Iron Catalysis and Water: A Synergy for Refunctionalization of Boron

John L. Wood, Ludovic D. Marciasini, Michel Vaultier, Mathieu Pucheault*

Institut des Sciences Moléculaires, UMR 5255 – 351 Cours de Libération – Bâtiment A11, Université de Bordeaux 1, 33405 Talence Cedex, France
Fax +33(5)40006632; E-mail: m.pucheault@ism.u-bordeaux1.fr

Received: 08.10.2013; Accepted after revision: 06.12.2013

Abstract: A new catalytic system has been optimized to promote the conversion of boron species into others. $FeCl_3$ associated with imidazole and water favors boron refunctionalization under mild conditions.

Key words: boron, iron, homogeneous catalysis, water, boronate

Boron derivatives have long been used in numerous synthetic transformations, including as coupling partners in organometallic catalyzed reactions such as the Suzuki–Miyaura cross-coupling. Several methods are available to prepare such derivatives, mostly by addition of a strong organometallic reagent onto a trialkylborate. Alternatively, the borylation of aryl halides or pseudo halides can be promoted by transition-metal complexes leading usually to pinacol boronates.[1] C–H activation by late-transition-metal complexes, such as iridium or rhodium, can afford the same compounds.[2] Many derivatives can be prepared from boronic acids, however, it is not always trivial to interconvert various groups on the boron without altering the carbon–boron bond.

For example, the classical method for transforming boronic acids into stable pinacol boronates stands in a classical esterification process with water azeotropic removal using a Dean–Stark apparatus or molecular sieves on small scale. Diaminonaphthyl boranes, used in the elegant chemistry developed by Suginome,[3] are similarly prepared by reaction of boronic acids with 1,8-diaminonaphthalene. Until recently, trifluoro(organo)borates, easily prepared by fluorination[4,5] of the corresponding dialkoxyboranes, were not easily hydrolyzed, and many groups have been looking for efficient methods to release the boronic acid from the borate. One other problem relies in the generation of boronic acids by hydrolysis of pinacolboronates. These derivatives, often obtained via transition-metal-catalyzed borylation,[6] are important stable building blocks due to the steric bulkiness of the pinacol group which prevents hydrolysis and protodeboronation. However, the down side of such derivatives is the poor reactivity in cross-coupling reactions as compared to the boronic acids parental molecule. As direct hydrolysis is often ineffective, therefore a fluorination–hydrolysis sequence has been developed to afford the boronic acids.[7,8] Overall, some transformations occur without any problem, while many others require harsh conditions eventually leading to side products on advance substrates. As part of our research focused on boron derivatives preparation, we looked for an efficient method allowing interconverting boron substituents, keeping in mind the simplicity, the cost effectiveness, and the sustainability of the process.

Trifluoro(organo)borates[9] are stable derivatives formed by fluorination[4] of the corresponding boronic acids or their esters. They are isolated by precipitation and purified by recrystallization, and as such can be stored on the shelf for an extended period of time. Nonetheless, these borates have been used in numerous catalytic transformations, using palladium,[10] copper,[11] nickel,[12] or rhodium[13] complexes as catalysts. Despite their attractiveness, many groups found that the corresponding boronic acids are often more reactive than the borate due to the vacancy on the boron atom.[7,14]

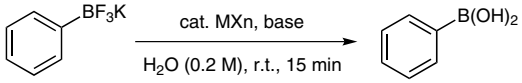
Classical methods, based on highly reactive Lewis acid ($SiCl_4$, TMSCl)[15] are not tolerated by many functionalities borne by the substrate. Lately some milder methods have emerged to prepare boronic acids by the hydrolysis of the corresponding trifluoroborates. Treatment of aryltrifluoroborates by alumina[16] under microwave or classical heating, or with silica[17] in a EtOAc–H_2O mixture led to the corresponding boronic acid. One of the simplest method has been reported by Kabalka and involves the use of 1.1 equivalents of iron trichloride in a THF–H_2O mixture.[18] Intrigued by the role of iron chloride, supposedly forming FeF_3 which would displace the equilibrium, we finally discovered that $FeCl_3$ could be used as a catalyst to promote many interconversions of boron species, including hydrolysis of trifluoroborates.

