JOC Article

Cross-Coupling and Dehalogenation Reactions Catalyzed by (*N*-Heterocyclic carbene)Pd(allyl)Cl Complexes

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A series of well-defined, air- and moisture-stable (NHC)Pd(allyl)Cl (NHC = *N*-heterocyclic carbene) complexes has been used in several catalytic reactions: Suzuki−Miyaura cross-coupling, catalytic dehalogenation of aryl halides, and aryl amination. The scope of the three processes using various substrates was examined. A general system involving the use of (IPr)Pd(allyl)Cl as catalyst and NaO^{t}Bu as base has proven to be highly active for the Suzuki−Miyaura cross-coupling of activated and unactivated aryl chlorides and bromides, for the catalytic dehalogenation of aryl chlorides, and for the catalytic aryl amination of aryl triflates. All reactions proceed in short reaction times and at mild temperatures. The system has also proven to be compatible with the microwave-assisted Suzuki−Miyaura cross-coupling and catalytic dehalogenation processes, affording yields similar to those of the conventionally heated analogous reactions.

Introduction

N-Heterocyclic carbenes (NHC) have become increasingly popular in homogeneous catalysis as they represent a unique family of ligands possessing strong M−NHC bonds and imparting thermal stability to organometallic complexes.[1,2] These important properties distinguish them from tertiary phosphines.[3] We have previously reported on the use of palladium/imidazolium salt systems in dehalogenation reactions[4] and cross coupling of aryl halides with amines,[5] organomagnesium,[6] organosilicon,[7] organotin,[8] and organoboron[9] reagents. Recently, we have focused our research efforts on the design and characterization of various monomeric (NHC)Pd(allyl)Cl species.[10] Studies focusing on their reactivity in cross-coupling reactions have been communicated in preliminary form.[10,11] We now wish to report an extended study of the catalytic behavior of (NHC)Pd(allyl)Cl complexes as catalysts in the Suzuki−Miyaura cross-coupling involving aryl chlorides and bromides, aryl amination of aryl triflates, and catalytic dehalogenation of aryl chlorides.

Suzuki−Miyaura Cross-Coupling Reactions. Cross-coupling reactions represent an extremely versatile tool in organic synthesis,[12] since C−C bond formation is a key step in a wide range of organic processes, from supramolecular chemistry[13] to natural product synthesis.[14] These reactions require the use of a transmetalating agent such as an organomagnesium,[15] organosilicon,[16] organotin,[17] or organozinc[18] reagents. When organoboron reagents are used in coupling with aryl halides or pseudohalides, the process is known as the Suzuki−Miyaura reaction.[19,20]

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(1) (a) Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 725−728. (b) Arduengo, A. J., III; Krafczyc, R. *Chem. Zeit.* **1998**, *32*, 6−14. (c) Herrmann, W. A.; Kocher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2163-2187.

(2) (a) Gstottmayr, C. W. K.; Bohm, V. P. W.; Herdtweck, E.; Grosche, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1363−1365. (b) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247−2250. (c) Kucucbay, H.; Cetinkaya, B.; Salaheddine, G.; Dixneuf, P. H. *Organometallics* **1996**, *15*, 2434−2439. (d) Grasa, G. A.; Hillier, A. C.; Nolan, S. P. *Org. Lett.* **2001**, *3*, 1077−1080. (e) Marshall, W. J.; Grushin, V. V.; *Organometallics* **2003**, *22*, 1591−1593.

(3) Phosphine ligands in homogeneous catalysis: (a) Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*; J. Wiley and Sons: New York, 1992. (b) Pignolet, L. H., Ed. *Homogeneous Catalysis with Metal Phosphine Complexes*; Plenum: New York, 1983.

(4) Viciu, M. S.; Grasa, G. A.; Nolan, S. P. *Organometallics* **2001**, *20*, 3607−3612.

(5) Huang, J.; Grasa, G. A.; Nolan, S. P. *Org. Lett.* **1999**, *1*, 1307−1309.

(6) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889−9890.

(7) Lee, H.-M.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 2053−2055.

(8) Grasa, G. A.; Nolan, S. P. *Org. Lett.* **2001**, *3*, 119−122.

(9) (a) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804−3805. (b) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866−2873.

(10) Viciu, M. S.; Germaneau, R. F.; Navarro-Fernandez, O.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2002**, *21*, 5470−5472.

(11) Viciu, M. S.; Germaneau, R. F.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 4053−4056.

(12) (a) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: New York, 1985. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science: Mill Valley, CA, 1987. (c) Diederich, F., Stang, P. J. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 1998.

(13) (a) Roncali, J. *J. Chem. Rev.* **1992**, *92*, 711−738. (b) Yamamura, K.; Ono, S.; Ogoshi, H.; Masuda, H.; Kuroda, Y. *Synlett.* **1989**, 18−19.

