JOC Article

Application of Silicon-Based Cross-Coupling Technology to Triflates

Shaundra Riggleman and Philip DeShong*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742

pd10@umail.umd.edu

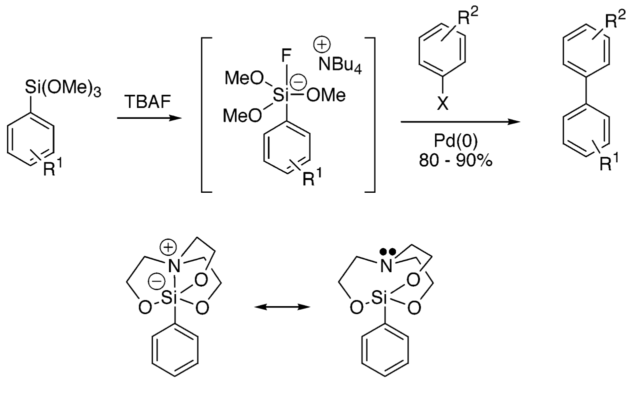
Received June 11, 2003

Aryl silatranes undergo fluoride-induced cross-coupling with aryl triflates to provide unsymmetrical biaryl derivatives in good to excellent yields. Silatranes also couple with aryl iodides and bromides, although the yields of adduct are lower than with the corresponding siloxane derivates. Aryl siloxanes (which had previously failed to couple with triflates) can be employed for triflate couplings using the Denmark modification, although the yields are lower than the corresponding silatrane reactions.

Introduction

Organosilicon reagents have played an increasingly important role in Pd(0)-catalyzed cross-coupling with organohalides.[1−18] Our laboratory has developed the Pd(0)-catalyzed fluoride-promoted reaction of aryl halides with aryl siloxanes. This methodology tolerates electron-deficient, electron-rich, and ortho-substituted systems to provide the unsymmetrical biaryl adduct in good to excellent yields (Scheme 1).[19,20]

SCHEME 1



1

While siloxanes undergo cross-coupling with aryl halides in excellent yields, they failed to efficiently couple with aryl triflates.[21] When phenyltrimethoxysilane was cross-coupled with an aryl triflate, the major product was the result of hydrolysis of the aryl triflate. The goal of this research was to explore the possibility of using phenylsilatrane as a cross-coupling reagent with aryl triflates, which are often more accessible than the halide derivatives.

It was initially thought that phenylsilatrane (**1**) would be adequately hypervalent to transfer its phenyl group without the need for activation by fluoride because silatrane and its derivatives constitute a class of formally pentacoordinate silicon compounds by virtue of the transannular Si−N bond.[22−24] One of the benefits of the silatrane derivatives is they have been found to be stable under standard hydrolysis and alcoholysis conditions.[25−28] Also, they are crystalline solids, do not polymerize, are

---

* To whom correspondence should be addressed. Tel: 301-405-1892. Fax: 301-314-9121.

[1] Hirabayashi, K.; Mori, A.; Kawashima, J.; Suguro, M.; Nishihara, Y.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 5342−5349.

[2] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483.

[3] Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359−1469.

[4] Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 421−453.

[5] Shibata, K.; Miyazawa, K.; Goto, Y. *Chem. Commun.* **1997**, 1309−1310.

[6] Kira, M.; Zhang, L. C. In *Chemistry of Hypervalent Compounds*; Akiba, K.-Y., Ed.; Wiley-VCH: New York, 1999; pp 147−169.

[7] Stille, J. K.; Echavarren, A. M.; Williams, R. M.; Hendrix, J. A. *Org. Synth.* **1993**, *71*, 97−106.

[8] Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051−6054.

[9] Ito, H.; Hosomi, A. *J. Synth. Org. Chem. Jpn.* **2000**, *58*, 274−284 and references therein.

[10] Hosomi, A.; Kohra, S.; Tominaga, Y. *Chem. Pharm. Bull.* **1988**, *36*, 4622−4625 and references therein.