Assuming the mechanism of the hydrolysis would proceed through a Lewis acid–basic ligand exchange, we investigated a series of chloride salts, known for their Lewis acidic properties, for example in Friedel–Crafts reactions. Among the various salts tested, aluminium chloride (85% yield, Table 1, entry 1), copper(II) chloride (85% yield, Table 1, entry 2), zinc chloride (85% yield, Table 1, entry 3), and iron(III) chloride (85% yield, Table 1, entry 4) displayed similar activity. Zinc chloride led to slightly purer compounds, but iron(III) chloride was chosen because of its relative environmental harmlessness and ease of use. Initially at 16 hours, reaction duration was lowered down to 15 minutes (Table 1, entries 5 and 6) as no further evolution could be observed for extended reaction time.

Base influence was investigated, and no better base than imidazole could be found. Classical amine base such as

SYNLETT 2014, 25, 0551–0555
Advanced online publication: 13.01.2014
DOI: 10.1055/s-0033-1340500; Art ID: ST-2013-B0948-L

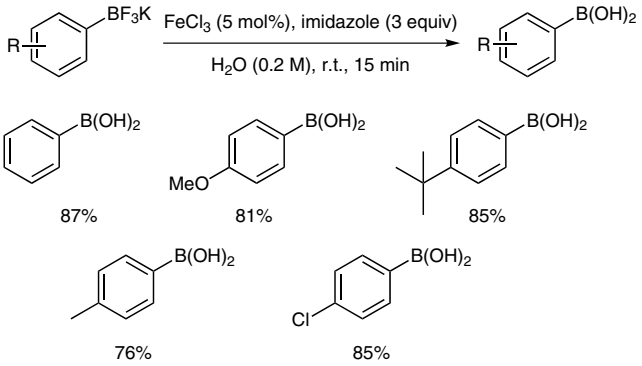
Table 1 Catalytic System Optimization: Trifluoroborate Hydrolysis



Entry	Catalyst MX_n (mol%)	Base (n equiv)	Solvent	Yield (%)[a]
1	$AlCl_3$ (10)	imidazole (3)	H_2O	85[b]
2	$CuCl_2$ (10)	imidazole (3)	H_2O	82[b]
3	$ZnCl_2$ (10)	imidazole (3)	H_2O	82[b]
4	$FeCl_3$ (10)	imidazole (3)	H_2O	84[b]
5	$ZnCl_2$ (10)	imidazole (3)	H_2O	83[c]
6	$FeCl_3$ (10)	imidazole (3)	H_2O	83[c]
7	$FeBr_3$ (10)	imidazole (3)	H_2O	82
8	$FeCl_3$ (10)	Et_3N (3)	H_2O	73
9	$FeCl_3$ (10)	pyridine (3)	H_2O	68
10	$FeCl_3$ (10)	piperidine (3)	H_2O	55
11	$FeCl_3$ (10)	K_2CO_3 (3)	H_2O	71
12	$FeCl_3$ (10)	$KHCO_3$ (3)	H_2O	72
13	$FeCl_3$ (10)	imidazole (3)	MeCN–H_2O	72
14	$FeCl_3$ (10)	imidazole (3)	THF–H_2O	45
15	$FeCl_3$ (10)	imidazole (3)	acetone–H_2O	69
16	$FeCl_3$ (10)	imidazole (3)	MeOH–H_2O	81
17	$FeCl_3$ (0)	imidazole (3)	H_2O	73
18	$FeCl_3$ (1)	imidazole (3)	H_2O	76
19	$FeCl_3$ (2.5)	imidazole (3)	H_2O	85
20	$FeCl_3$ (5)	imidazole (3)	H_2O	87
21	$FeCl_3$ (5)	imidazole (3)	H_2O	80[d]
22	$FeCl_3$ (5)	imidazole (3)	H_2O	75[e]

[a] Isolated yield as referred to analytically pure material.
[b] Reaction time: 16 h.
[c] Reaction time: 15 min.
[d] Reaction concentration: 0.1 M.
[e] Reaction concentration: 0.5 M.

triethylamine (73% yield, Table 1, entry 8), pyridine (68% yield, Table 1, entry 9), piperidine (55% yield, Table 1, entry 10) showed significantly lower yields, and in most cases the product was contaminated by the ammonium salt. Inorganic bases such as $KHCO_3$ (71% yield, Table 1, entry 11) or K_2CO_3 (85% yield, Table 1, entry 12) led to a mere 70% yield. The addition of organic solvent to improve the reaction rate or solubility had only a detrimental effect on the reaction. Acetonitrile (72% yield, Table 1, entry 13), tetrahydrofuran (45% yield, Table 1, entry 14), acetone (69% yield, Table 1, entry 15), or methanol (81% yield, Table 1, entry 16) led only to poorer conversion but



Scheme 1 Hydrolysis of aryltrifluoroborates under optimized conditions

most importantly products were obtained in all cases as impure materials.