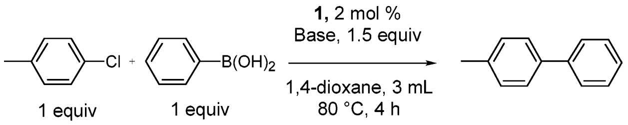
(14) (a) Torssell, K. B. G. *Natural Product Chemistry*; Wiley: Chichester, 1983. (b) Thomson, R. H. *The Chemistry of Natural Products*; Blackie and Son: Glasgow, 1985. (c) Huth, A.; Beetz, I.; Schumann, I. *Tetrahedron* **1989**, *45*, 6679−6682. (d) Ennis, D. S.; McManus, J.; Wood-Kaczmar, W.; Richardson, J.; Smith, G. E.; Carstairs, A. *Org. Process Res. Dev.* **1999**, *3*, 248−252. (e) Baudoin, O.; Cesario, M.; Guenard, Daniel; Gueritte, F. *J. Org. Chem.* **2002**, *67*, 1199−1207.

(15) (a) Yamamura, M.; Moritani, I.; Murahashi, S. *J. Organomet. Chem.* **1975**, *91*, C39−C42. (b) Tamao, K.; Kiso, Y.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 9268−9269. (c) Sekiya, A.; Ishikawa, N. *J. Organomet. Chem.* **1976**, *118*, 349−354.

(16) Hatanaka, Y.; Hiyama, T. *Synlett.* **1991**, 845−853.

10.1021/jo035834p CCC: $27.50

TABLE 1. Effect of the Base on the Suzuki–Miyaura Cross-Coupling Reaction



base	yield (%)[a]
Cs_2CO_3	47
CsF	66
KF	39
K_3PO_4	20
KO^{t}Bu	65
NaO^{t}Bu	74
$Ba(OH)_2$	62

[a] GC yields, average of two runs.

Despite the fact that they are air-sensitive and degrade at high temperatures,[3] monodentate tertiary phosphines are usually employed as ancillary ligands in the Suzuki–Miyaura reaction. Most palladium/tertiary phosphine systems require the use of excess ligand,[21] and very active systems achieve high performance at the expense of complex stability.[22] Some recent examples of the use of bulky tertiary phosphines in this reaction are found in the work of Hartwig, Buchwald, and Fu.[22,23] The Fu group has reported on methods to circumvent the air-sensitive nature of trialkylphosphines.[24] We have tested the performance of (NHC)Pd(allyl)Cl catalysts as substitutes for phosphine-based systems in the Suzuki–Miyaura reaction.

Our studies began using (IMes)Pd(allyl)Cl (**1**) (IMes = (*N*,*N′*-bis(2,4,6-trimethylphenyl)imidazol)-2-ylidene) and a variety of bases (Table 1). 4-Chlorotoluene (1 equiv) was coupled with phenylboronic acid in the presence of 1.5 equiv of base using 2 mol % of **1** at 80 °C in 3 mL of 1,4-dioxane. Under these conditions of low base concentration, we found that NaO^{t}Bu and KO^{t}Bu were much more efficient than the commonly used KF or Cs_2CO_3.

SCHEME 1. *N*-Heterocyclic Carbenes Used as Ancillary Ligands and General Structure of the (NHC)Pd(allyl)Cl Complexes

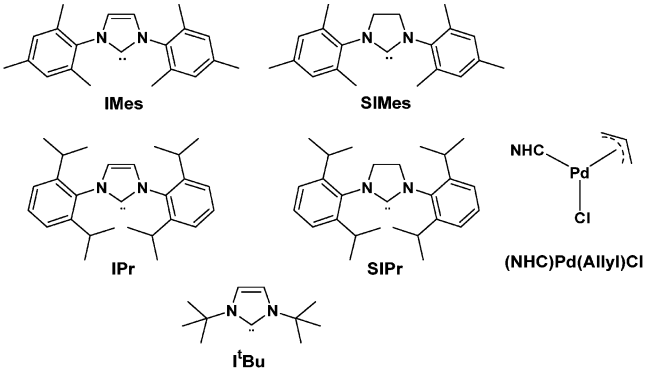
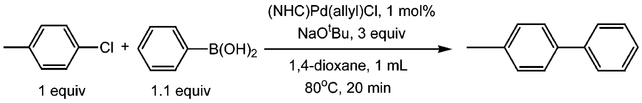


TABLE 2. Effect of NHC Ligand on the Suzuki–Miyaura Cross-Coupling



(NHC)Pd(allyl)Cl	yield (%)[a]
(IMes)Pd(allyl)Cl (**1**)	80
(SIMes)Pd(allyl)Cl (**2**)	70
(IPr)Pd(allyl)Cl (**3**)	80
(SIPr)Pd(allyl)Cl (**4**)	62
(I^{t}Bu)Pd(allyl)Cl (**5**)	68

[a] GC yields, average of two runs.

Once NaO^{t}Bu had been selected as the most effective base, the next optimization step involved testing for the optimum ancillary ligand. Several (NHC)Pd(allyl)Cl catalysts were tested: (IMes)Pd(allyl)Cl (**1**); (SIMes)Pd(allyl)Cl (**2**) (SIMes = (*N*,*N′*-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol)-2-ylidene); (IPr)Pd(allyl)Cl[25] (**3**) (IPr = (*N*,*N′*-bis(2,6-diisopropylphenyl)imidazol)-2-ylidene); (SIPr)Pd(allyl)Cl (**4**) (SIPr = (*N*,*N′*-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol)-2-ylidene); (I^{t}Bu)Pd(allyl)Cl (**5**) (I^{t}Bu = (*N*,*N′*-bis(2,6-*tert*-butyl)imidazol)-2-ylidene) (Scheme 1). Results for the catalytic reactions after 20 min are presented in Table 2. As observed in the *in situ* catalyst generated palladium/imidazolium salt systems, catalysts bearing IPr or IMes NHCs display the best catalytic behavior.[9b] The use of **3** leads to complete conversion of 4-chlorotoluene after 1 h at 80 °C. When compared to the palladium/imidazolium salt systems, a shorter reaction time is required using the well-defined system. An induction period was initially observed in the *in situ* generated system since an interval was required to generate the free NHC ligand. In the present case, the active Pd(0) species is obtained rapidly from the (NHC)Pd(allyl)Cl complex by reaction with the alkoxide.

