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Selective amination of aryl chlorides catalysed by Ni(PMe₃)₄†

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C.N-coupling reactions of arvl chlorides and arvl amines catalyzed by a nickel catalyst are reported. 17 new amines are synthesized in yields of 57-99%. 2,6-Dichloro substituted imines can be selectively aminated. Both mono- and di-aminated products are obtained. Different substrates and amines are tested to look into the influence of electronic effects and steric hindrance to the reaction. An inexpensive and convenient base, NaOH, is used. It is an efficient way to gain access to new amines and imines.

C,N-coupling reactions are important in the synthesis of amines. The palladium catalyzed Buchwald-Hartwig reaction and the copper catalyzed Ullman amination reaction are known as the most significant C-N formation pathways.¹⁻³ A lot of examples of Pd or Cu catalyzed aryl halogen amination have been reported, with application to small molecules, total synthesis of natural products⁴ and organic electroactive materials.5 The Ullman type reactions usually need excess copper with bromides or iodides as substrates.⁶

Nickel catalysts have attracted great interest in the amination of aryl halides. Buchwald demonstrated the first nickelcatalyzed amination of aryl chlorides,⁷ and developed a highly active dppf-ligated Ni precatalyst for C,N-cross-coupling reactions.8 Hartwig reported Ni complexes containing a bisphosphine ligand with a side-bound benzonitrile ligand that catalyzed the coupling of aryl electrophiles with primary amines or ammonia.9 Ni(π)-(σ-aryl) complexes were employed as catalysts by Yang in the amination of aryl chlorides¹⁰ and the reaction can also occur using Ni(PCy₃)₂Cl₂ with the help of iPrMgCl.¹¹ Nickel complexes containing NHC ligands¹² or other suitable ligands^{13,14} could also catalyze the C,N-coupling reactions.

In previous work, nickel catalysts were reported, but the catalyst scope is still narrow compared to the palladium or

†Electronic supplementary information (ESI) available: ¹H NMR, ¹³C NMR,

copper catalysts. As an inexpensive and readily available metal, nickel has a lot of advantages in catalytic reactions. The selectivity of C-Cl amination for polychloro substances has proven to be poor. It is important to find a way to functionalize C-Cl bonds specifically in molecules.

We report here the Ni(PMe₃)₄-catalyzed selective amination of aryl chlorides using NaOH as a base. As shown in Table 1, several nickel complexes were used as catalysts in the model

Base, Additive solvent, temp, t

Table 1 Optimization of reaction conditions for C,N-coupling reaction^a

				Additivo/	
	Cat. ^e /mol	Base	Solvent	mol	Yield ^b /%
	$10\% \text{ NiL}_4$	NaOH	Toluene	None	95
2	5% NiL ₄	NaOH	Toluene	None	95
3	$3\% \text{ NiL}_4$	NaOH	Toluene	None	34
ŀ	10% Ni(PPh ₃) ₂ Cl ₂	NaOH	Toluene	None	0
5	10% NiL ₂ Cl ₂	NaOH	Toluene	None	0
5	5% NiL4	KOH	Toluene	None	84
7	5% NiL_4	Na_2CO_3	Toluene	None	_
3	5% NiL_4	Et ₃ N	Toluene	None	0
)	5% NiL	NaOMe	Toluene	None	_
0	5% NiL ₄	KO ^t Bu	Toluene	None	60
1	5% NiL_4	NaOH	Toluene	None	94^c
2	5% NiL_4	NaOH	Toluene	5% TBAB	95^d
3	$4\% \text{ NiL}_4$	NaOH	Toluene	5% TBAB	95^d
4	$4\% \text{ NiL}_4$	NaOH	DMSO	5% TBAB	0^d
5	$4\% \text{ NiL}_4$	NaOH	CH ₃ CN	5% TBAB	Impurities ^d
.6	$4\% \text{ NiL}_4$	NaOH	DMF	5% TBAB	Impurities ^d
7	4% NiL ₄	NaOH	Toluene	5% TBAI	72^d
8	$4\% \text{ NiL}_4$	NaOH	Toluene	$MgSO_4$	30
9	$4\% \text{ NiL}_4$	NaOH	Toluene	5% TEBAC	65^d

^a Reaction conditions: aryl chloride (0.15 mmol), amine (0.15 mmol), NaOH (0.15 mmol), 80 °C, 24 h in toluene (2 mL). ^b Isolated yield by column chromatography using 50:1 petroleum ether: Et₃N. ^c Reaction temperature 100 °C, reaction time 21 h. d Reaction time 12 h. $e L = PMe_3$.