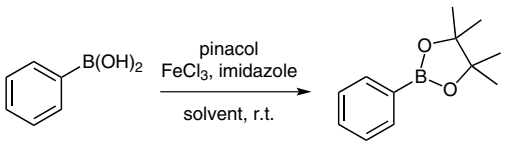
Finally, catalyst loading and reaction concentration were optimized to complete the study. We found out that the optimal catalyst loading was 5 mol% (87% yield, Table 1, entry 20). In short, 1 mol% catalyst is not enough to see improvement on the reaction, 10 mol% and more of $FeCl_3$ induce lower yields due to faster side reactions. Reaction conditions were applied to the hydrolysis of few other trifluoro(organo)borates (Scheme 1). Indeed, the optimized catalytic systems afforded the corresponding boronic acids in good yields. Strikingly, no boroxine was formed under these reactions conditions in contrast to classical organometallic addition onto trialkylborates. However, despite its intrinsic interest, we envisioned that other nucleophiles could be used in place of water. In that case, it would allow the transformation of trifluoro(organo)borates into other boron derivatives. Even if pinacol is not known to be the most nucleophilic diol, it is nonetheless the most employed substituent of boron. Therefore we decided to adapt the conditions developed above to the synthesis of pinacol boronates from trifluoro(organo)borates. Indeed, under the same reaction conditions, simply adding one equivalent of pinacol in the reaction mixture, reaction of trifluorophenylborate afforded the pinacolphenylborane in 65% yield. Studies showed that water was required to perform this reaction in good yield, indicating that the reaction probably proceeded through a hydrolysis of the borate into the boronic acid followed by esterification of the intermediate acid.

Encouraged by this observation we envisioned that the same catalytic system could be employed to transform boronic acids into 1,3,2-dioxaborolanes. Namely, the esterification of boronic acids into its esters can be tricky, especially with low nucleophilic alcohols such as pinacol or pinanediol. The classical method involves refluxing the reaction mixture with azeotropic removal of the generated water.[19] Some milder alternatives have been described,[17] using mechanochemistry[20] for example.

When the previous catalytic system was directly applied to the esterification of boronic acids, isolated yields were deceptively low (Table 2, entry 1). Indeed, pinacol is bare-

ly soluble in neat water and reactivity is therefore decreased. Replacement of water by anhydrous solvents turned out to be unsuccessful. For example, reaction in acetonitrile led to a mere 60% yield (Table 2, entry 2). Using an aqueous 1:1 mixture of water and miscible solvents such as acetonitrile (Table 2, entry 3), acetone (Table 2, entry 4), or tetrahydrofuran (Table 2, entry 5) a clear improvement of conversion was observed. Finally, a 4:1 acetonitrile–water mixture afforded the best conversions (Table 2, entry 6). Reaction time was optimized, and after a 30 minutes reaction time (Table 2, entry 7) the best yields were obtained. Longer reaction times only provided higher proportion of side products (Table 2, entry 8). An excess of diol (Table 2, entries 9 and 10) or boronic acid (Table 2, entry 11) showed no improvement. Finally, we checked the requirement of adding iron chloride (Table 2, entry 12) and three equivalents of base (Table 2, entries 13 and 14). In both cases, isolated yields were below 70%.