Under these reaction conditions, no sign of catalyst decomposition (Pd black formation) was observed. To test the activation threshold leading to a Pd–NHC species, the reaction temperature was reduced to 60 °C. To compensate for the decreased solubility of phenyl boronic acid, the amount of solvent was increased to 1.5 mL. Both factors led to a slower reaction yet a 90% conversion was achieved in 2 h. The reaction did not proceed to completion even after longer reaction times. An increase in the amount of benzene appearing in the GC at 60 °C in comparison to the one at 80 °C indicated decomposition of phenyl boronic acid; therefore, the boronic acid loading was increased to 1.2 equiv. Under these conditions, the reaction reached to completion in 4 h. Further reducing

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(17) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508–524. (b) Farina, V.; Krishnamurthy, V.; Scott, W. *Org. React.* **1997**, *50*, 1–652. (c) Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 167–202 and references therein. (d) Handy, S. T.; Zhang X. *Org. Lett.* **2001**, *3*, 233–236.

(18) Erdik, E. *Tetrahedron* **1992**, *48*, 9577–9648.

(19) For reviews, see: (a) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11–59. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483. (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147–168.

(20) Herrmann, W. A.; Reisinger, C.-P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93–96.

(21) Herrmann, W. A.; Kocher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2163-2187.

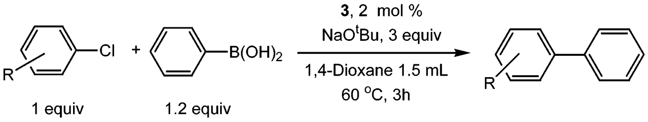
(22) Stambuli, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4746–4748.

(23) (a) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020–4028 and references cited therein. (b) Netherton, M. R.; Dai, C.; Neuschuetz, K.; Fu. G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100. (c) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163.

(24) Netherton, M. R.; Fu, G. C.; *Org. Lett.* **2001**, *3*, 4295–4298.

(25) (IPr)Pd(allyl)Cl is now commercially available from Strem Chemicals.

TABLE 3. Suzuki–Miyaura Cross-Coupling of Aryl Chlorides with Phenylboronic Acid



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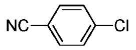
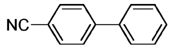
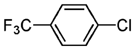
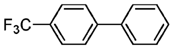
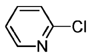
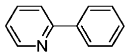
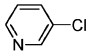
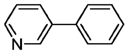
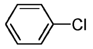
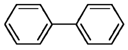
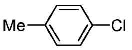
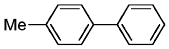
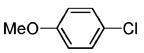
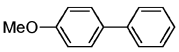
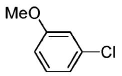
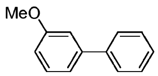
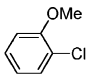
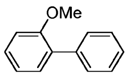
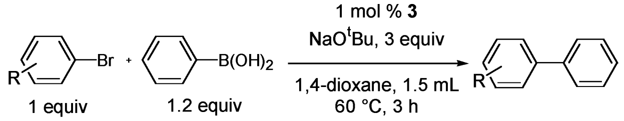
1			94 (88)
2			98 (94)
3			97 (93)
4			97 (91)
5			100(100)
6			98 (93)[b]
7			98 (93)
8			96 (92)
9			97 (93)

[a] GC yield (isolated yield), average of two runs. [b] 4 h.

TABLE 4. Suzuki–Miyaura Cross-Coupling of Aryl Bromides with Phenylboronic Acid



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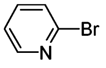
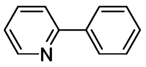
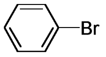
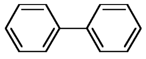
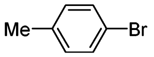
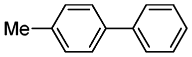
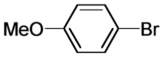
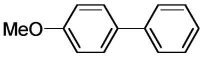
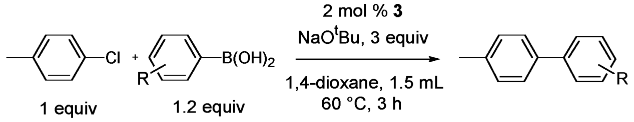
1			97 (90)
2			98 (93)[b]
3			97 (91)
4			93 (89)

[a] GC yield (isolated yield), average of two runs. [b] 2 h.