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¹⁹F NMR and ESI-MS data for the new compounds. See DOI: 10.1039/c5dt02298c

reaction and only Ni(PMe₃)₄ showed activity. It is possible to activate one C-Cl bond selectively in a di-chlorinated system by controlling the amount of the amine added. The loading of the catalyst was initially intended to be at least 5 mol% for the complete conversion of the substrate in 24 h. Then bases were tested. Surprisingly, NaOH behaved better than other bases, giving a 95% yield. NaOH is inexpensive and convenient compared to the typical bases used in C,N-coupling, such as KO^tBu or Cs₂CO₃. The reaction temperature was set at 80 °C because the time saved by raising the temperature from 80 °C to 100 °C was small. As NaOH cannot completely dissolve in organic solvents, the phase transfer catalyst TBAB (tetra-n-butylammonium bromide), or TEBAC (benzyltriethylammonium chloride) or TBAI (tetrabutylammonium iodide), was taken into consideration to improve the reaction conditions. When the phase transfer catalyst TBAB was added to 5 mol% substrate, the best conversion was achieved. It not only doubled the reaction efficiency, but also lowered the catalyst loading to 4 mol%. The model reaction was also tried in different solvents. Reaction in DMSO led to no yield. CH₃CN and DMF resulted in uncontrollable impurities. Therefore, the best reaction conditions for this catalytic system are 4 mol% $Ni(PMe_3)_4$ as the catalyst, NaOH as the base and 5 mol% TBAB in toluene for 12 h (entry 13, Table 1).

The substrates explored are shown in Schemes 1–3. The amination of different types of chlorinated Schiff bases with aryl amines was studied. Initially, amines that were the same as the ones in the preparation of the Schiff bases were tested (Scheme 1). One equivalent of the amine was added to obtain the mono-aminated product. It was reported that it is difficult to obtain the mono-(C,N)-coupling product from di- or tri-chlorinated compounds.¹⁴ In this catalytic system, all the yields are high when using aryl amines. Mono-aminated products were the only products obtained by controlling the







Scheme 3 Different Schiff bases coupling with 4-methylaniline. Reaction conditions: aryl chloride (1.5 mmol), amine (1.5 mmol), NaOH (1.5 mmol), ⁿBu₄NBr (0.075 mmol), Ni(PMe₃)₄ (0.060 mmol), toluene (4 mL), 80 °C, 12 h. Isolated yield by column chromatography using 50:1 petroleum ether : Et₃N. ^aThe imine product is reduced with NaBH₄. ^bThe reaction time is 24 h.

amount of the amine added. The anchoring group, the imine group, is also of great importance in the selective amination. Alkyl amines are not fit for this reaction.

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The reaction was carried out with different aryl amines (Scheme 2). It turned out that 1-naphthylamine had the highest yield (2h). It was disclosed that the amines containing electron-withdrawing groups have lower activities.¹⁵ In our case 2e and 2g showed a yield of 80% and 82%, respectively. Even for 4-fluoro amine (2i) the yield is 80%. To obtain 2i, the related Schiff base had to be reduced to the corresponding amine with NaBH₄. The reduction procedure was almost quantitative.

