Amido pincer complex of nickel-catalysed Kumada cross-coupling reactions†

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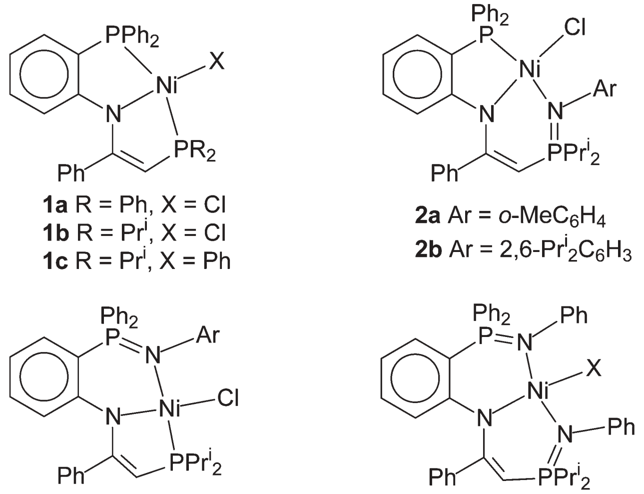
Novel nickel complexes bearing P,N,P-, P,N,N- and N,N,N-amido pincer ligands exhibited highly catalytic activity in Kumada coupling reactions.

Group 10 metal catalysed C–C coupling between Grignard reagents and aryl halides has been extensively investigated and widely used in modern synthetic organic chemistry[1] since the pioneering work of Kumada and Corriu.[2] However, exploration of the catalytic systems for unactivated electrophilic substrates is still challenging.[3] Recent promising catalytic systems spurred much attention towards new catalysts for use of relatively unreactive but cheaper and more widely available aryl chlorides as starting materials.[1c,4] Several types of nickel and palladium complexes have been reported to catalyse the coupling of Grignard reagents with aryl chlorides effectively.[4,5] Herein we report a new series of catalytic nickel complexes with amido pincer ligands for Kumada coupling reactions.

The amido pincer complexes of nickel chloride **1a**, **1b** and **2a–4a** (Fig. 1) were synthesised by ligand transfer reaction between $(Et_3P)_2NiCl_2$ and the corresponding amido lithium complexes. **1b** and **4a** were further transformed into the respective phenyl or butyl derivative, **1c** and **4b**, by reaction with PhMgBr and $LiBu^n$, respectively. Complexes **1a–4a** were air stable in the solid state at room temperature and **4b** decomposed slowly when exposed to air. They were quite soluble in CH_2Cl_2 and THF and soluble in toluene. Each of **1a–3c** was diamagnetic and characterised by ^1H, ^{13}C and ^{31}P NMR spectroscopy and elemental analyses. The structures of **1c**, **2b** and **3c** were also characterised by single-crystal X-ray diffraction techniques‡ and the results showed that in each complex the nickel atom has a distorted square planar geometry. An ORTEP view of **3c** as a representative example is presented in Fig. 2. Complex **4a** was paramagnetic and characterised by elemental analysis and HRMS. The paramagnetism is probably due to excessive distortion from square planar coordinate geometry at the nickel atom. Attempts to grow its single crystals for X-ray diffraction analysis were unsuccessful. However, its butyl derivative **4b** was diamagnetic and was fully characterised by NMR spectroscopy and elemental analysis. Single-crystal diffraction result also confirmed the square planar geometry around the central nickel atom.‡



1a R = Ph, X = Cl
1b R = Pr^i, X = Cl
1c R = Pr^i, X = Ph

2a Ar = o-MeC_6H_4
2b Ar = 2,6-$Pr^i_2C_6H_3$

3a Ar = Ph
3b Ar = o-MeC_6H_4
3c Ar = 2,6-$Pr^i_2C_6H_3$

4a X = Cl
4b X = Bu^n

Fig. 1 Amido pincer complexes of nickel **1–4**.