TABLE 5. Suzuki–Miyaura Cross-Coupling of 4-Chlorotoluene with Different Boronic Acids



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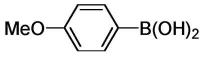
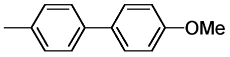
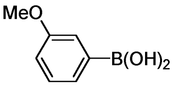
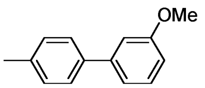
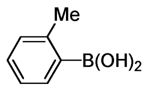
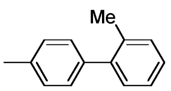
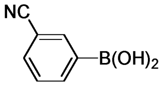
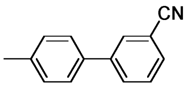
1			98 (96)
2			97 (92)
3			81 (75)
4			79 (72)

[a] GC yield (isolated yield), average of two runs.

the reaction temperature to 40 °C led to complete conversion only after 20 h;[26] thus, we conducted a substrate survey at 60 °C. Substrates and reactions tested are presented in Table 3. Both activated (entries 1–4) and unactivated chlorides (entries 6–9) reached total conversion in 4 h or less. When aryl bromides were used as substrates, the amount of catalyst could be reduced to 1 mol % without loss of activity (Table 4). In all cases examined (aryl chlorides and bromides), only traces of homocoupling and dehalogenation products were formed (<5%).

Aryl iodides, although not extensively tested here, are also compatible with the catalyst system. Functional group compatibility at the boronic acid was also tested (Table 5). For demanding substrates, entries 3 (sterically hindered) and 4 (with an electron-withdrawing substituent), good yields were obtained in 3 h.

Microwave-assisted reactions have gained popularity as a facile screening method since it was first reported in 1986.[27] Since several microwave-assisted cross-coupling reactions have been reported in the literature,[28] we decided to apply that concept to our system. Results are listed in Table 6. Results very similar to the ones obtained by conventional heating are obtained. Under these high thermal conditions, the catalysts appear stable and no palladium black is formed.

Catalytic Dehalogenation of Aryl Chlorides. The dehalogenation of aryl halides, specifically aryl chlorides, represents an important chemical transformation in organic synthesis[29] and due to the high toxicity of polychlorinated biphenyls is of importance to environmental remediation.[30] Palladium is the most frequently used transition metal in hydrodehalogenation reactions, either in homogeneous or in heterogeneous processes, and a plethora of systems and conditions have already been reported to achieve dehalogenation.[31] Fort and co-workers recently reported a very efficient nickel(0)/imidazolium

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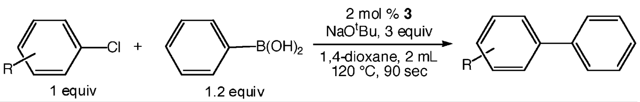
(26) The reaction was done in 2 mL of 1,4-dioxane because of the low solubility of the PhB(OH)$_2$ at that temperature. This factor certainly contributed to increase the reaction time.

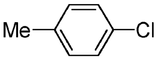
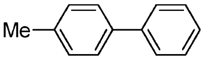
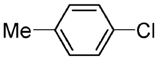
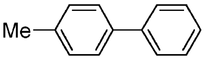
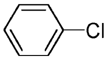
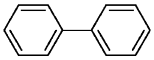
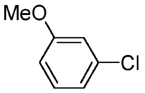
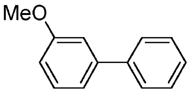
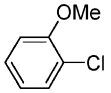
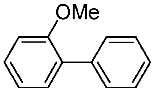
(27) (a) Larhed, M.; Hallberg, A. *J. Org. Chem.* **1996**, *61*, 9582–9584. (b) Larhed, M.; Hallberg, A.; Lindeberg, G. *Tetrahedron Lett.* **1996**, *37*, 8219–8222.

(28) (a) Larhed, M.; Hoshino, M.; Hadida, S.; Curran, D. P.; Hallberg, A. *J. Org. Chem.* **1997**, *62*, 5583–5587. (b) Erdelyi, M.; Gogoll, A. *J. Org. Chem.* **2001**, *66*, 4165–4169. (c) Leadbeater, N. E.; Marco, M. *J. Org. Chem.* **2003**, *68*, 888–892. (d) Blettner, C. G.; Koenig, W. A.; Stenzel, W.; Schotten, T. *J. Org. Chem.* **1999**, *64*, 3885–3890.

(29) (a) Pinder, A. R. *Synthesis* **1980**, 425–452 (b) Terstiege, I.; Maleczka, R. E., Jr. *J. Org. Chem.* **1999**, *64*, 342–343. (c) Parry, R. J.; Li, Y.; Gomez, E. E. *J. Am. Chem. Soc.* **1992**, *114*, 5946–5959. (d) Dorman, G.; Olszewski, J. D.; Prestwich, G. D.; Hong, Y.; Ahem, D. G. *J. Org. Chem.* **1995**, *60*, 2292–2297.

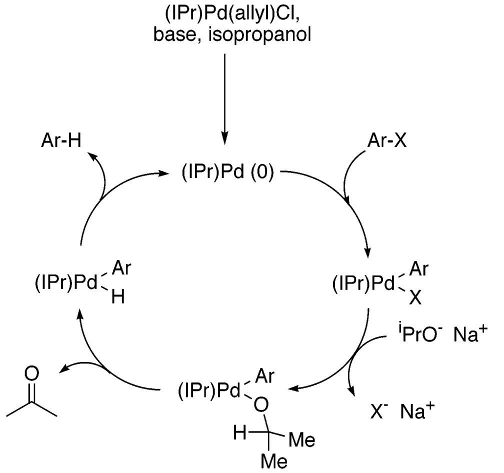
TABLE 6. Microwave-Assisted Suzuki–Miyaura Cross-Coupling of Aryl Chlorides with Phenylboronic Acid



entry	aryl chloride	product	yield(%)[a]
1			0[b]
2			97
3			99
4			88
5			97

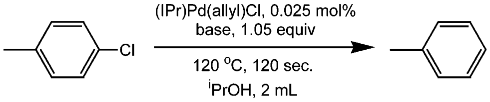
[a] GC yield, average of two runs. [b] No catalyst added.

