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Palladium-catalyzed chemo- and regioselective cross-coupling reactions of 2,3-dichloronaphthalene-1,4-bistriflate

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ABSTRACT

Palladium-catalyzed chemoselective and regioselective cross-coupling reactions of 2,3-dichloro-1,4-(trifluoromethanesulfonyloxy)naphthalene with aryl boronic acids selectively afforded a variety of mono-, di-, and tetraphenylnaphthalenes. These reactions proceeded with excellent chemoselectivity in favor of the triflate functional group at the C-1 and C-4 positions of naphthalene.

Predictive reactivity and selective control of Pd-catalyzed transformations is an attractive aspect of cross-coupling chemistry. Significant efforts have been made in recent years to realize Pd-catalyzed cross-coupling reactions with regard to the choice of nucleophiles,[1] development of versatile ligands[2] and various catalysts,[3] as well as employing aromatic halides and pseudo-halides as reaction partners.[4] Pd-catalyzed carbon—carbon bond forming processes, particularly the selective Suzuki–Miyaura coupling reaction of arenes and heteroarenes, have been extensively investigated in terms of substrate scope and reactivity, as well as to categorize important features that determine their regio-, chemo-, and stereoselectivity.[5] Selectivity in the Suzuki–Miyaura coupling reaction depends heavily on electronic effects and the steric properties of both coupling partners, together with the precise structure of the substrates, which constitute the cores of many types of polymers,[6] ligands,[7] natural products, and pharmaceuticals.[8]

In recent years, selective cross-coupling reactions of polyhalogenated substrates have been extensively studied[5a–f] and employed as key intermediates in the synthesis of important biological targets or their direct precursors.[5g–i] The development of phenol-derived pseudo-halide electrophiles in coupling reactions is highly attractive as the hydroxyl group is present in many organic compounds, and they have been employed as versatile alternatives to halides in cross-coupling reactions.[9] Nevertheless, the implementation of this strategy is often not as simple as for aryl halides, largely due to a higher C—O bond strength relative to the carbon—halogen bond. Aryl triflates are one of the most common electrophiles in coupling reactions but have some drawbacks such as difficult purification due to ease of hydrolysis and degradation at room temperature which offers the opportunity for improvement. Multi-substituted arenes containing mixed triflates and halides (two or more reactive sites) have scarcely been studied and in spite of the significant recent advances in transition metal-catalyzed processes, many noteworthy challenges remain. Among them are the coupling of hindered reaction partners, control of chemo- and/or regioselectivity using substrates with multiple reaction centers, and the coupling of abundant aryl chlorides.[10]

One key substrate class on which we have focused our efforts is symmetrical 1,4-bis-triflates of naphthalene bearing mixed halide/triflate substituents. The ability to effect selective functionalization can be a powerful tool as the resulting products are important synthetic motifs in organic synthesis, the pharmaceutical industry, and materials science.[11] Substituted naphthalenes are important as drugs and lead structures in medicinal chemistry.[11g]

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The primary focus of our efforts was the selective substitution at the C-1 and/or C-4 positions. Previous reports were disappointing, and almost none of the desired Suzuki coupling product was observed (see Scheme 2, top).[12] All efforts resulted in sluggish reactions and low overall yields. This unexpected behavior of 1,4-bis-triflates as evidenced by the prevalence of hydrolysis/redox products under catalytic reaction condition was probably due to the abstractable proton (two transferable hydrogen atoms of 1,4-dihydroxybenzenes that easily lead to stable quinones and hydroquinones which are common redox mediators).[13] Herein, we report a highly chemo- and regioselective palladium-catalyzed Suzuki–Miyaura reaction of 1,4-(trifluoromethanesulfonyloxy)-2,3-chloronaphthalene, which allowed the direct synthesis of a number of mono-, di-, and tetraphenyl substituted naphthalene products.

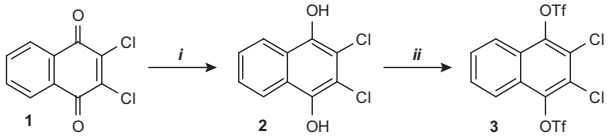
2,3-Dichloronaphthalene-1,4-diol **2** was synthesized in high yield from inexpensive, commercially available 2,3-dicloro-1,4-naphthaquinone (DCNQ) **1** by reduction with aqueous $Na_2S_2O_4$ (94%), followed by transformation to the corresponding 2,3-dichloronaphthalene-1,4-diylbis(trifluoromethanesulfonate) **3** (96%) (Scheme 1).