[11] Hosomi, A.; Hayashida, H.; Tominaga, Y. *J. Org. Chem.* **1989**, *54*, 3254−3256.

[12] Denmark, S. E.; Pan, W. *Org. Lett.* **2001**, *3*, 61−64.

[13] Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317−1350.

[14] Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448.

[15] Denmark, S. E.; Pan, W. *Org. Lett.* **2003**, *5*, 1119−1122.

[16] Mateo, C.; Fernandez-Rivas, C.; Cardenas, D. J.; Echavarren, A. M. *Organometallics* **1998**, *17*, 3661−3669.

[17] Babudri, F.; Farinola, G. M.; Naso, F.; Panessa, D. *J. Org. Chem.* **2000**, *65*, 1554−1557.

[18] Hiyama, T.; Shirakawa, E. In *Cross-Coupling Reactions*; Miyaura, N., Ed.; Springer-Verlag: Berlin, 2002; Vol. 219, pp 61−85.

[19] Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3266−3270.

[20] Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 1684−1688.

[21] Mowery, M. E. PhD, University of Maryland College Park, 2000.

[22] Frye, C. L.; Vogel, G. E.; Hall, J. A. *J. Am. Chem. Soc.* **1961**, *83*, 996−997.

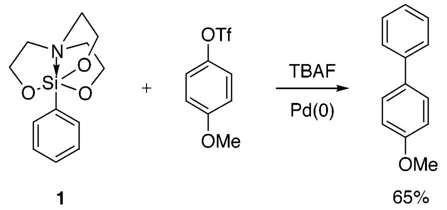
[23] Frye, C. L.; Vincent, G. A.; Finzel, W. A. *J. Am. Chem. Soc.* **1971**, *93*, 6805−6811.

[24] Turley, J. W.; Boer, F. P. *J. Am. Chem. Soc.* **1968**, *90*, 4026−4030.

[25] Verkade, J. G. *Coord. Chem. Rev.* **1994**, *137*, 233−295.

10.1021/jo034809g CCC: $25.00

SCHEME 2



stable at room temperature, and are easily prepared from their siloxane precursors. The most common method for synthesis of aryl silatranes is the alcoholysis of the corresponding trialkoxysilane by triethanolamine, which leads to the exclusive formation of crystalline monomeric product in excellent yield.[22,23] In turn, the siloxane precursors for the synthesis of silatrane derivatives can be easily prepared using either a palladium(0) or rhodium(I) catalyst.[29−31]

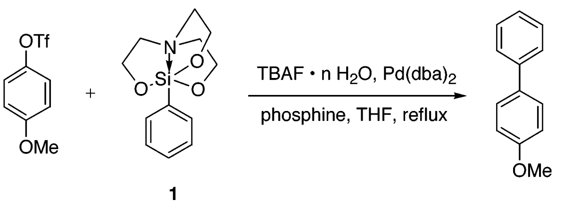
The initial studies involving phenylsilatrane as a phenyl-transfer agent revealed that the dative bond in this pentacoordinate silicon system was not sufficient to promote transfer of phenyl. However, with TBAF activation, phenylsilatrane was found to couple with aryl triflates (Scheme 2).

Recently, Denmark reported that the addition of water to his silanol coupling reactions would slow the rate of triflate hydrolysis, enabling a higher yield of coupled product.[32] The original reaction conditions for couplings utilized TBAF as a 1 M solution with a 3:1 mole ratio of H_2O to TBAF (Table 1, entry 1). In an attempt to increase the yield of coupled product, the amount of water in the TBAF solution was increased. Table 1 describes the results of varying first the amount of water added and then changing the phosphine ligand.

Upon addition of 20 equiv of water to 1 equiv of TBAF to the coupling medium, no hydrolyzed product was detected (Table 1, entry 3) and an excellent yield of the coupled adduct was obtained. Entries 1 and 2 showed less than 10% hydrolyzed product, and addition of water did not affect reaction time until after 30 equiv of water had been added as seen in entry 4.