SCHEME 2. Proposed Mechanism for the Catalytic Dehalogenation of Aryl Halides



chloride catalyzed reduction of aryl halides[32] which is very similar to the one we reported some time ago using a palladium/imidazolium chloride system.[4] In both systems, alkoxide attack at the metal center followed by reductive elimination of the arene from the metal(II)–hydride complex is suggested as a likely pathway (see Scheme 2). While conducting our studies on the Suzuki–Miyaura reaction, we noticed that, under certain conditions, the dehalogenation of the aryl halide was promoted, and we decided to examine the performance of the present systems in dehalogenation chemistry.

TABLE 7. Effect of the Base on the Microwave-Assisted Dehalogenation



base	yield (%)[a]
NaO^tBu	100
KO^tBu	96
NaOMe	37
KOMe	91

[a] GC yields, average of two runs.

Studies were conducted in technical grade 2-propanol with the idea of generating the working base (isopropoxide) *in situ* in an attempt to formulate an easy, scalable, and economical process. The catalyst selected was the one leading to the best results in the Suzuki–Miyaura cross-coupling reaction since it has been suggested that the rate-determining step for dehalogenation is the oxidative addition of the aryl chloride.[4,33] (IPr)Pd(allyl)Cl (**3**) was then the catalyst of choice for this reaction.

We initiated this section of the study using microwave-assisted heating. A minimum of 2 mL of solvent was required because of the specifications of the microwave reactor. By using 1.05 equiv of NaO^tBu, the amount of catalyst required to dehalogenate 1 equiv of 4-chlorotoluene was reduced to 0.025 mol % of (IPr)Pd(allyl)Cl (reaction at 120 °C, 120 s). Use of a larger amount of base decreased the yields, presumably because of a competition between the *tert*-butoxide and the isopropoxide for the addition to the metal center. To confirm the importance of the ancillary NHC ligand, a reaction was carried out using 1 mol % of $[Pd(allyl)Cl]_2$ as catalyst under these same conditions and afforded the toluene product in only 45% yield with the concomitant formation of a large amount of metallic palladium. Reactions without catalyst or base afforded no product.

A survey of various bases was performed, and results of this optimization exercise are shown in Table 7. Once the optimum base was identified (NaO^tBu), the scope of the reaction was tested. Few examples of microwave-assisted dehalogenation of aryl halides have been reported. Such studies have mainly focused on bromides and iodides and required much harsher reaction conditions.[32] With the present palladium system, several aryl chlorides were successfully dehalogenated (Table 8).

Having demonstrated the compatibility of the system with a microwave-assisted process, conventional heating was also tested in these reactions. The optimization process can be followed in Table 9, which shows temperatures and times to perform total conversion of 4-chlorotoluene into toluene. It is important to remark that, in all cases, the reaction reached 85% to 90% conversion in half of the time required for complete conversion. The subsequent reactions were carried at 60 °C with 0.5 mol % of (IPr)Pd(allyl)Cl, affording very good results. Results illustrating the scope of this reaction are presented in Table 10.

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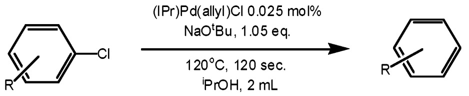
(30) (a) Hutzinger, O.; Safe, S.; Zitko, V. *The Chemistry of PCBs*; CRC Press: Cleveland, OH, 1974. (b) Mincher, B. J.; Curry, R. D.; Clevenger, T. E.; Golden, J. U.S. Patent 6 132 561, 2000. (c) McNab, W. W. Jr.; Ruiz, R.; Pico, T. M. U.S. Patent 6 214 202, 2001. (d) Morra, M. J.; Borek, V.; Koolpe, J. *J. Environ. Qual.* **2000**, *29*, 706–715.

(31) For a review, see: Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2002**, *102*, 4009–4091.

(32) Desmarets, C.; Kuhl, S.; Schneider, R.; Fort, Y. *Organometallics* **2002**, *21*, 1554–1559.

(33) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176–4211.

TABLE 8. Microwave-Assisted Dehalogenation of Aryl Chlorides[a]



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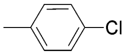
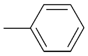
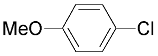
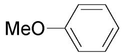
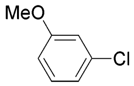
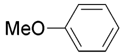
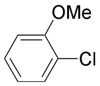
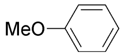
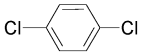
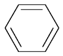
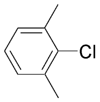
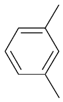
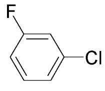
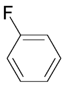
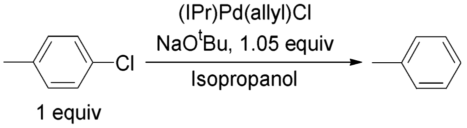
1			100
2			100
3			100
4			100
5			95[c]
6			99
7			100

[a] Reaction times not optimized. [b] GC yields, average of two runs. [c] 0.05 mol % of catalyst, 2.1 equiv of base.