2,3-Dichloronaphthalene-1,4-bistriflate (**3**) is stable and can be stored for a long time (more than six months) at room temperature. In order to obtain a crystal structure, layering techniques were applied and well-defined crystals were grown from (CH_2Cl_2/EtOH, 2:1). The X-ray structure showed that both triflate groups were twisted out of plane (Fig. 1).[20]

The Suzuki–Miyaura reaction of **3** with arylboronic acids **4a–e** (4.5 equiv) afforded 1,2,3,4-tetraarylnaphthalenes **5a–e** in 58–76% yields (Scheme 2, Table 1). Both electron-poor and electron-rich arylboronic acids were successfully employed. The reactions were quite clean, although in some cases, small amounts of biaryl derivatives, due to homocoupling of the organoboron reagents, were also observed. The best yields were obtained in 1,4-dioxane at 120 °C using $Pd(PPh_3)_4$ (5 mol %) as the catalyst and KF (10.0 equiv) as the base.

Next, the Suzuki–Miyaura coupling was examined for the synthesis of unsymmetrical substituted naphthalenes. A highly selective mono-coupling reaction was achieved after careful optimization of the reaction parameters including base (3.0 equiv KF), temperature (50 °C) and solvents. Selective Suzuki coupling of **3** with various arylboronic acids (1.0 equiv) afforded the unsymmetrical 1-aryl-2,3-dichloronaphthalene-4-trifluoromethanesulfonates **6a–c** in 68–72% yields (Table 2). The reactions proceeded with good selectivity for monosubstitution in favor of the triflate at the C-1 position, while the C-4 triflate remained unreacted under strict control of the reaction conditions. During optimization, it proved crucial to use dried solvents, KF as base and Pd $(PPh_3)_4$ (3 mol %) as catalyst. The reaction course was selective and predominantly led to the product of OTf-displacement (Scheme 3, Table 2).

The structures of the compounds were elucidated by extensive spectral analysis; 1D and 2D (COSY, HMBC, HMQC, NOESY) NMR spectroscopy. In order to obtain crystal structures, layering techniques were applied and well-defined crystals were grown from (CH_2Cl_2/EtOH, 2:1). The structure of compound **6a** was unambiguously confirmed by single crystal X-ray analysis (Fig. 2).[20]



Scheme 1. Synthesis of **2** and **3**. Reagents and Conditions: (i) **1** (1.0 equiv), $Na_2S_2O_4$ (3.0 equiv), 1 h; (ii) **2** (1.0 equiv), Tf_2O (3.0 equiv), pyridine (2.0 equiv), CH_2Cl_2, 20 °C, 6 h.

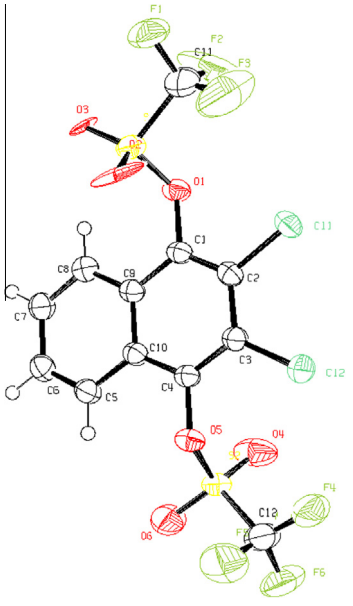
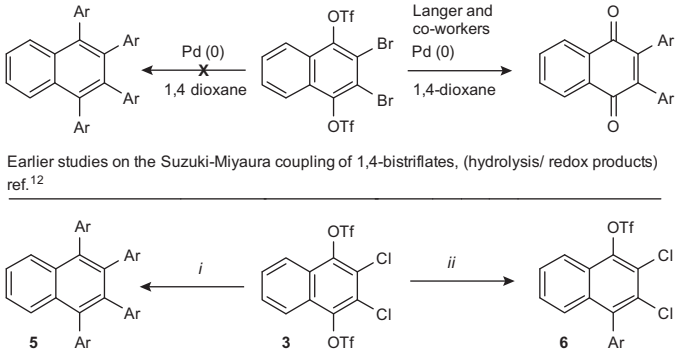


Figure 1. Crystal structure of **3**.



