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# Carbamic acid 2-trimethylsilylethyl ester as a new ammonia equivalent for palladium-catalyzed amination of aryl halides

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ABSTRACT

Carbamic acid 2-trimethylsilylethyl ester (Teoc-$NH_2$) serves as an ammonia equivalent in the palladium-catalyzed amination of aryl bromides and aryl chlorides. Anilines with sensitive functional groups can be readily prepared using these amine derivatives.

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Significant progress has been made in the development of transition metal-catalyzed aminations of aryl halides. Despite the existence of copper- and nickel-catalyzed versions of this reaction, palladium remains the metal of choice for this transformation. This is due principally to the higher efficiency of palladium complexes in aryl amination, benefitting from developments in related palladium-catalyzed cross-coupling reactions.[1–3]

As a result, a wide variety of secondary aryl amines can be prepared efficiently using this methodology. Primary aryl amines have been largely prepared by palladium-catalyzed coupling of aryl halides with ammonia surrogates. Allylamine was used as an ammonia equivalent and the allyl group from the resulting aryl alkyl amine was cleaved conveniently using methanesulfonic acid and palladium on carbon.[4] Benzophenone imine has frequently been used as an effective ammonia equivalent. The coupling reactions with this imine are high yielding and can be performed under extremely mild reaction conditions. Moreover, the resulting *N*-aryl imines can be cleaved using several orthogonal methods that are compatible with a variety of protecting groups.[5] The groups of Hartwig and Buchwald independently reported the use of inexpensive silyl reagents such as [$LiN(SiMe_3)_2$] and $Ph_3SiNH_2$ as ammonia equivalents for palladium-catalyzed aminations and the resulting aryl silylamines were deprotected easily.[6] Amidine hydrochloride has recently been used as an ammonia equivalent for copper-catalyzed couplings with aryl halides to prepare anilines.[7] Hydroxylamine *O*-benzyl ether as an ammonia equivalent in the catalytic amination of aryl halides has been reported.[8]

Toluene sulfonamides have been used as ammonia surrogates for palladium-catalyzed aminations.[9] Unfortunately, the resulting sulfonamide requires strong acidic conditions for its cleavage. Fluorinated carbamates have been used as ammonia equivalents for palladium-catalyzed coupling with aryl halides.[10] *N,N*-Dialkylhydrazines were also used as ammonia equivalents for the palladium-catalyzed coupling of aryl halides, and the resulting aryl hydrazines were cleaved using palladium on carbon under transfer hydrogenation conditions to give anilines.[11] Very recently, ammonia itself has been used as an amine reagent for the palladium-catalyzed coupling of aryl halides to afford primary aryl amines.[12] Aqueous ammonia and ammonium chloride were used recently for the synthesis of primary aryl amines using copper as the catalyst.[13]

We recently used 2-(trimethylsilyl)ethanesulfonyl amide (SES-$NH_2$) as an ammonia surrogate and the 2-(trimethylsilyl)ethanesulfonyl group was cleaved using CsF in DMF at a relatively high temperature (100 °C) and requiring a long reaction time.[14] In the search for other suitable and stable ammonia surrogates we found that carbamic acid 2-trimethylsilylethyl ester (Teoc-$NH_2$) was an ammonia surrogate for the palladium-catalyzed amination