Scheme 3 shows the catalytic reactions of the Schiff bases containing diverse backbones with 4-methylaniline. Some products were reduced to provide the corresponding amines (2i, 2k, 2l, 2p). It can be concluded from 2j and 2n that the steric hindrance effect (the butyl group) and the electron-withdrawing group (the ortho-Cl group) of the backbone influenced the reaction negatively. The mono-chloro substituted imine reacted slowly (2p), giving 17% product in 12 h and 70% yield in 24 h. The same situation occurred in the di-amination of two chlorine atoms of the substrate (20). The reason for the difference in the reaction rates between mono- and di-chlorinated substrates can be the electronic effect of the other chlorine atom on the aryl ring. The second chlorine atom makes the C-Cl activation easier. To improve the production yield, the reaction time was doubled and the yield of the di-amination product rose to 65%. Finally, hexachlorobenzene was coupled with p-toluidine to give a moderate yield of the product (Scheme 4). In the case of 2q, only one chlorine atom could be activated slowly, indicating the importance of the anchoring group. In Schiff bases, C=N is the anchoring group, directing the metal selectively and activating the ortho-(C-Cl) bond effectively.

The mechanism of this catalytic cycle is considered to be a $Ni(0)/Ni(\pi)$ procedure (Scheme 5). Previous work in our group showed that the oxidative addition of Ni(0) to the C–Cl bond in Schiff bases formed Ar–Ni(π)–Cl species.¹⁶ After the coordination of the anchoring group imine, the oxidative addition of the C–Cl bond at the Ni(0) center occurs to provide nickel(π) intermediate **A**. Replacement of one trimethylphosphine ligand of **A** by one amine molecule gives rise to intermediate **B**. In the presence of NaOH, **B** transforms into intermediate **C** with the formation of NaCl and H₂O. The amines have to be both basic enough to coordinate to the nickel center and acidic enough to undergo deprotonation.¹⁵ The reductive elimination between the Ni–N and Ni–C bonds of **C** delivers the final product, the *ortho*-aminated imine, with the regeneration of the catalyst Ni(PMe₃)₄.



Scheme 4 Preparation of 2q



Scheme 5 Proposed mechanism of the C,N-coupling reactions.

Conclusions

In conclusion, a C,N-coupling reaction of di-chlorinated Schiff bases with aryl amines catalyzed by $Ni(PMe_3)_4$ is described. The di-chlorinated substrates could be both mono-aminated and di-aminated selectively. Different amines and Schiff bases are tested, giving good yields. NaOH is used as a base instead of expensive and unstable bases. This catalytic system establishes an effective strategy to functionalize aryl C–Cl bonds effectively.

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Notes and references

- 1 (a) M. A. Topchiy, A. F. Asachenko and M. S. Nechaev, Eur. J. Org. Chem., 2014, 3319; (b) G.-D. Roiban, G. Mehler and M. T. Reetz, Eur. J. Org. Chem., 2014, 2070; (c) S. M. Crawford, C. B. Lavery and M. Stradiotto, Chem. -Eur. J., 2013, 19, 16760; (d) S. M. Raders, J. N. Moore, J. K. Parks, A. D. Miller, T. M. Leißing, S. P. Kelley, R. D. Rogers and K. H. Shaughnessy, J. Org. Chem., 2013, 78, 4649; (e) K. D. Collins and F. Glorius, Nat. Chem., 2013, 5, 597; (f) T. Iwai, T. Harada, K. Hara and M. Sawamura, Angew. Chem., Int. Ed., 2013, 52, 12322; (g) S. Guo, Y. Wang, C. Sun, J. Li, D. Zou, Y. Wu and Y. Wu, Tetrahedron Lett., 2013, 54, 3233; (h) R. K. Rao, I. Karthikeyan and G. Sekar, Tetrahedron, 2012, 68, 9090; (i) L. L. Hill, J. L. Crowell, S. L. Tutwiler, N. L. Massie, C. C. Hines, S. T. Griffin, R. D. Rogers, K. H. Shaughnessy, G. A. Grasa and J. C. Christopher, J. Org. Chem., 2010, 75, 6477.
- 2 (a) Y. Zhang, V. César, G. Storch and N. Lugan, Angew. Chem., Int. Ed., 2014, 53, 6482; (b) B. Mu, J. Li and Y. Wu, Appl. Organomet. Chem., 2013, 27, 537; (c) S. Meiries, G. L. Duc, A. Chartoire, A. Collado, K. Speck, K. S. A. Arachchige, A. M. Z. Slawin and S. P. Nolan,