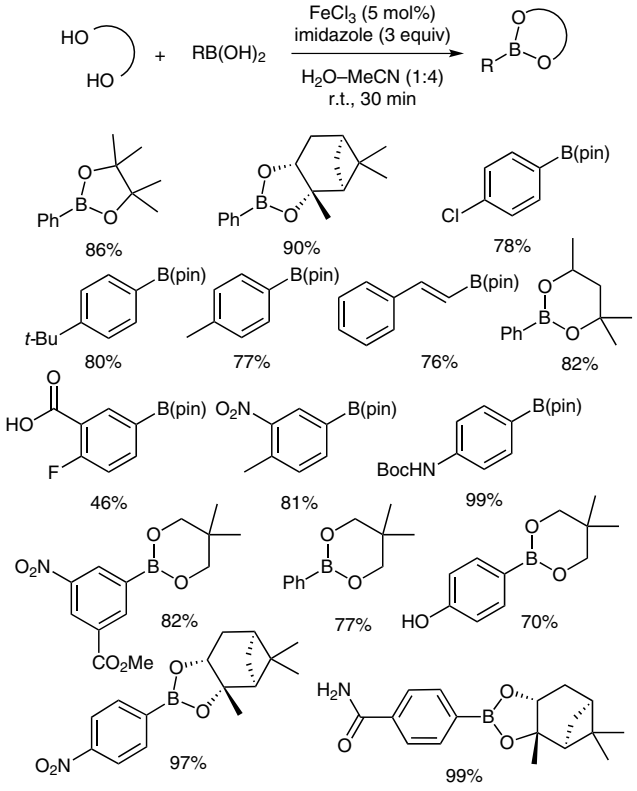
Table 2 Catalytic System Optimization: Formation of Boronates



Entry	$FeCl_3$ (mol%)	Imidazole (equiv)	Solvent	Time (min)	Yield (%)[a]
1	5	3	H_2O	15	57
2	5	3	MeCN	15	60
3	5	3	MeCN–H_2O (1:1)	15	68
4	5	3	acetone–H_2O (1:1)	15	65
5	5	3	THF–H_2O (1:1)	15	66
6	5	3	MeCN–H_2O (4:1)	15	71
7	5	3	MeCN–H_2O (4:1)	30	86
8	5	3	MeCN–H_2O (4:1)	60	66
9	5	3	MeCN–H_2O (4:1)	30	76
10	5	3	MeCN–H_2O (4:1)	30	74[b]
11	5	3	MeCN–H_2O (4:1)	30	55[c]
12	–	3	MeCN–H_2O (4:1)	30	66[d]
13	5	–	MeCN–H_2O (4:1)	30	61
14	5	1	MeCN–H_2O (4:1)	30	65

[a] Isolated yield as referred to analytically pure material.
[b] Conditions: 1.05 equiv of pinacol were used.
[c] Conditions: 1.1 equiv of pinacol were used.
[d] Conditions: 0.9 equiv of pinacol were used.

With this optimized catalytic system in hand, we extended the reaction to the use of other diols such as pinanediol, neopentylglycol, or 2,4-dihydroxy-2-methyl pentane. The corresponding boronates were obtained in 90%, 77%, and 82% yield, respectively. Similarly, few other boronic acids were tested. The *para*-substituted arylboronic acids led to 77–80% yield, and reaction with styryl boronic acid afforded 76% of the vinylboronate (Scheme 2).



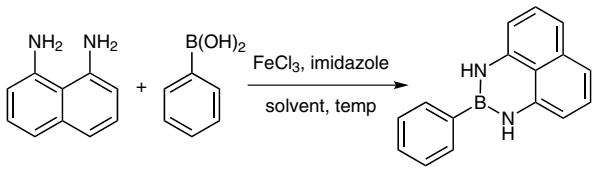
Scheme 2 Esterification of boronic acids

Diazaborolanes[21] have dragged a considerable interest since Suginome reported the use of 1,8-diamino naphthalene as boron masking group, leading to an elegant strategy for an iterative Suzuki–Miyaura cross-coupling sequence.[3] However, despite its attractiveness, the synthesis of these diazaborolanes requires high temperature (toluene reflux for 2 h) with azeotropic removal of water followed by a quick purification on silica gel.[3,22]

We thought that our method could be advantageously adapted to prepare these compounds. Indeed, after a quick optimization of reaction conditions, we found that high temperature was not required for the transformation, but the presence of imidazole was mandatory (Table 3, entry 2). Overall at room temperature, after two hours in the presence of 5 mol% $FeCl_3$, conversion was complete (Table 3, entry 2).