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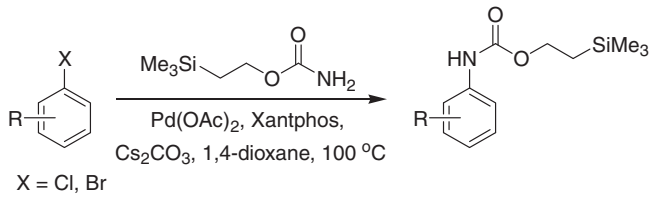
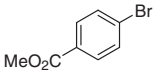
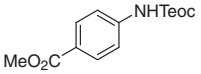
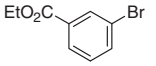
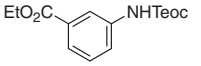
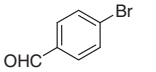
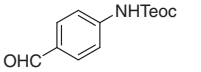
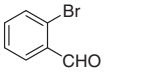
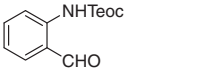
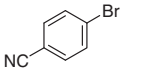
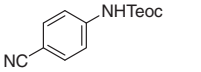
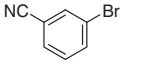
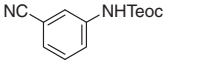
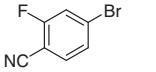
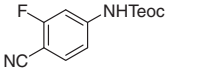
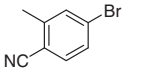
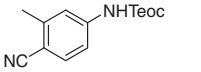
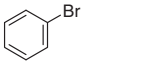
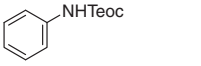
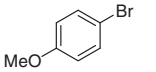
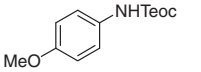
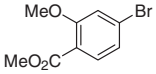
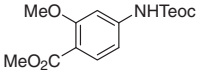
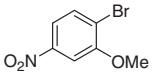
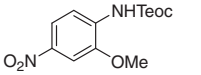
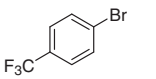
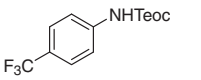
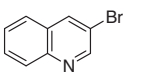
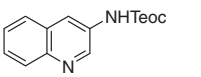
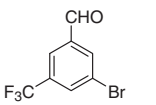
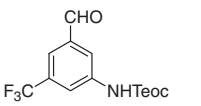
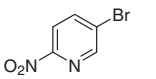
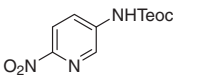
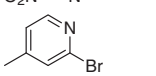
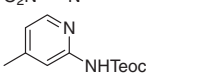


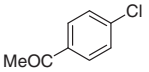
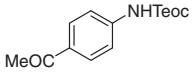
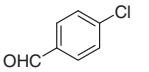
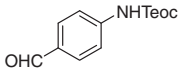
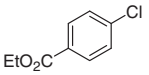

**Scheme 1.** Synthesis of Teoc-protected anilines.

**Table 1**
Teoc-NH2 as an ammonia surrogate in the palladium-catalyzed coupling of aryl and heterocyclic bromides[a]

| Entry | Substrate | Product | Yield[b] (%) |
|---|---|---|---|
| 1 |  |  | 97 |
| 2 |  |  | 98 |
| 3 |  |  | 93 |
| 4 |  |  | 96 |
| 5 |  |  | 93 |
| 6 |  |  | 92 |
| 7 |  |  | 90 |
| 8 |  |  | 95 |
| 9 |  |  | 90 |
| 10 |  |  | 71 |
| 11 |  |  | 97 |
| 12 |  |  | 98 |
| 13 |  |  | 95 |
| 14 |  |  | 87 |
| 15 |  |  | 93 |
| 16 |  |  | 75 |
| 17 |  |  | 86 |

[a] Reaction conditions: aryl bromide (1 mmol), Teoc-$NH_2$ (1.2 mmol), $Pd(OAc)_2$ (0.03 mmol), Xantphos (0.06 mmol), $Cs_2CO_3$ (2.0 mmol) 1,4-dioxane (7 ml), Schlenk tube, 100 °C, 15 h.
[b] Isolated yield.