Chem. – Eur. J., 2013, **19**, 17358; (d) G. Le Duc, S. Meiries and S. P. Nolan, Organometallics, 2013, **32**, 7547; (e) A. Chartoire, A. Boreux, A. R. Martin and S. P. Nolan, *RSC Adv.*, 2013, **3**, 3840; (f) S. Meiries, K. Speck, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, Organometallics, 2013, **32**, 330; (g) M. Hoyos, R. S. Sprick, C. Wang, M. L. Turner and O. Navarro, J. Polym. Sci., Part A: Polym. Chem., 2012, **50**, 4155; (h) A. Chartoire, X. Frogneux, A. Boreux, A. M. Z. Slawin and S. P. Nolan, Organometallics, 2012, **31**, 6947; (i) A. K. K. Lewis, S. Caddick, F. G. N. Cloke, N. C. Billingham, P. B. Hitchcock and J. Leonard, J. Am. Chem. Soc., 2003, **125**, 10066.

- 3 (a) P. Wagner, M. Bollenbach, C. Doebelin, F. Bihel, J.-J. Bourguignon, C. Salomé and M. Schmitt, Green Chem., 2014, 16, 4170; (b) C. Salomé, P. Wagner, M. Bollenbach, F. Bihel, J.-J. Bourguignon and M. Schmitt, Tetrahedron, 2014, 70, 3413; (c) S. Borjian, D. M. Tom and M. C. Baird, Organometallics, 2014, 33, 3928; (d) C. A. Wheaton, J.-P. J. Bow and M. Stradiotto, Organometallics, 2013, 32, 6148; (e) R. N. Prabhu and R. Ramesh, Tetrahedron Lett., 2013, 54, 1120; (f) R. J. Burton, M. L. Crowther, N. J. Fazakerley, S. M. Fillery, B. M. Hayter, J. G. Kettle, C. A. McMillan, P. Perkins, P. Robins and P. M. Smith, Tetrahedron Lett., 2013, 54, 6900; (g) P. G. Alsabeh, R. J. Lundgren, R. McDonald, C. C. Johansson Seechurn, T. J. Colacot and M. Stradiotto, Chem. - Eur. J., 2013, 19, 2131; (h) M. Beller, C. Breindl, T. H. Riermeier and A. Tillack, J. Org. Chem., 2001, 66, 1403.
- 4 (a) P. Tao, J. Liang and Y. Jia, Eur. J. Org. Chem., 2014, 5735;
 (b) J. Liang, W. Hu, P. Tao and Y. Jia, J. Org. Chem., 2013, 78, 5810;
 (c) M. K. Ghorai and Y. J. Nanaji, Org. Chem., 2013, 78, 3867;
 (d) A. Gangjee, O. A. Namjoshi, S. Raghavan, S. F. Queener, R. L. Kisliuk and V. J. Cody, Med. Chem., 2013, 56, 4422;
 (e) R. Ding, J.-G. Fu, G.-Q. Xu, B.-F. Sun and G.-Q. Lin, J. Org. Chem., 2013, 79, 240;
 (f) D. Waghray, J. Zhang, J. Jacobs, W. Nulens, N. Basarić, L. V. Meervelt and W. Dehaen, J. Org. Chem., 2012, 77, 10176;
 (g) R. Ding, B.-F. Sun and G.-Q. Lin, Org. Lett., 2012, 14, 4446.
- 5 (a) C. Wetzel, A. Mishra, E. Mena-Osteritz, A. Liess, M. Stolte, F. Würthner and P. Bäuerle, Org. Lett., 2013, 16, 362; (b) D. Waghray, A. Cloet, K. Van Hecke, S. F. Mertens, S. De Feyter, L. Van Meervelt, M. Van der Auweraer and W. Dehaen, Chem. Eur. J., 2013, 19, 12077; (c) I. S. Perețeanu and T. J. Müller, Org. Biomol. Chem., 2013, 11, 5127; (d) D. Sakamaki, A. Ito, K. Tanaka, K. Furukawa, T. Kato and M. Shiro, Angew. Chem., Int. Ed., 2012, 51, 8281.