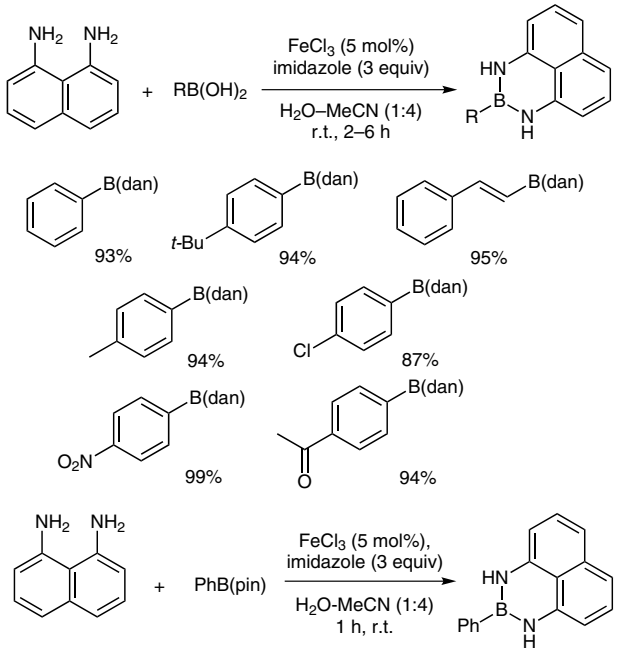
Consequently, we quickly checked on various substrates the generality of the system. In all cases, similar to those reported in the previous sections, yields (87–95%) were high enough to prove the utility of this method to prepare diazaborolanes. Interestingly, the same catalytic system allowed the direct conversion of the pinacolic ester into the diaminonaphthalenyl derivative in 82% yield (Scheme 3).

Table 3 Catalytic System Optimization: Diaminoborane Formation



Entry	$FeCl_3$ (mol%)	Imidazole (equiv)	Temp (°C)	Time (h)	Yield (%)[a]
1	5	3	80	2	89
2	5	–	80	2	57
3	5	3	80	1	89
4	5	3	r.t.	2	93

[a] Isolated yield as referred to analytically pure material.



Scheme 3 Conversion of boronic aicds into diazaborolanes

Overall we developed a simple cost effective but yet efficient method to interconvert boron substituents, that is, fluorine, alkoxy, and amino. The iron(III) chloride–imidazole–water system displayed a unexpected versatility to transform aryl boronic derivatives into one another. If potassium 4-methoxyphenyltrifluoroborate and $FeCl_3$ in a 1:1 mixture led to the formation of the boronic acid in CD_3CN, no change in ^{11}B NMR was witnessed when adding $FeCl_3$ to boronic acid. Imidazole reacts with the boronic acid (δ = 28 ppm) by making a weak complex (δ = 20.3 ppm) but without forming the borate. Imidazole and iron chloride unsurprisingly form an iron–imidazole complex as witnessed by a weak downfield shift of imidazole protons upon complexation. The mechanism is thought to proceed via classical activation by this iron complex as Lewis acids, followed by sequential addition–elimination steps on the boron center. These steps are promoted by the imidazole/imidazolium system acting as a acido-basic buffer and by imidazole-stabilizing intermediate by forming ate complexes. In most cases, a mixture of acetonitrile and water turned out to be the optimal solvent system leading to compounds in good yields at room temperature.

Acknowledgment

L. M. and J. L.W. thank the Région d'aquitaine for funding. We gratefully thank M. N. Rager of the Ecole Nationale Supérieure de Chimie de Paris for NMR analyses. This work has been funded by the CNRS, Université de Bordeaux 1 and Conseil Régional d'Aquitaine.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