To evaluate the catalytic activity of complexes **1a–4b** in the Kumada coupling reaction, we first carried out the catalytic reaction of aryl iodides p-RC_6H_4I with p-MeC_6H_4MgBr (Table 1).§ Each of complexes **1a–4b** was capable of catalysing the cross-coupling reactions in toluene at room temperature to yield the

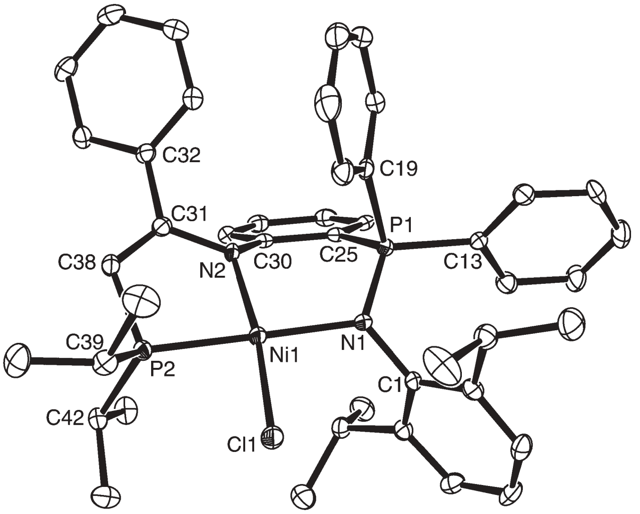


Fig. 2 ORTEP view (50% probability) of complex **3c**. Selected interatomic distances (Å) and angles (°): Ni1–N1 1.9773(18), Ni1–N2 1.9386(17), Ni1–P2 2.1399(10), Ni1–Cl1 2.1769(8); N1–Ni1–N2 95.26(7), N1–Ni1–P2 176.29(5), N1–Ni1–Cl1 92.34(6), N2–Ni1–P2 86.21(6), N2–Ni1–Cl1 172.39(5), P2–Ni1–Cl1 86.18(4).

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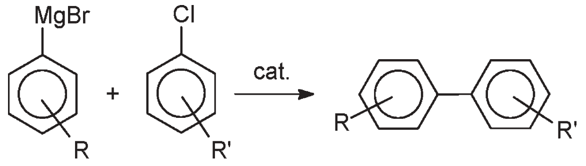
Table 1 Evaluation of complexes **1–4** in the cross-coupling reactions of p-MeC$_6$H$_4$MgBr with p-RC$_6$H$_4$I[a]

Entry	Catalyst (mol%)	R	Time/h	Yield[b] (%)
1	**1a** (0.5)	H	11	99
2	**1b** (0.5)	H	12	>99
3	**1b** (0.5)	OMe	12	99
4	**1c** (1)	H	13	97.8
5	**2a** (0.02)	H	12	>99
6	**2a** (0.02)	OMe	22	>99
7	**2b** (0.1)	H	3	>99
8	**3a** (0.02)	H	12	91
9	**3a** (0.05)	H	12	99
10	**3b** (0.02)	H	12	99
11	**3b** (0.02)	OMe	12	99
12	**3c** (0.2)	H	3	>99
13	**4a** (0.005)	H	12	89
14	**4a** (0.01)	H	12	>99
15	**4a** (0.01)	OMe	12	98.4
16	**4b** (0.005)	H	12	98.5

[a] Reaction was carried out in toluene at room temperature. [b] Yields of isolated products.

desired biaryls in high isolated yield. No homocoupling product of the Grignard reagent was observed. Among the catalysts tested, the nickel complexes with P,N,P-chelate ligands, **1a–1c**, showed relatively low catalytic activity, while each of **2a–4b** displayed excellent catalytic activity. For example, in the reaction of p-MeC$_6$H$_4$MgBr and iodobenzene 0.02 mol% of **2a**, **3a** or **3b** could catalyse the coupling reaction to approach completion within 12 h, giving almost quantitative cross-coupling products (Table 1, entries 5, 8 and 10). Increasing amount of the catalysts could significantly reduce the reaction time. Excessive steric hindrance of ligands resulted in a decrease of catalytic activity of the catalysts. For example, 0.02 mol% of **2a** could catalyse the reaction of C$_6$H$_5$I with p-MeC$_6$H$_4$MgBr to go to completion within 12 h, giving coupling product in >99% yield (Table 1, entry 5); while the reaction catalysed by 0.02 mol% **2b** under the same conditions gave only 21% yield of coupling product. Comparison between **3b** and **3c** revealed a similar result. Both **4a** and **4b** were highly active catalysts in the coupling reaction of p-MeC$_6$H$_4$MgBr with aryl iodides. 0.01 mol% **4a** or 0.005 mol% of **4b** could catalyse the reaction of p-MeC$_6$H$_4$MgBr with C$_6$H$_5$I to reach completion (Table 1, entries 14 and 16). These complexes could also catalyse the coupling reaction of deactivated p-MeOC$_6$H$_4$I with p-MeC$_6$H$_4$MgBr effectively. Representative examples are presented in Table 1 (entries 3, 6, 11 and 15). In addition, the reactions performed in THF gave either cross-coupling products or Grignard homocoupling product depending on the reactants and catalysts employed.