- 6 (a) C. Xi, X. Yan and X. Yang, *Catal. Sci. Technol.*, 2014, 4, 4169; (b) F. Monnier and M. Taillefer, *Angew. Chem., Int. Ed.*, 2009, 48, 6954.
- 7 J. P. Wolfe and S. L. Buchwald, J. Am. Chem. Soc., 1997, 119, 6054.
- 8 N. H. Park, G. Teverovskiy and S. L. Buchwald, Org. Lett., 2014, 16, 220.
- 9 (a) R. A. Green and J. F. Hartwig, Angew. Chem., Int. Ed., 2015, 54, 3768; (b) S. Ge, R. A. Green and J. F. Hartwig, J. Am. Chem. Soc., 2014, 136, 1617.
- 10 C. Chen and L.-M. Yang, J. Org. Chem., 2007, 72, 6324.
- 11 X.-L. Li, W. Wu, X.-H. Fan and L.-M. Yang, Org. Biomol. Chem., 2014, **12**, 1232.
- 12 (a) M. Nirmala, G. Prakash, R. Ramachandran, P. Viswanathamurthi, J. G. Malecki and W. Linert, J. Mol. Catal. A: Chem., 2015, 397, 56; (b) A. R. Martin, D. J. Nelson, S. Meiries, A. M. Slawin and S. P. Nolan, Eur. J. Org. Chem., 2014, 3127; (c) N. F. Fine Nathel, J. Kim, L. Hie, X. Jiang and N. K. Garg, ACS Catal., 2014, 4, 3289; (d) A. R. Martin, Y. Makida, S. b. Meiries, A. M. Slawin and S. P. Nolan, Organometallics, 2013, 32, 6265: K. Matsubara, S. Miyazaki, Y. Koga, Y. Nibu, (*e*) T. Hashimura and T. Matsumoto, Organometallics, 2008, 27, 6020; (f) R. A. Kelly, N. M. Scott, S. Díez-González, E. D. Stevens and S. P. Nolan, Organometallics, 2005, 24, 3442; (g) R. Omar-Amrani, A. Thomas, E. Brenner, R. Schneider and Y. Fort, Org. Lett., 2003, 5, 2311; (h) C. Desmarets, R. Schneider and Y. Fort, J. Org. Chem., 2002, 67, 3029; (i) B. Gradel, E. Brenner, R. Schneider and Y. Fort, Tetrahedron Lett., 2001, 42, 5689.
- 13 (a) G. Manolikakes, A. Gavryushin and P. J. Knochel, Org. Chem., 2008, 73, 1429; (b) E. Brenner and Y. Fort, Tetrahedron Lett., 1998, 39, 5359.
- 14 (a) C. Desmarets, R. Schneider and Y. Fort, *Tetrahedron Lett.*, 2001, 42, 247; (b) C. Desmarets, R. Schneider and Y. Fort, *Tetrahedron*, 2001, 57, 7657.
- 15 M. Pompeo, J. L. Farmer, R. D. Froese and M. G. Organ, *Angew. Chem., Int. Ed.*, 2014, 53, 3223.
- 16 (a) Q. Niu, X. Zhang, S. Zhang, X. Li and H. Sun, Inorg. Chim. Acta, 2015, 426, 165; (b) J. Li, X. Li, L. Wang, Q. Hu and H. Sun, Dalton Trans., 2014, 43, 6660; (c) J. Li, X. Li and H. Sun, Organomet. Chem., 2013, 743, 114; (d) J. Li, C. Wang, X. Li and H. Sun, Dalton Trans., 2012, 41, 8715; (e) Y. Shi, M. Li, Q. Hu, X. Li and H. Sun, Organometallics, 2009, 28, 2206; (f) Y. Chen, H. Sun, U. Flörke and X. Li, Organometallics, 2008, 27, 270; (g) R. Cao, H. Sun and X. Li, Organometallics, 2008, 27, 1944.