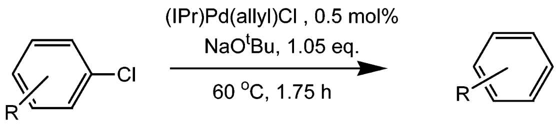
TABLE 9. Optimization Reactions for the Dehalogenation of Aryl Chlorides with Conventional Heating

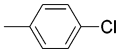
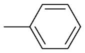
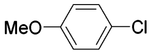
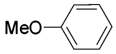
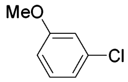
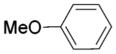
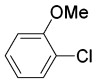
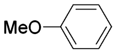
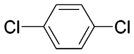
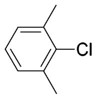
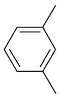
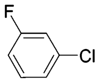
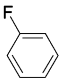
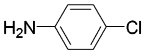
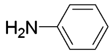
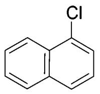
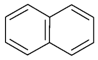
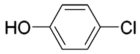
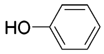
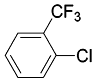
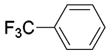


catalyst loading (mol %)	solvent (mL)	T (°C)	time[a]
1	2	60	40 min
1	1.5	60	40 min
0.5	1.5	60	90 min
0.5	1.5	50	8 h
0.25	1.5	60	3.5 h

[a] Times required to obtain >95% of toluene, GC yield; average of two runs.

TABLE 10. Conventionally Heated Dehalogenation of Aryl Chlorides



entry	aryl chloride	product	yield (%)[a]
1			98
2			98
3			99
4			95
5			97[b]
6			91
7			98
8			95
9			100
10			100
11			99

[a] GC yields, average of two runs. [b] 1 mol % catalyst, 2.1 equiv of base.

Aryl Amination of Aryl Triflates. Several studies have been reported on the palladium-catalyzed preparation of a wide variety of arylamines from aryl halides.[34] Most of these reaction procedures make use of catalysts bearing phosphine ligands.[35] In the past few years, the aryl amination reaction has been reported to be efficient with aryl triflates as the coupling partner.[36] The importance of aryl triflates is significant as they can be easily synthesized from readily available phenols[37] and their use has already has been demonstrated in Stille and Suzuki−Miyaura couplings.[37−39] Uncatalyzed coupling of secondary amines with activated aryl triflates in polar solvents is known but requires several days to lead to product formation.[40] Catalytic amination of aryl triflates

---

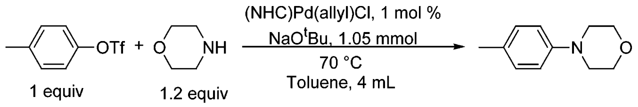
(34) See, for example: (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J. F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805−818. (b) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852−860.

(35) (a) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609−3612. (b) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348−1350. (c) Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215−7216. (d) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217−7218. (e) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046−2067. (f) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575−5580. (g) Kuwano, R.; Utsunomiya, M.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 6479−6486.

(36) (a) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264−1267. (b) Ahman, J.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6363−6366. (c) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig. J. F. *J. Org. Chem.* **1997**, *62*, 1268−1273. (d) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158−1174.

(37) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478−5486.

TABLE 11. Effect of Different NHC on the Aryl Amination Reaction



(NHC)Pd(allyl)Cl	time (h)	yield (%)[a]
(IPr)Pd(allyl)Cl	3	94
(IMes)Pd(allyl)Cl	24	11
(I^{t}Bu)Pd(allyl)Cl	24	41

[a] GC yields.

has been previously achieved using systems involving Pd/BINAP,[36a,b] Pd/dppf,[36c] and Pd/(*o*-biphenyl)P(^{t}Bu)$_2$.[36d] The active species in these systems is generated *in situ*; however, the ligands employed are susceptible to thermal degradation and are usually difficult to remove from the product.

We turned our attention to triflates as substrates and examined their compatibility with the (NHC)Pd(allyl) Cl presented here. Various (NHC)Pd(allyl)Cl complexes were tested in the coupling of morpholine and *p*-tolyl triflate. From the results presented in Table 11, (IPr)-Pd(allyl)Cl was selected to conduct the amination reactions.

A variety of amines were coupled with aryl triflates in the presence of NaO^{t}Bu as base using toluene as solvent. Dialkylamines, secondary arylamines and primary amines were suitable substrates for the amination reaction and results are presented in Table 12.