Table 2 Catalytic coupling of aryl Grignard reagents and aryl chlorides by complexes **1–4**[a]



Entry	Catalyst (mol%)	R	R′	Reaction conditions	Yield[b] (%)
1	**1a** (2.5)	p-Me	H	RT, 24 h	80
2	**1a** (2.5)	p-Me	H	80 °C,[c] 6 h	91
3	**1b** (2.5)	p-Me	H	RT, 24 h	92.8
4	**1b** (2.5)	p-Me	H	80 °C,[c] 6 h	99
5	**1b** (2.5)	o-Me	H	RT, 24 h	97
6[d]	**1b** (2.5)	p-Me	p-OMe	80 °C,[c] 24 h	46
7	**1b** (4)	p-Me	p-OMe	RT, 67 h	89
8[d]	**1b** (4)	p-Me	p-OMe	80 °C,[c] 12 h	94
9	**2a** (2.5)	p-Me	H	RT, 24 h	91
10	**2a** (2.5)	p-Me	H	80 °C,[c] 6 h	95.6
11	**2a** (2.5)	o-Me	H	RT, 24 h	99
12[d]	**2a** (2.5)	p-Me	p-OMe	80 °C,[c] 6 h	92
13	**2a** (4)	p-Me	p-OMe	RT, 66 h	80
14	**2b** (2.5)	p-Me	H	RT, 24 h	>99
15	**3a** (2.5)	p-Me	H	RT, 18 h	>99
16	**3b** (2.5)	p-Me	H	RT, 12 h	98.4
17	**3b** (2.5)	o-Me	H	RT, 16 h	97
18	**3b** (2.5)	o-Me	o-Me	RT, 28 h	99
19	**3b** (2.5)	p-Me	p-OMe	RT, 24 h	87.5
20[d]	**3b** (2.5)	p-Me	p-OMe	80 °C,[c] 6 h	98
21	**3b** (4)	p-Me	p-OMe	RT, 30 h	93
22	**3b** (2.5)	o-Me	p-OMe	RT, 24 h	89
23	**3c** (2.5)	p-Me	H	RT, 24 h	95
24	**3c** (2.5)	p-Me	p-OMe	RT, 40 h	64
25[d]	**3c** (2.5)	p-Me	p-OMe	80 °C,[c] 10 h	80
26	**3c** (4)	p-Me	p-OMe	RT, 40 h	92.3
27	**4a** (2.5)	p-Me	H	RT, 24 h	94
28	**4a** (2.5)	o-Me	H	RT, 24 h	89
29	**4a** (4)	p-Me	p-OMe	RT, 70 h	88
30[d]	**4a** (2.5)	p-Me	p-OMe	80 °C,[c] 6 h	98.6
31	**4b** (2.5)	p-Me	H	RT, 24 h	89.3

[a] Reaction was carried out in THF unless otherwise stated. [b] Yields of isolated products. [c] Bath temperature. [d] A mixed solvent of THF and toluene (1 : 1).