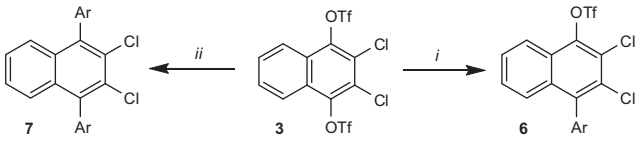
Scheme 2. Synthesis of **5a–e** and **6a–e**. Reagents and conditions: (i) **3** (1.0 equiv), $ArB(OH)_2$ (4.5 equiv), $Pd(PPh_3)_4$ (3 mol %), KF (10.0 equiv), 1,4-dioxane, 120 °C, 8 h, (ii) **3** (1.0 equiv), $ArB(OH)_2$ (1.0 equiv), $Pd(PPh_3)_4$ (3 mol %), KF (3.0 equiv), 1,4-dioxane, 50 °C, 4 h.

Table 1
Synthesis of 1,2,3,4-tetraarylnaphthalenes **5a–e**

Entry	$ArB(OH)_2$ (**4**)	**5**	Yield (%)
1	4-(MeO)C_6H_4	**a**	76
2	4-MeC_6H_4	**b**	72
3	4-ClC_6H_4	**c**	66
4	3,5-MeC_6H_3	**d**	58
5	3,4,5-MeC_6H_2	**e**	62

Table 2
Synthesis of **6a–c** and **7a–c**

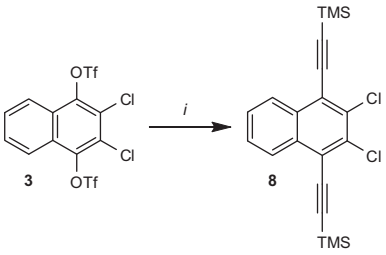
Entry	$ArB(OH)_2$ (**4**)	**6**	Yields (%)	**7**	Yields (%)
1	4-MeOC_6H_4	**a**	72	**a**	77
2	4-MeC_6H_4	**b**	70	**b**	52
3	4-ClC_6H_4	**c**	68	**c**	60



Scheme 3. Synthesis of **6a–c** and **7a–c**. Reagents and conditions: (i) **3** (1.0 equiv), $ArB(OH)_2$ (1.0 equiv), $Pd(PPh_3)_4$ (3 mol %), KF (3.0 equiv), 1,4-dioxane, 50 °C, 4 h; (ii) **3** (1.0 equiv), $ArB(OH)_2$ (2.0 equiv), $Pd(PPh_3)_4$ (3 mol %), KF (6.0 equiv), 1,4-dioxane, 80 °C, 4–6 h.

In earlier reports it was observed that the catalyst source, ligand, and solvent, had a direct role on the selectivity for an aryl chloride in preference to an aryl triflate.[14,15] The competition of C—Cl versus C—OTf functionalization and the reversal of selectivity in Pd cross-coupling in polar solvents have been investigated using a combination of computational and experimental studies.[16] The reactivity in a polar solvent is consistent with anionic Pd(0) and in a nonpolar solvent with neutral Pd(0) catalysis.[16b] It is believed that a polar solvent might stabilize the oxidative addition transition state to C—OTf more strongly than for C—Cl and the actual active catalytic species differs in a polar solvent.[17] However, based on our initial consideration of steric hindrance, selectivity for the cross-coupling due to the increased size of the substituents can cause differentiation, and indeed, this was observed. For the symmetrical framework, a general selectivity mode is not apparent. The use of KF as base and purging the reaction mixture with argon for 10–15 min have significant advantages over the previous procedures, particularly regarding the sensitive 1,4 bistriflate core, which would otherwise be labile under prolonged exposure to basic conditions and where the optimal procedures for chemoselective Suzuki–Miyaura coupling are ineffective.[18]