**Table 2**
Teoc-$NH_2$ as an ammonia surrogate in the palladium-catalyzed coupling of aryl and heterocyclic chlorides[a]

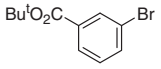
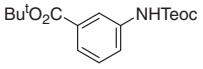
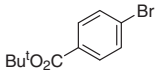
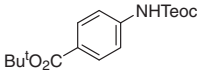
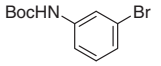
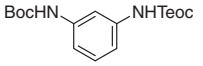
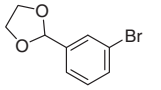
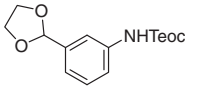
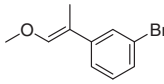
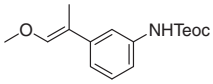
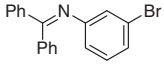
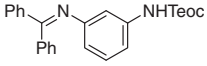
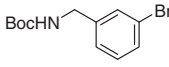
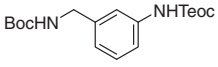
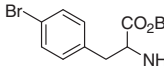
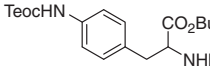
| Entry | Substrate | Product | Yield[b] (%) |
|---|---|---|---|
| 1 |  |  | 93 |
| 2 |  |  | 92 |
| 3 |  |  | 97 |
| 4 |  |  | 93 |
| 5 |  |  | 89 |
| 6 |  |  | 91 |
| 7 |  |  | 83 |
| 8 |  |  | 88 |
| 9 |  |  | 90 |
| 10 |  |  | 41[c] |
| 11 |  |  | 43[c] |
| 12 |  |  | 79 |
| 13 |  |  | 72 |
| 14 |  |  | 90 |
| 15 |  |  | 88 |

[a] Reaction conditions: aryl chloride (1 mmol), Teoc-$NH_2$ (1.2 mmol), $Pd(OAc)_2$ (0.03 mmol), Xantphos (0.06 mmol), $Cs_2CO_3$ (2.0 mmol) 1,4-dioxane (7 ml), Schlenk tube, 120 °C, 15 h.
[b] Isolated yield.
[c] Incomplete reaction; the Teoc group cleaved and the product was isolated as the free amine.

(Scheme 1). The Teoc-protecting group can be removed under mild conditions using a fluoride source. The fluoride ion attacks the silicon atom which leads to β-elimination and this releases the deprotected amine and volatile products such as fluorotrimethylsilane and ethylene. Teoc-$NH_2$ can be prepared from the reaction of phenyl chloroformate and trimethylsilyl ethanol in the presence of pyridine and the resulting carbonate can be transformed directly into the Teoc carbamate (Teoc-$NH_2$) using ammonia.[15] Teoc-$NH_2$ can also be prepared from trimethylsilyl ethanol by the reaction with CDI.[16]

In the present investigation, we studied the potential of Teoc-$NH_2$ as a reagent for the synthesis of primary arylamines from methyl 4-bromobenzoate using a palladium source such as

**Table 3**
Teoc-$NH_2$ as an ammonia surrogate in the palladium-catalyzed coupling of aryl bromides containing sensitive functional groups and selective Teoc group cleavage[a]

| Entry | Substrate | Product | Yield[b] (%) |
|---|---|---|---|
| 1 |  |  | 96 (98) |
| 2 |  |  | 96 (94) |
| 3 |  |  | 80 (93) |
| 4 |  |  | 92 (90) |
| 5 |  |  | 88 (95) |
| 6 |  |  | 79 (96) |
| 7 |  |  | 80 (96) |
| 8 |  |  | (52)[c] |

[a] Reaction conditions: aryl bromide (1 mmol), Teoc-$NH_2$ (1.2 mmol), $Pd(OAc)_2$ (0.03 mmol), Xantphos (0.06 mmol), $Cs_2CO_3$ (2.0 mmol) 1,4-dioxane (7 ml), Schlenk tube, 100 °C, 15 h.
[b] Isolated yield of coupled product. Yield of free amine after Teoc deprotection is given in the brackets.
[c] Incomplete reaction; the Teoc group of the crude product was cleaved and the product was isolated as the free amine.

$Pd(OAc)_2$ or $Pd_2(dba)_3$ with *rac*-BINAP in toluene or 1,4-dioxane as solvent. The maximum yield obtained using this system was only 60%.