References

(1) Chow, W. K.; Yuen, O. Y.; Choy, P. Y.; So, C. M.; Lau, C. P.; Wong, W. T.; Kwong, F. Y. *RSC Adv.* **2013**, *3*, 12518.
(2) Hartwig, J. F. *Chem. Soc. Rev.* **2011**, *40*, 1992.
(3) (a) Noguchi, H.; Shioda, T.; Chou, C.-M.; Suginome, M. *Org. Lett.* **2008**, *10*, 377. (b) Noguchi, H.; Hojo, K.; Suginome, M. *J. Am. Chem. Soc.* **2007**, *129*, 758.
(4) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.
(5) Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2012**, *51*, 9385.
(6) (a) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *Synthesis* **2000**, 778. (b) Billingsley, K. L.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 5589. (c) Marciasini, L.; Richy, N.; Vaultier, M.; Pucheault, M. *Chem. Comm.* **2012**, *48*, 1553. (d) Ma, Y.; Song, C.; Jiang, W.; Xue, G.; Cannon, J. F.; Wang, X.; Andrus, M. B. *Org. Lett.* **2003**, *5*, 4635. (e) Willis, D. M.; Strongin, R. M. *Tetrahedron Lett.* **2000**, *41*, 8683. (f) Wang, L.; Li, J.; Cui, X.; Wu, Y.; Zhu, Z.; Wu, Y. *Adv. Synth. Catal.* **2010**, *352*, 2002. (g) Tang, W.; Keshipeddy, S.; Zhang, Y.; Wei, X.; Savoie, J.; Patel, N. D.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2011**, *13*, 1366. (h) PraveenGanesh, N.; Demory, E.; Gamon, C.; Blandin, V.; Chavant, P. Y. *Synlett* **2010**, 2403. (i) Lu, J.; Guan, Z.-Z.; Gao, J.-W.; Zhang, Z.-H. *Appl. Organomet. Chem.* **2011**, *25*, 537. (j) Kawamorita, S.; Ohmiya, H.; Iwai, T.; Sawamura, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 8363. (k) Billingsley, K. L.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 5589. (l) Broutin, P.-E.; Čerňa, I.; Campaniello, M.; Leroux, F.; Colobert, F. *Org. Lett.* **2004**, *6*, 4419. (m) Praveen Ganesh, N.; Chavant, P. Y. *Eur. J. Org. Chem.* **2008**, 4690. (n) Euzenat, L.; Horhant, D.; Ribourdouille, Y.; Duriez, C.; Alcaraz, G.; Vaultier, M. *Chem. Commun.* **2003**, 2280. (o) Euzenat, L.; Horhant, D.; Brielles, C.; Alcaraz, G.; Vaultier, M. *J. Organomet. Chem.* **2005**, *690*, 2721. (p) Marciasini, L. D.; Richy, N.; Vaultier, M.; Pucheault, M. *Adv. Synth. Catal.* **2013**, *355*, 1083. (q) Pucheault, M.; Marciasini, L.; Vaultier, M. EP 123058547, **2012**.
(7) Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899.
(8) Inglis, S. R.; Woon, E. C. Y.; Thompson, A. L.; Schofield, C. J. *J. Org. Chem.* **2010**, *75*, 468.
(9) (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275. (b) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2007**, *108*, 288. (c) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623.

(10) (a) Darses, S.; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393. (b) Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875.
(11) Joubert, N.; Baslé, E.; Vaultier, M.; Pucheault, M. *Tetrahedron Lett.* **2010**, *51*, 2994.
(12) Han, F.-S. *Chem. Soc. Rev.* **2013**, *42*, 5270.
(13) (a) Pucheault, M.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, 3552. (b) Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 6155. (c) Pucheault, M.; Darses, S.; Genêt, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 15356. (d) Pucheault, M.; Michaut, V.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2004**, *45*, 4729. (e) Navarre, L.; Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2005**, *46*, 4247. (f) Pucheault, M.; Darses, S.; Genêt, J.-P. *Chem. Commun.* **2005**, 4714.
(14) (a) Amatore, C.; Jutand, A.; Le Duc, G. *Angew. Chem. Int. Ed.* **2012**, *51*, 1379. (b) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393. (c) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302. (d) Butters, M.; Harvey, J. N.; Jover, J.; Lennox, A. J. J.; Lloyd-Jones, G. C.; Murray, P. M. *Angew. Chem.* **2010**, *122*, 5282.
(15) Kim, B. J.; Matteson, D. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3056.
(16) Kabalka, G. W.; Coltuclu, V. *Tetrahedron Lett.* **2009**, *50*, 6271.
(17) Molander, G. A.; Cavalcanti, L. N.; Canturk, B.; Pan, P.-S.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 7364.
(18) Blevins, D. W.; Yao, M.-L.; Yong, L.; Kabalka, G. W. *Tetrahedron Lett.* **2011**, *52*, 6534.
(19) Sugihara, J. M.; Bowman, C. M. *J. Am. Chem. Soc.* **1958**, *80*, 2443.
(20) (a) Schnurch, M.; Holzweber, M.; Mihovilovic, M. D.; Stanetty, P. *Green Chem.* **2007**, *9*, 139. (b) Kaupp, G.; Naimi-Jamal, M. R.; Stepanenko, V. *Chem. Eur. J.* **2003**, *9*, 4156.
(21) Pailer, M.; Fenzl, W. *Monatsh. Chem.* **1961**, *92*, 1294.
(22) Slabber, C. A.; Grimmer, C.; Akerman, M. P.; Robinson, R. S. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2011**, *67*, o1995.