These complexes were also able to catalyse the cross coupling of aryl chlorides and aryl Grignard reagents efficiently (Table 2).§ It was proved that THF or a 1 : 1 mixture of THF and toluene rather than toluene alone was a suitable solvent for the catalytic reactions. Due to low reactivity of aryl chlorides, the amounts of the catalysts used were greatly increased compared with those in the reaction with aryl iodides. In general, the reactions using aryl chlorides were run with 2.5 mol% of metal catalysts. When deactivated p-MeOC$_6$H$_4$Cl was employed as electrophilic substrate, it was necessary to further increase the amount of the catalysts or raise the reaction temperature to ensure the reactions to be completed. Steric congestion of reactants did not significantly affect the reactions tested. The coupling of o-MeC$_6$H$_4$MgBr with PhCl catalysed by **1b**, **2a**, **3b** and **4a**, respectively, gave similar yields to those of p-MeC$_6$H$_4$MgBr and PhCl under the same reaction conditions. The reaction of o-MeC$_6$H$_4$MgBr with o-MeC$_6$H$_4$Cl catalysed by **3b** gave also a similar result to that of o-MeC$_6$H$_4$MgBr and PhCl, but longer reaction time was required. In these catalytic reactions, the nickel complexes with N,N,P-chelate ligands, **2b**, **3a** and **3b**, exhibited excellent catalytic activities, while **4a** showed lower activity than **2b**, **3a** and **3b**. This order is different from that in the reactions of aryl iodides with p-MeC$_6$H$_4$MgBr. The hindrance of ligand in **2b** did not markedly affect its catalytic activity (Table 2, entry 14), but the reaction catalysed by **3c** was slower than those catalysed by **3a** and **3b**, respectively.

We examined the reaction of **1c** with 6 equiv. of p-MeC$_6$H$_4$MgBr and the result showed by the ^{31}P NMR spectrum that no reaction occurred between them or between PhI and **1c** or **1b**. Hence we guess that the first step of the catalytic coupling reaction proceeds through the single electron transfer (SET) from a Grignard reagent to an aryl halide, forming a radical anion. The radical anion reduces the Ni^{II} complex to a Ni^0 or Ni^I complex which catalyses the following coupling reaction. Namely, aryl halides act as an intermedium of the SET at the initial stage of the reaction and such behavior of aryl halides as intermedia in SET processes have been proved.[6] Reactions of Grignard reagents with organic compounds *via* SET processes have also been reported.[7]

In the catalytic system we tested, the coupling reactions using an aryllithium instead of a Grignard reagent often gave different results. For example, reaction of *p*-MeC_6H_4Li with PhCl catalysed by 2.5 mol% of **3b** in toluene at 70 °C gave the homocoupling product of *p*-MeC_6H_4Li in 75.2% yield (based on the amount of *p*-MeC_6H_4Li added), while the reaction of *p*-MeC_6H_4MgBr with PhCl under the same conditions afforded the sole cross-coupling product in 97.8% yield. This showed that metal ion on nucleophiles played an important role in the reaction. Recently, Nakamura and co-workers indicated that a Ni/Mg bimetallic synergy accelerated nickel-catalysed Kumada cross-coupling reactions.[5c] The selectivity of the reactions we tested may be also a result of Ni/Mg bimetallic cooperation.

In summary, we have demonstrated that amido pincer complexes of nickel are highly active catalysts in cross-coupling of aryl Grignard reagents and aryl halides. Among the catalysts tested, the P,N,P-chelate nickel complexes showed relatively low catalytic activity compared with those with N,N,P- and N,N,N-chelate ligands. Steric congestion of reactants did not intensively affect the reactions tested. However, excessive steric hindrance of ligands led to a decline of catalytic activity of the complexes in most cases. The reactions probably proceed through single electron transfer processes from Grignard reagents to aryl halides at the initial stage of the reactions.

Notes and references

‡ CCDC 632195–632198 for complexes **1c**, **2b**, **3c** and **4b**. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b702027a

§ *Representative procedure* (Table 2, entry 16): A Schlenk tube was charged with **3b** (33.9 mg, 0.0489 mmol), THF (2 cm^3) and chlorobenzene (0.22 g, 1.95 mmol). To the homogeneous solution formed was added dropwise a solution of *p*-MeC_6H_4MgBr in THF (2.2 mmol, *ca.* 1 M in THF) at room temperature with stirring. Stirring was continued at room temperature for 12 h. The reaction was ceased by addition of water (6 cm^3). The mixture was extracted with Et_2O (3 × 5 cm^3) and the combined organic layers were dried over anhydrous Na_2SO_4. The Na_2SO_4 was removed by filtration and washed with Et_2O. The resulting Et_2O solution was concentrated by rotary evaporation and the residue was purified by column chromatography on silica gel (hexane) to afford *p*-MeC_6H_4Ph (0.323 g, 98.4%) as colorless crystals.

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