Although the yield was moderate, the product formation from Teoc-$NH_2$ was convincing and thus we screened different catalysts. Changing the ligand from BINAP to Xantphos resulted in an increase in the yield. Also, by changing the solvent, base, and reaction temperature, we were able to obtain a 97% isolated yield of product from methyl 4-bromobenzoate using a $Pd(OAc)_2$–Xantphos–$Cs_2CO_3$ catalyst system in 1,4-dioxane at 100 °C for 15 h. Aryl bromides with various functional groups such as cyano, ester, nitro, aldehyde, and methoxy reacted under the above-optimized conditions without undergoing any other side reactions (Table 1).[17]

Having been successful with aryl bromides, we next extended this reaction to aryl chlorides. Aryl chloride bond activation is an industrially important field of research due to the lower cost of aryl chlorides compared to aryl bromides and aryl iodides.[18] We used the same reaction conditions for the coupling of Teoc-$NH_2$ with aryl chlorides, but the temperature was increased from 100 °C to 120 °C. The reaction worked well with aryl chlorides possessing different substituents such as cyano, ester, keto, nitro, and aldehyde, and the yields obtained were more than 80% in most cases. Surprisingly, this reaction only worked moderately well with aryl chlorides with electron-donating groups (Table 2, entries 10 and 11), whereas heterocyclic aryl chlorides reacted well with Teoc-$NH_2$ (Table 2).

The aminated aryl trimethylsilylethyl ester products were very stable and could be used for further transformations without affecting the Teoc group. The Teoc group was cleaved selectively using CsF in DMF without affecting other functional groups.[19] We have carried out Teoc deprotection with several products having acid-sensitive groups, for example, the Teoc group was cleaved selectively from products containing acid-sensitive groups such as *tert*-butyl ester, enol ether, *tert*-butyl carbamate, aldol, and imine. (Table 3).

In summary, we have reported the synthesis of several aryl carbamic acid 2-trimethylsilylethyl esters from aryl bromides and aryl chlorides using Teoc-$NH_2$. The Teoc group can be cleaved selectively without affecting other functional groups and establishes Teoc-$NH_2$ as a useful ammonia surrogate for aryl amination reactions. Further studies on N-substituted Teoc-$NH_2$ are in progress.

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## Supplementary data

Supplementary data (experimental and analytical data for new compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.100.