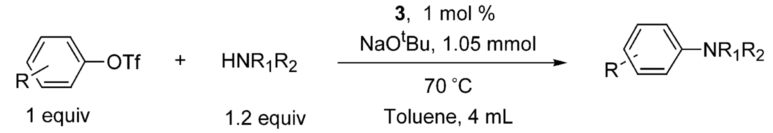
Conclusions

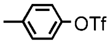
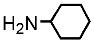
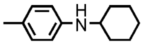
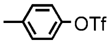
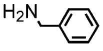
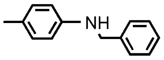
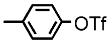
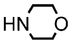
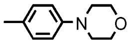
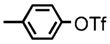
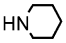
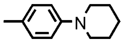
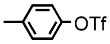
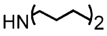
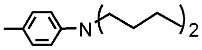
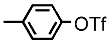
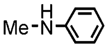
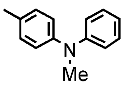
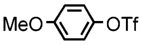
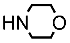
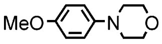
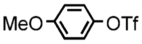
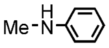
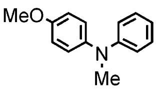
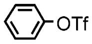
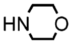
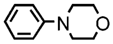
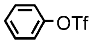
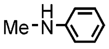
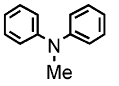
The catalytic behavior of a series of well-defined, air- and moisture-stable (NHC)Pd(allyl)Cl complexes has been examined. A general system involving the use of (IPr)Pd(allyl)Cl and NaO^{t}Bu was shown to be suitable for the Suzuki−Miyaura cross-coupling of activated and unactivated aryl chlorides and bromides, also efficient in the catalytic dehalogenation of aryl chlorides and in the catalytic aryl amination involving aryl triflates. All reactions proceed in short times and at mild temperatures. Investigations focusing on mechanistic aspects and reactivity of this series of complexes in related cross-coupling reactions are ongoing in our laboratories.

Experimental Section

General Considerations. All aryl halides, boronic acids, amines, and aryl triflates were used as received. Technical grade 2-propanol was also used as received. 1,4-Dioxane (anhydrous) and toluene were distilled under argon from

TABLE 12. Catalytic Amination of Aryl Triflates



entry	triflate	amine	product	time (h)	yield (%)[a]
1				3	84(80)
2				3	77(71)
3				3	92(90)
4				6	84(75)
5				6	91(85)
6				3	92(90)
7				3	93(90)
8				3	95(88)
9				6	85(77)
10				3	93(90)

[a] GC yield (isolated yield), average of two runs.

sodium benzophenone ketyl prior to use. Cesium carbonate, potassium and cesium fluoride, potassium phosphate, potassium and sodium *tert*-butoxide, and barium hydroxide were stored under argon in an inert atmosphere glovebox or in desiccators over anhydrous calcium carbonate. The palladium complexes (IMes)Pd(allyl)Cl (**1**) (IMes = (*N*,*N′*-bis(2,4,6-trimethylphenyl)imidazol)-2-ylidene), (SIMes)Pd(allyl)Cl (**2**) (SIMes = (*N*,*N′*-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol)-2-ylidene), (IPr)Pd(allyl)Cl (**3**) (IPr = (*N*,*N′*-bis(2,6-diisopropylphenyl)imidazol)-2-ylidene), (SIPr)Pd(allyl)Cl (**4**) (SIPr = (*N*,*N′*-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol)-2-ylidene), and (I^tBu)Pd(allyl)Cl (**5**) (I^tBu = (*N*,*N′*-bis(2,6-*tert*-butylphenyl)-imidazol)-2-ylidene) were prepared according to reported procedures.[10] All reactions were carried out under an atmosphere of argon in screw cap vials and stirred in a Lab-Line Orbit bench shaker if conventionally heated or in sealed cap vials and placed in an Enrys Optimizer microwave reactor if microwave heated. Flash chromatography was performed using silica gel 60 (230−400 mesh) using hexanes/ethyl acetate mixtures. NMR spectra were recorded on a 300 or 400 MHz spectrometer at ambient temperature in $CDCl_3$.

Conventional and Microwaved-Assisted Suzuki-Miyaura Cross-Coupling Reactions. Effect of the Base on the Suzuki−Miyaura Cross-Coupling. General Procedure. In a glovebox, **1** (2 mol %, 9.8 mg), base (1.5 mmol), and phenylboronic acid (1 mmol, 122 mg) were added in turn to a vial and closed with a screw cap fitted with a septum. Outside the glovebox, 4-chlorotoluene (1 mmol, 118 mL) and 1,4-dioxane (3 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 80 °C for 4 h. The mixture was then analyzed by gas chromatography.

Effect of Different NHC on the Suzuki−Miyaura Cross-Coupling. General Procedure. In a glovebox, catalyst (2 mol %), NaO^tBu (3 mmol, 288 mg), and phenylboronic acid (1.1 mmol, 134 mg) were added in turn to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, 4-chlorotoluene (1 mmol, 118 μL) and 1,4-dioxane (1 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 80 °C for 20 min. The mixture was then analyzed by gas chromatography.

Catalytic Suzuki−Miyaura Cross- Coupling of Aryl Chlorides with Phenylboronic Acid. General Procedure. In a glovebox, **3** (2 mol %, 11.4 mg), NaO^tBu (3 mmol, 288 mg), and phenylboronic acid (1.2 mmol, 146 mg) were added in turn to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, the aryl chloride (1 mmol) and 1,4-dioxane (1.5 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 80 °C for 3−4 h and subsequently allowed to cool to room temperature. After analysis by gas chromatography, silica gel was added to the vial, the solvent was evaporated in vacuo, and the product was isolated by flash chromatography. The isolated product yields are the average of two runs.