In addition to the Suzuki–Miyaura reaction, we also explored the Sonogashira coupling reaction (Scheme 4). The product distribution of Sonogashira reactions is not necessarily the same as the Suzuki–Miyaura coupling reaction of the same substrates and the degree of selectivity of Sonogashira reactions is not predictable based on the results of the analogous Suzuki reactions. In Pd-catalyzed Suzuki couplings, the outcome of competition between aryl halides and aryl triflates varies with the nucleophilic partner; R–B species generally follow a different pattern from other R–M species.[19] The results obtained using 2.2 equiv of trimethylsilylacetylene were in line with that observed for Suzuki–Miyaura coupling. Our study found that the $Pd(PPh_3)_4/CuI/Et_3N$ in a THF system furnished 1,4-diethynyltrimethylsilyl-2,3-dichloronaphthalene product **8** in 72% yield.



Scheme 4. Synthesis of **8**. Reagents and conditions: (i) **3** (1.0 equiv), trimethylsilylacetylene (2.2 equiv), $Pd(PPh_3)_4$ (3 mol %), dry CuI (3 mol %) Et_3N (2.0 equiv), THF, 40–50 °C, 2–3 h.

In conclusion, we have reported a highly chemoselective and regioselective palladium-catalyzed Suzuki–Miyaura and Sonogashira coupling reactions of 2,3-dichloronaphthalene-1,4-bistriflate. These controllable coupling reactions proceeded with excellent chemoselectivity in favor of the triflate groups and afforded a variety of diversified, mono-, di-, and 1,2,3,4-tetraphenylnaphthalene structures.

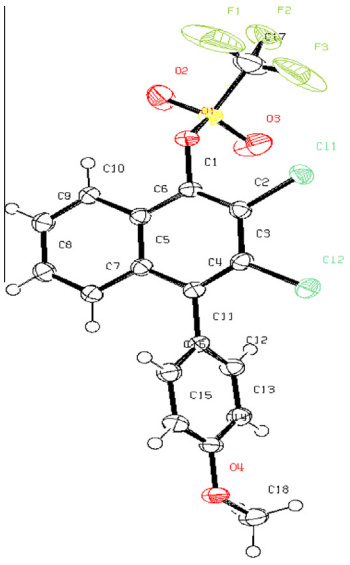


Figure 2. Crystal structure of **6a**.

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Supplementary data

Supplementary data (experimental procedures, and spectral/characterization data) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.11.013.

References and notes

1. (a) Nakao, Y.; Hiyama, T. *Chem. Rev.* **2011**, *105*, 4893; (b) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417; (c) Denmark, S.; Regens, C. *Acc. Chem. Res.* **2008**, *41*, 1486.
2. (a) Perez, H. F.; Etayo, P.; Panossian, A.; Ferran, A. V. *Chem. Rev.* **2011**, *111*, 2119; van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Claver, C.; Pamies, O.; Dieguez, D. *Chem. Rev.* **2011**, *111*, 2077; (b) Gregory, C. Fu *Acc. Chem. Res.* **2008**, *41*, 1555; (c) Martin, R.; Buchwald, S. *Acc. Chem. Res.* **2008**, *41*, 1461; (d) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125.
3. (a) Netherton, M. R.; Fu, G. C. *Top. Organomet. Chem.* **2005**, *14*, 85108; (b) Organ, M. G.; Chass, G. A.; Fang, D.-C.; Hopkinson, A. C.; Valente, C. *Synthesis* **2008**, 2776; (c) Valente, C.; Belowich, M. E.; Hadei, N.; Organ, M. G. *Eur. J. Org. Chem.* **2010**, 4343; (d) Glorius, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 8347; (e) Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525; (f) Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674; (g) Sherry, B. D.; Furstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500; (h) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1435; (i) Phapale, V. B.; Cardenas, D. J. *Chem. Soc. Rev.* **2009**, *38*, 1598; (j) Rudolph; Lautens, A. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656.
4. (a) Sellars, J. D.; Steel, P. G. *Chem. Soc. Rev.* **2011**, *40*, 5170; (b) Anbarasan, P.; Schareina, T.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 5049; (c) Kambe, N.; Iwasaki, N.; Terao, J. *Chem. Soc. Rev.* **2011**, *40*, 4937; (d) Chau, M. S.; Kwong, F. Y. *Chem. Soc. Rev.* **2011**, *40*, 4963; (e) Anderson, K. W.; Mendez-Perez, M.; Priego, J.; Buchwald, S. L. *J. Org. Chem.* **2003**, *68*, 9563; (f) Badone, D.; Cecchi, R.; Guzzi, U. *J. Org. Chem.* **1992**, *57*, 6321; (g) Roth, G. P.; Fuller, C. E. *J. Org. Chem.* **1991**, *56*, 3493.
5. (a) Rossi, R.; Bellina, F.; Lessi, M. *Adv. Synth. Catal.* **2012**, *354*, 1181; (b) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283; (c) Schroter, S.; Stock, C.; Bach, B. *Tetrahedron* **2005**, *61*, 2245; (d) Hassan, Z.; Patonay, T.; Langer, P. *Synlett* **2013**, 412; (e) Farlamb, I. S. *Chem. Soc. Rev.* **2007**, *36*, 1036; (f) Wang, J.-R.; Manabe, K. *Synthesis* **2009**, 1405; (g) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem.*,