## References and notes

1. Palladium-catalyzed aryl amination: (a) Hartwig, J. F. *Handb. Organopalladium Chem. Org. Syn.* **2002**, *1*, 1051; (b) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131; (c) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046; (d) Ali, M. H.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 2560; (e) Kuwano, R.; Utsunomiya, M.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 6479; (f) Stambuli, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4746; (g) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553; (h) Viciu, M. S.; Germaneau, R. F.; Navarro-Fernandez, O.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2002**, *21*, 5470; (i) Stauffer, S. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 6977; (j) Hooper, M. W.; Utsunomiya, M.; Hartwig, J. F. *J. Org. Chem.* **2003**, *68*, 2861; (k) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653; (l) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 13978; (m) Viciu, M. S.; Kelly, R. A., III; Stevens, E. D.; Naud, F.; Studer, M.; Nolan, S. P. *Org. Lett.* **2003**, *5*, 1479; (n) Urgaonkar, S.; Xu, J.-H.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 8416; (o) Rataboul, F.; Zapf, A.; Jackstell, R.; Harkal, S.; Riermeier, T.; Monsees, A.; Dingerdissen, U.; Beller, M. *Chem. Eur. J.* **2004**, *10*, 2983; (p) Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 9135; (q) Charles, M. D.; Schultz, P.; Buchwald, S. L. *Org. Lett.* **2005**, *7*, 3965; (r) Xie, X.; Zhang, T. Y.; Zhang, Z. *J. Org. Chem.* **2006**, *71*, 6522; (s) Marion, N.; Navarro, O.; Mei, J.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101; (t) Klingensmith, L. M.; Strieter, E. R.; Barder, T. E.; Buchwald, S. L. *Organometallics* **2006**, *25*, 82; (u) Shekhar, S.; Ryberg, P.; Hartwig, J. F.; Mathew, J. S.; Blackmond, D. G.; Strieter, E. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 3584; (v) Li, J. J.; Wang, Z.; Mitchell, L. H. *J. Org. Chem.* **2007**, *72*, 3606; (w) Kienle, M.; Dubbaka, S. R.; Brade, K.; Knochel, P. *Eur. J. Org. Chem.* **2007**, 4166; (x) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338; (y) Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 13848; (z) Shen, Q.; Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6586; (aa) So, C. M.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 6402; (ab) Lipshutz, B. H.; Chung, D. W.; Richa, B. *Adv. Synth. Catal.* **2009**, *351*, 1717; (ac) Lundgren, R. J.; Sappong, K. A.; Stradiotto, M. *Chem. Eur. J.* **2010**, *16*, 1983.
2. Nickel-catalyzed aryl amination: (a) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029; (b) Omar-Amrani, R.; Thomas, A.; Brenner, E.; Schneider, R.; Fort, Y. *Org. Lett.* **2003**, *5*, 2311; (c) Chen, C.; Yang, L.-M. *Org. Lett.* **2005**, *7*, 2209; (d) Kelly, R. A., III; Scott, N. M.; Dıez-Gonzalez, S.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 3442; (e) Chen, C.; Yang, L.-M. *J. Org. Chem.* **2007**, *72*, 6324; (f) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624; (g) Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 2929.
3. Copper-catalyzed aryl amination: (a) Antilla, J. C.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 2077; (b) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 793; (c) Okano, K.; Tokuyama, H.; Fukuyama, T. *Org. Lett.* **2003**, *5*, 4987; (d) Lu, Z.; Twieg, R. J.; Huang, S. D. *Tetrahedron Lett.* **2003**, *44*, 6289; (e) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578; (f) Ran, C.; Dai, Q.; Harvey, R. G. *J. Org. Chem.* **2005**, *70*, 3724; (g) Hu, T.; Li, C. *Org. Lett.* **2005**, *7*, 2035; (h) Rao, H.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2005**, *70*, 8107; (i) Moriwaki, K.; Satoh, K.; Takada, M.; Ishino, Y.; Ohno, T. *Tetrahedron Lett.* **2005**, *46*, 7559; (j) Lu, Z.; Twieg, R. J. *Tetrahedron* **2005**, *61*, 903; (k) Jerphagnon, T.; van Klink, G. P. M.; de Vries, J. G.; van Koten, G. *Org. Lett.* **2005**, *7*, 5241; (l) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120; (m) Zhang, Z.; Mao, J.; Zhu, D.; Wu, F.; Chen, H.; Wan, B. *Tetrahedron* **2006**, *62*, 4435; (n) Wolf, C.; Liu, S.; Mei, X.; August, A. T.; Casimir, M. D. *J. Org. Chem.* **2006**, *71*, 3270; (o) Barros, O. S. R.; Nogueira, C. W.; Stangherlin, E. C.;

Menezes, P. H.; Zeni, G. *J. Org. Chem.* **2006**, *71*, 1552; (p) Shafir, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 8742; (q) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 2779; (r) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2007**, *9*, 643; (s) Altman, R. A.; Koval, E. D.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 6190; (t) Dawei, M.; Qian, C. *Acc. Chem. Res.* **2008**, *41*, 1450.