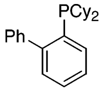
Assorted phosphines were surveyed as additives in the coupling reaction (Table 1**,** entries 5−7). On the basis of the results summarized in Table 1, the optimal reaction conditions for coupling of 4-methoxyphenyl triflate were 20:1 H_2O/TBAF and the use of the Buchwald ligand (**2**) (Table 1, entry 3).[33−35]

TABLE 1. Optimization of the Coupling of 4-Methoxyphenyl Triflate with Phenylsilatrane

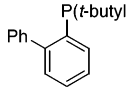


entry	n^a	phosphine	time (h)	yield (%)
1	3	**2**	12	65
2	10	**2**	12	83
3	20	**2**	12	90
4	30	**2**	24	93
5	20	**3**	24	35
6	20	PPh_3	48	<5^b
7	20	P(*o*-tol)$_3$	48	<5^c

[a] Hydrated levels of TBAF were made by premixing appropriate amounts of water with the TBAF·3 H_2O. [b] 85% starting material recovered. [c] 80% starting material recovered.

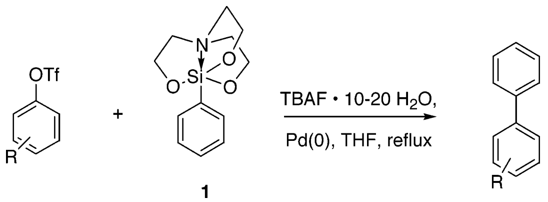


2



3

TABLE 2. Coupling of Phenylsilatrane with Aryl Triflates[a,b]



entry	R	time (h)	yield (%)
1	4-OMe	12	90
2	2-OMe	12	90
3	2,3-dimethoxy	12	73
4	2,6-dimethoxy	48	0^{c,d}
5	4-H	12	75
6	4-Me	12	87
7	4-NO_2	1	50^d
8	4-Ac	1	56^d
9	4-CO_2Me	1	21^d

[a] Hydrated levels of TBAF were made by premixing appropriate amounts of water with the TBAF·3H_2O. [b] Conditions for entries 1−5 utilized 20 equiv of H_2O and 2-(dicyclohexylphosphino)biphenyl; entries 6−8 utilized 10 equiv of H_2O and PPh_3. [c] 56% starting material recovered. [d] Mass balance was hydrolyzed triflate.

After optimization of the coupling of phenylsilatrane with 4-methoxyphenyl triflate, other triflate substrates were investigated (Table 2). Interestingly, an electron-donating ortho substituent on the aryl triflate ring did not affect the coupling reaction (Table 2, entries 2 and 3). Unfortunately, the sterically hindered 2,6-dimethoxyphenyl triflate does not couple with phenylsilatrane. Presumably, it is unable to undergo oxidative addition with the Pd(0) catalyst. Aryl substrates bearing strong electron-donating groups gave the best yields, although weaker donating groups also gave good yields of adduct (Table 2, entries 5 and 6). We also saw efficient coupling with 1-naphthalene triflate (68%). With electron-deficient aryl triflates, (Table 2, entries 7−9), the yields were lower

---

(26) Garant, R. J.; Daniels, L. M.; Das, S. K.; Janakiraman, M. N.; Jacobson, R. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1991**, *113*, 5728−5735.

(27) Sidorkin, S. F.; Pestunovich, V. A.; Voronkov, M. G. *Russ. Chem. Rev. Engl. Transl.* **1980**, *49*, 414−427.

(28) Yoshikawa, A.; Gordon, M. S.; Sidorkin, V. F.; Pestunovich, V. A. *Organometallics* **2001**, *20*, 927−931.

(29) Murata, M.; Suzuki, K.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, *62*, 8569−8571.

(30) Manoso, A. S.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449−7455.

(31) Murata, M.; Shimazaki, R.; Watanabe, S.; Masuda, Y. *Synthesis* **2001**, 2231−2233.