Int. Ed. **2005**, *44*, 4442; (h) Furstner, A.; Weintritt, H. *J. Am. Chem. Soc.* **1998**, *120*, 2817; (i) Furstner, A.; Gastner, T.; Weintritt, H. *J. Org. Chem.* **1999**, *64*, 2361.
6. Kertesz, M.; Choi, C. H.; Yang, S. *Chem. Rev.* **2005**, *105*, 3448.
7. Kaye, S.; Fox, J. M.; Hicks, F. A.; Buchwald, S. L. *Adv. Synth. Catal.* **2001**, *343*, 789.
8. Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.
9. (a) Ritter, K. *Synthesis* **1993**, 735.
10. Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.
11. (a) Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 2867; (b) Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2009**, *11*, 5198; (c) Signorelli, P.; Ghidoni, R. *J. Nutr. Biochem.* **2005**, *16*, 449; (d) Viswanathan, G. S.; Wang, M.; Li, C. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 2138; (e) Koziki, B.; Burgie, Z. J.; Sepiot, J. J.; Wilamowski, J.; Kuczynski, M.; Góra1, M. *Environ. Biotechnol.* **2006**, 20; (f) Dai, J.; Liu, Y.; Zhou, Y.-D.; Nagle, D. G. *J. Nat. Prod.* **2007**, *70*, 1824; (g) Brasholz, M.; Sorgel, S.; Azap, C.; Reissig, H.-U. *Eur. J. Org. Chem.* **2007**, 3801.
12. (a) Hassan, Z.; Ullah, I.; Ali, I.; Knepper, I.; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron* **2013**, *69*, 460; (b) Best, W. M.; Sims, C. G.; Winslade, M. *Aust. J. Chem.* **2001**, *54*, 401.
13. (a) Husain, A. M.; Schätzle, M. A.; Ludeke, S.; Müller, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 9806; (b) Warren, J. J.; Tronic, A. T.; Mayer, J. M. *Chem. Rev.* **2010**, *110*, 6961.
14. Littke, A. F.; Dai, C. Y.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020.
15. For reviews, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147; (c) Miyaura, N. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; ; JAI: London, 1998; Vol. 6, pp 187–243; (d) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998. Chapter 2; (e) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263.
16. (a) Proutiere, F.; Schoenebeck, F. *Synlett* **2012**, 645; (b) Proutiere, F.; Schoenebeck, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 8192.
17. (a) Cramer, C. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2009**, *11*, 10757; (b) Anstaett, P.; Schoenebeck, F. *Chem. Eur. J.* **2011**, *17*, 12340.
18. (a) Hassan, Z.; Hussain, M.; Villinger, A.; Langer, P. *Tetrahedron* **2012**, *68*, 6305; (b) Hassan, Z.; Hussain, M.; Langer, P. *Synlett* **2011**, 1827.
19. Espino, G.; Kurbangalieva, A.; Brown, J. M. *Chem. Commun.* **2007**, 1742.
20. CCDC 1434114 and CCDC 1434115 contain all crystallographic details reported in this Letter for the structures **3** and **6a** and are available at www.ccdc.cam.ac.uk/conts/retrieving.html.