Catalytic Suzuki−Miyaura Cross-Coupling of Aryl Bromides with Phenylboronic Acid. General Procedure. In a glovebox, **3** (1 mol %, 5.7 mg), NaO^tBu (3 mmol, 288 mg), and phenylboronic acid (1.2 mmol, 146 mg) were added in turn to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, the aryl bromide (1 mmol) and 1,4-dioxane (1.5 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 60 °C for 3 h and subsequently allowed to cool to room temperature. After analysis by gas chromatography, silica gel was added to the vial, the solvent was evaporated in vacuo, and the product was isolated by flash chromatography. The amounts of isolated product are the average of two runs.

Catalytic Suzuki−Miyaura Cross-Coupling of 4-Chlorotoluene with Different Boronic Acids. General Procedure. In a glovebox, **3** (2 mol %, 11.4 mg), NaO^tBu (3 mmol, 288 mg), and the boronic acid (1.2 mmol) were added in turn to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, 4-Cl-toluene (1 mmol, 120 mL) and 1,4-dioxane (1.5 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 60 °C for 3 h and subsequently allowed to cool to room temperature. After analysis by gas chromatography, silica gel was added to the vial, the solvent was evaporated in vacuo, and the product was isolated by flash chromatography. The amounts of isolated product are the average of two runs.

Microwave-Assisted Catalytic Suzuki−Miyaura Cross-Coupling of Aryl Chlorides with Phenylboronic Acid. General Procedure. In a glovebox, **3** (2 mol %, 11.4 mg), NaO^tBu (3 mmol, 288 mg), and phenylboronic acid (1.2 mmol, 146 mg) were added in turn to a microwave vial containing a magnetic stirring bar and the vial sealed with a cap fitted with a septum. Outside the glovebox, the aryl chloride (1 mmol) and 1,4-dioxane (2 mL) were injected into the vial in that order. The vial was then placed in a microwave reactor set at 120 °C for 90 s and subsequently allowed to cool to room temperature. The mixture was then analyzed by gas chromatography.

Conventional and Microwave-Assisted Catalytic Dehalogenation of Aryl Chlorides. Effect of the Base on the Microwave-Assisted Dehalogenation. General Procedure. In a glovebox, base (1.05 mmol) was added to a microwave vial containing a magnetic stirring bar and the vial sealed with a cap fitted with a septum. Outside the glovebox, 4-chlorotoluene (1 mmol, 118 μL) and 2 mL of a stock solution of **3** in technical grade 2-propanol (1.5 mg in 20 mL, 0.025 mol % in 2 mL) were injected into the vial in that order. The vial was then placed in a microwave reactor set at 120 °C for 120 s and subsequently allowed to cool to room temperature. The mixture was analyzed by gas chromatography and compared with an authentic sample of the product.

Microwave-Assisted Dehalogenation of Aryl Chlorides. General Procedure. In a glovebox, NaO^tBu (1.05 mmol, 101 mg) was added to a microwave vial containing a magnetic stirring bar and the vial sealed with a cap fitted with a septum. Outside the glovebox, aryl chloride (1 mmol) and 2 mL of a stock solution of **3** in technical grade 2-propanol (1.5 mg in 20 mL, 0.025 mol % in 2 mL) were injected into the vial in that order. The vial was then placed in a microwave reactor set at 120 °C for 120 s and subsequently allowed to cool to room temperature. The mixture was analyzed by gas chromatography and compared with an authentic sample of the product.

Dehalogenation of Aryl Chlorides. General Procedure. In a glovebox, NaO^tBu (1.05 mmol, 101 mg) was added to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, the aryl chloride (1 mmol) and 1.5 mL of a stock solution of **3** in technical grade 2-propanol (57 mg in 30 mL, 0.5 mol % in 1.5 mL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 60 °C for 1.75 h and subsequently allowed to cool to room temperature. The mixture was analyzed by gas chromatography and compared with an authentic sample of the product.

Catalytic Amination of Aryl Triflates. Effect of Different NHC on the Catalytic Amination of Aryl triflates. In a glovebox, catalyst (1 mol %), NaO^tBu (1.05 mmol, 101 mg), and dry toluene (4 mL) were added in turn to a vial which was closed with a screw cap fitted with a septum. Outside the glovebox, *p*-tolyl triflate (1 mmol, 179 μL) and morpholine (1.2 mmol, 105 μL) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 70 °C, and the reaction was monitored by gas chromatography.

Catalytic Amination of Aryl Triflates. General Procedure. In a glovebox, **3** (1 mol %), NaO^tBu (1.05 mmol, 101

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(38) Oh-e, T.; Miyaura, N.; Suzuki. A. *J. Org. Chem.* **1993**, *58*, 2208−2201.

(39) Ritter, K. *Synthesis* **1993**, 735−762.

(40) Kotsuki, H.; Kobayashi, S.; Suenaga, H.; Nishizawa, H. *Synthesis* **1990**, 1145−1147.

mg), and dry toluene (4 mL) were added in turn to a vial that was then closed with a screw cap fitted with a septum. Outside the glovebox, aryl triflate (1 mmol) and amine (1.2 mmol) were injected into the vial in that order. The vial was then placed in a benchtop shaker set at 70 °C. After analysis by gas chromatography, silica gel was added to the vial, the solvent was evaporated *in vacuo*, and the product isolated by flash chromatography. The amounts of isolated product reported are the average of two runs.

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Supporting Information Available: Experimental procedures and product isolation protocol. This material is available free of charge via the Internet at http://pubs.acs.org.

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