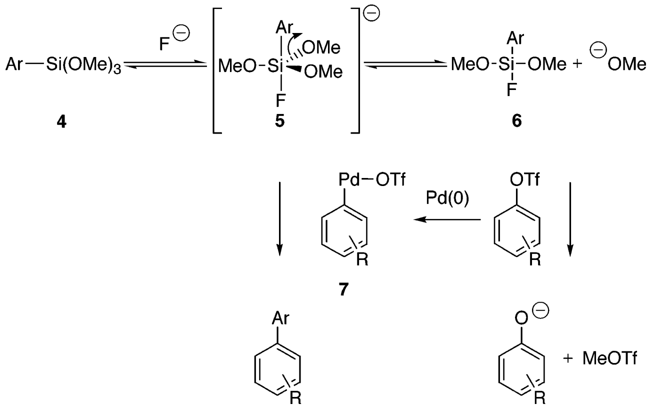
(32) Denmark, S. E.; Sweis, R. F. *Org. Lett.* **2002**, *4*, 3771−3774.

(33) Torraca, K. E.; Kuwabe, S. I.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12907−12908.

(34) Harris, M. C.; Huang, X.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 2885−2888.

(35) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369−4378.

SCHEME 3



SCHEME 4

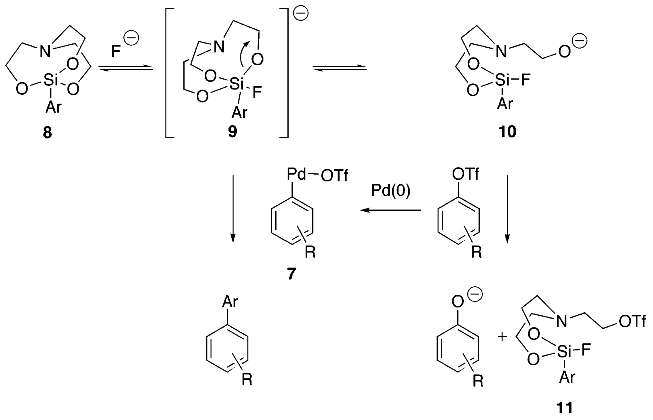
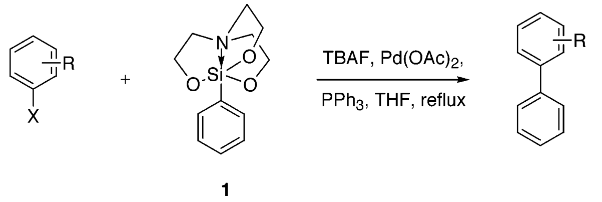


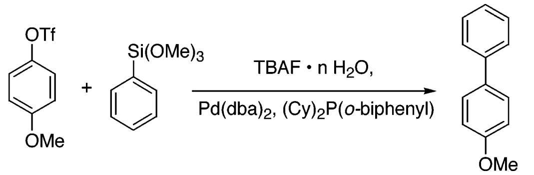
TABLE 3. Phenylsilatrane Coupling with Aryl Halides



entry	X	R	yield (%) (siloxane yields^a (%))
1	I	4-acetyl	80 (77^b)
2	I	4-methoxy	78 (91^b)
3	Br	4-acetyl	71 (86^a)
4	Br	4-methoxy	73 (74^a)
5	Br	2,6-dimethyl	65 (85^a)

[a] Results of the reaction with phenyltrimethoxysilane as reported by Mowery and DeShong: Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137−2140. [b] Results of the reaction with phenyltrimethoxysilane using the method of Mowery and DeShong: Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137−2140.