4. Jaime-Figueroa, S.; Liu, Y.; Muchowski, J. M.; Putman, D. G. *Tetrahedron Lett.* **1998**, *39*, 1313.
5. (a) Wolfe, J. P.; Åhman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6367; (b) Mann, G.; Hartwig, J. F.; Driver, M. S.; Fernandez-Rivas, C. *J. Am. Chem. Soc.* **1998**, *120*, 827; (c) Cioffi, C. L.; Berlin, M. L.; Herr, R. J. *Synlett* **2004**, 841; (d) Grossman, O.; Rueck-Braun, K.; Gelman, D. *Synthesis* **2008**, 537.
6. (a) Lee, S.; Jorgensen, M.; Hartwig, J. F. *Org. Lett.* **2001**, *3*, 2729; (b) Huang, X.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 3417.
7. Gao, X.; Fu, H.; Qiao, R.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2008**, *73*, 6864.
8. Bedford, R. B.; Betham, M. *Tetrahedron Lett.* **2007**, *48*, 8947.
9. (a) Yin, J.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 1101; (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043; (c) He, H.; Wu, Y.-J. *Tetrahedron Lett.* **2003**, *44*, 3385; (d) Deng, W.; Liu, L.; Zhang, C.; Liu, M.; Guo, Q.-X. *Tetrahedron Lett.* **2005**, *46*, 7295.
10. Trabanco, A. A.; Vega, J. A.; Fernandez, M. A. *J. Org. Chem.* **2007**, *72*, 8146.
11. Liu, X.; Barry, M.; Tsou, H. –R. *Tetrahedron Lett.* **2007**, *48*, 8409.
12. (a) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10028; (b) Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354; (c) Schulz, T.; Torborg, C.; Enthaler, S.; Schaeffner, B.; Dumrath, A.; Spannenberg, A.; Neumann, H.; Boerner, A.; Beller, M. *Chem. Eur. J.* **2009**, *15*, 4528; (d) Vo, G. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11049.
13. (a) Kim, J.; Chang, S. *Chem. Commun.* **2008**, 3052; (b) Wang, D.; Cai, Q.; Dinga, K. *Adv. Synth. Catal.* **2009**, *351*, 1722; (c) Xia, N.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 337; (d) Wu, X. –F.; Darcel, C. *Eur. J. Org. Chem.* **2009**, 4753; (e) Elmkaddem, M. K.; Fischmeister, C.; Thomas, C. M.; Renaud, J.-L. *Chem. Commun.* **2010**, *46*, 925.
14. Anjanappa, A.; Mullick, D.; Selvakumar, K.; Sivakumar, M. *Tetrahedron Lett.* **2008**, *49*, 4585.
15. Fessenden, R. J.; Coon, M. D. *J. Med. Chem.* **1965**, *8*, 604.
16. Reddy, K. L.; Dress, K. R.; Sharpless, K. B. *Tetrahedron Lett.* **1988**, *39*, 3667.
17. *General procedure*: An oven-dried Schlenk tube was charged with $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), Xantphos (34.7 mg, 0.06 mmol), Teoc-$NH_2$ (193 mg, 1.2 mmol), and $Cs_2CO_3$ (650 mg, 2.0 mmol). The Schlenk tube was evacuated and back-filled with argon. 3-Bromobenzoic acid *tert*-butyl ester (257 mg, 1.0 mmol) and 1,4-dioxane (7 ml) were added and the Schlenk tube was sealed with a Teflon screw cap and placed in a preheated oil bath at 100 °C for aryl bromides and 120 °C for aryl chlorides for 15 h. After cooling to room temperature, $H_2O$ (10 ml) was added and the reaction mixture extracted with EtOAc (20 ml). The combined organic layer was washed with brine (10 ml), dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The product was purified by flash chromatography. Yield: 324 mg, 96%.
18. (a) Bedford, R. B.; Cazin, C. S. J.; Holder, D. *Coord. Chem. Rev.* **2004**, *248*, 2283; (b) Beller, M.; Zapf, A. *Top. Catal.* **2002**, *19*, 101.
19. (a) Carbino, L. A.; Sau, A. C. *J. Chem. Soc., Chem. Commun.* **1979**, 514; (b) Roush, W. R.; Coffey, D. S.; Mandar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 11331; (c) Van Maarseveen, J. H.; Scheeren, H. W. *Tetrahedron* **1993**, *49*, 2325.