		t-BuOK	 9	98
2		t-BuOK	 25	63
3		K_3PO_4	 25	45
4		t-BuOK	 25	76
5		K_3PO_4	 25	71
6		t-BuOK	 25	87
7		K_3PO_4	 25	90
8		K_3PO_4	 26	34
9		K_3PO_4	 27	39
10		K_3PO_4	 28	63
11		K_3PO_4	 29	42
12[b]		t-BuOK	 30	93
13[b]		t-BuOK	 31	84

[a] Isolated yields after purification with silica column chromatography. [b] With potassium vinyltrifluoroborate (0.15 mmol).

Table 4. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Boronic Acids and Esters with Aryl Bromides

$$Ar^1{-}B(OH)_2 \; + \; Ar^2{-}X \xrightarrow[\text{16 h, 120-135 °C, base, toluene}]{\text{6 (2 mol \%)}} Ar^1{-}Ar^2$$

entry	Ar^1-B(OH)$_2$	Ar^2-Br	product	yield[a] [%]
1			 32	87
2			 33	94
3			 12	86
4			 34	88
5[b]			 9	97
6			 19	81
7			 35	85

[a] Isolated yields after purification with silica column chromatography. [b] With phenylboronic acid pinacol ester (0.15 mmol).

aryl and heteroaryl halides and "pseudo halides" (triflates, tosylates, mesylates, pivalates, and carbamates) with phenyl boronic acid. The results of the couplings catalyzed by complex **6** are summarized in Table 2. In general, good to excellent isolated yields were observed for most substrates containing electron-donating groups (OH, OMe, NH_2) or electron-withdrawing groups (CN, NO_2, acyl, formyl) thus not following any obvious trend. Also heteroaryl halides (based on benzoxazole, thiazole, pyridine, pyrimidine, thiophene, thiazole) afforded good yields. This is particularly interesting in the case of pyridines and pyrimidines due their coordinating properties (Table 2, entries 18–20). Chlorobenzene (Table 2, entry 2) and 4-bromobenzaldehyde (Table 2, entry 16) were also suitable substrates, although the isolated yield was moderate in the case of the latter (44%). This may be attributed to side reactions of the substrate with a base under these reaction conditions.

Moreover, we tested the reactivity of some nonactivated primary and secondary aliphatic bromides and "pseudo halides" for the cross-coupling with phenyltrifluoroborates and vinyltrifluoroborate (Table 3). This reaction proceeds in good isolated yields (63–98%).

In particular, the vinylation of 4-bromo toluene and 4-bromo pyridine afforded high yields of 4-methylstyrene and 4-vinylpyridine (Table 3, entries 12 and 13). Only with butyl bromide (with K_3PO_4 as base), isopropyl and cyclohexyl triflates (Table 3, entries 2, 8 and 9), and vinyl triflate (Table 3, entry 11) lower yields were observed. The lower yields may be due to elimination reactions of the alkyl chain under basic conditions at elevated temperature.

Finally, we also varied the organoboronate reagent and investigated the coupling of several aryl and heteroarylboronic acids and one arylboronic acid ester with aryl bromides. The results of this study are shown in Table 4 revealing in all cases good to excellent isolated yields.

In conclusion, air-stable, thermally robust, and well-defined cationic Ni(II) PNP pincer complexes based on the 2,4-diaminotriazine scaffold are synthesized. The cationic Ni(II) complexes are readily deprotoanted to give neutral complexes. This has been shown on one example which has been isolated and even structurally characterized. With these easy to handle Ni(II) complexes, we have developed a protocol for the arylation, alkylation, and vinylation of a wide range of aryl, heteroaryl, alkyl halides, and pseudohalides with different organoboronate reagents using the Suzuki–Miyaura coupling. In most cases, high yields of isolated products are obtained. Deprotonated neutral Ni(II) complexes seem to be key intermediates in the catalytic reaction. In one case, it has been exemplarily shown that such a species is indeed an active catalyst.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01398.

Crystallographic data **3** and **6** (CCDC entries 1472541 (**3**) and 1472542 (**6**)) (CIF)

Complete crystallographic data, synthetic procedures, ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra of all complexes and organic products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: kkirch@mail.tuwien.ac.at.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

M.M. and K.K. gratefully acknowledge the financial support by the Austrian Science Fund (FWF) (Project No. P28866-N34). The X-ray center of the Vienna University of Technology is acknowledged for financial support and for providing access to the single-crystal diffractometer.

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