TABLE 4. Coupling 4-Methoxyphenyl Triflate with Phenyltrimethoxysilane



entry	n^a	time (h)	yield (%)
1	0^b	12	<10^c
2	3	12	36^c
3	10	12	53^c
4	20	12	79
5	30	24	72

[a] Hydrated levels of TBAF were made by premixing appropriate amounts of water with the TBAF$\cdot$3H_2O. [b] Using "anhydrous" TBAF solutions purchased from Acros (contains <5% water). Results from Mowery and DeShong, ref 21. [d] Mass balance was hydrolyzed triflate.

due to competing hydrolysis of aryl triflate. It is noteworthy that the rate of hydrolysis of the triflates in these instances is faster than the rate of the cross-coupling reaction.

There are two main strategies in dealing with the hydrolysis of the aryl triflate: (1) the use of silatrane derivates to decrease hydrolyzed triflate and (2) the use of water to control the rate of hydrolysis. We propose that hydrolysis of the aryl triflate occurs via the mechanism described in Scheme 3. First, the siloxane **4** undergoes hypervalent silicate formation with fluoride to give silicate **5**. Presumably, silicate **5** is in equilibrium with silyl fluoride **6** and methoxide, and it is the alkoxide that is responsible for hydrolysis of the aryl triflate. If the rate of hydrolysis of the triflate is faster than either aryl transfer of silicate **5** to aryl palladium intermediate **7** or the rate of oxidative addition of Pd(0) into the triflate, then hydrolysis of the triflate will occur faster than oxidative addition and cross-coupling. The goal was to inhibit hydrolysis either by decreasing the effective concentration of methoxide or by decreasing the rate of triflate hydrolysis.

One effective tactic to accomplish this goal was to employ silatrane **8** rather than siloxane reagents. The rate of hydrolysis of the triflate substrate was dramatically reduced when using phenylsilatrane. Fluoride addition to silatrane **8** gave silicate **9** which can undergo alkoxide loss (**10** in Scheme 4). Unlike the situation with siloxane reagents, however, the effective concentration of compound **10** is low because of the intramolecular (unimolecular) return to silicate. The bimolecular hydrolysis reaction becomes less competitive. The end result is that the rate of coupling exceeds the rate of hydrolysis.

Having demonstrated that aryl triflates underwent coupling with phenylsilatrane, aryl halides were also coupled to phenylsilatrane (Table 3). As with phenyltrimethoxysilane, phenylsilatrane gives higher yields with aryl iodides (Table 3, entries 1 and 2) than with aryl bromides (Table 3, entries 3−5). Electron-withdrawing and -donating groups did not greatly effect the reactivity of iodides or bromides. Entry 5 is particularly noteworthy, demonstrating that phenylsilatrane will couple with ortho-ortho hindered systems. Phenylsilatrane does not couple well with aryl chlorides (0−30%).

Previously, we had reported that aryl triflates were not viable substrates for coupling with siloxanes due to rapid hydrolysis of the triflate under the coupling conditions.[21] However, by adding excess water to the reaction mixture as noted by Denmark,[32] hydrolysis of the triflate was dramatically suppressed and the coupling of the siloxane derivatives proceeded in good yields as summarized in Table 4. In entry 4, Table 4, no hydrolysis of starting material was observed with 20 equiv of water in the

TBAF solution, while there was significant hydrolysis of the triflate with lesser amounts of water in the reaction media.

In conclusion, phenylsilatrane has been shown to undergo palladium-catalyzed cross-coupling with aryl triflates and halides to give unsymmetrical biaryls in good yields. Phenylsilatrane has been found to be stable to standard hydrolysis and alcoholysis conditions.[25−28] Also, it is a crystalline solid, does not polymerize, is stable at room temperature, and is easily prepared from the commercially available phenyltrimethoxysilane precursor. Addition of water to the reaction medium was observed to increase the yields of the coupled adduct and enabled the parent siloxane derivative to couple with aryl triflates in good yield.

Acknowledgment. We thank Dr. Yiu-Fai Lam for his assistance in obtaining NMR spectra. The generous financial support of the National Institutes of Health (CA 82169-01) is acknowledged.

Supporting Information Available: Experimental procedures and ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO034809G