Cross-Coupling Reactions of Hypervalent Siloxane Derivatives: An Alternative to Stille and Suzuki Couplings†

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Palladium-catalyzed cross-coupling of phenyl, vinyl, and allyl siloxane derivatives proceeded in good to excellent yield with aryl iodides, electron-deficient aryl bromides, and allylic benzoates. Methyl and 2,2,2-trifluoroethyl siloxane derivatives can be employed in the coupling reaction. Electron-donating and -withdrawing groups are tolerated on the aryl halide without affecting the coupling. The scope and limitations of this alternative to Stille and Suzuki couplings is outlined.

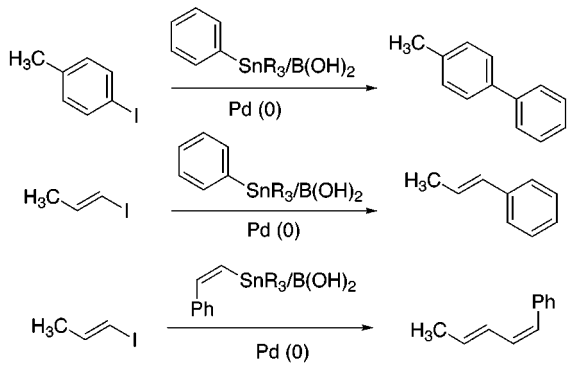
Introduction

Palladium-catalyzed cross-coupling reactions are versatile methods for the synthesis of carbon−carbon bonds in either a catalytic or a stoichiometric manner.[1] The Stille and Suzuki coupling protocols have achieved prominence because of the high yields, tolerance for functional groups, and excellent stereochemistry that is observed (Scheme 1).[1−3] However, there are serious limitations associated with each of these processes. In the Stille coupling, toxic tin(IV) substrates are used, and multiple equivalents of the tin reagent are required. Subsequently, the removal of tin byproducts poses a problem.

Although the Stille methodology is powerful, it has largely been supplanted by the Suzuki coupling technology, in which tin reagents have been replaced by boronic acid derivatives. As outlined in Scheme 1, Suzuki coupling between an aryl iodide and a boronic acid in the presence of Pd(0) results in formation of the cross-coupled product in excellent yield. However, this methodology is also limited by the availability of boronic acid derivatives.[4]

We chose to employ silicon reagents in our cross-coupling protocol for several reasons. One advantage of this approach over the Stille methodology is that it replaces the toxic tin reagents with environmentally benign silicon compounds.[5] Also, unlike the boronic acid derivatives employed in Suzuki couplings, silicon reagents are readily prepared by a variety of methods and are stable to many of the reaction conditions employed in organic synthesis.[5] The silicon activating group, unlike a boronic acid functionality, can be carried through several synthetic transformations prior to activation for coupling. Hiyama and Hatanaka have developed Pd-catalyzed, fluoride-promoted cross-coupling reactions of organohalosilanes with alkenyl- and aryl-substituted halides and triflates.[6,7] Typically, the organohalosilanes employed include alkenyl or aryl fluorosilanes. Although some of the organohalosilanes are commercially available, most have to be prepared using several different methodologies which often require multistep procedures and/or employ the use of caustic reagents.[6,7] Also, the major limitation of the Hiyama/Hatanaka protocol is the

Scheme 1



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† This manuscript is dedicated to the memory of George H. Büchi.

(1) (a) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Eds.; Pergamon: Oxford, 1982; Vol. 8, pp 799−938.(b) Tamao, K. *Ibid*. Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 435-480. (c) Knight, D. W. *Ibid*. Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 481−578. (d) Tsuji, T. *Palladium Reagents and Catalysis*; John Wiley & Sons: New York, 1985.

(2) (a) Stille, J. K.; Echavarren, A. M.; Williams, R. M.; Hendrix, J. A. *Org. Synth*. **1992**, *71*, 97−106 and references therein. (b) Del Valle, L.; Stille, J. K.; Hegedus, L. S. *J. Org. Chem*. **1990**, *55*, 3019−3023. (c) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc*. **1987**, *109*, 5478−5486. (d) Stille, J. K.; Groh, B. L. *Ibid*. **1987**, *109*, 813−817. (e) Stille, J. K. *Angew. Chem., Int. Ed. Engl*. **1986**, *25*, 508−524. (f) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc*. **1986**, *108*, 3033−3040. (g) Stille, J. K. *Pure Appl. Chem*. **1985**, *57*, 1771−1780.

(3) (a) Kalivretenos, A.; Stille, J. K.; Hegedus, L. S. *J. Org. Chem*. **1991**, *56*, 2883−2894 and references cited therein. (b) Gyorkos, A. C.; Stille, J. K.; Hegedus, L. S. *J. Am. Chem. Soc*. **1990**, *112*, 8465−8472. (c) Stille, J. K.; Sweet, M. P. *Tetrahedron Lett*. **1989**, *30*, 3645−3648.

(4) Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457−2483.

(5) Siloxanes have been widely used industrially in the production of fluids, resins, elastomers, rubbers, polymers, and miscellaneous products. Because many siloxane polymers are readily prepared by hydrolysis of functionalized siloxane monomers, the preparation of these monomers is well-developed. For more information, see: (a) Freeman, G. G. *Silicones: An Introduction to Their Chemistry and Applications*; The Chapel River Press Ltd.: Andover, Hants, England, 1962; pp 1−21 and 105−110. (b) Mehrotra, R. C. In *Chemistry and Technology of Silicon and Tin*; Kumar Das, V. G., Weng, N. G., Gielen, M., Eds.; Oxford University Press: New York, 1992; pp 93−109. For information regarding toxicology studies of silicone products, see: (c) Freeman, G. G. *Silicones: An Introduction to Their Chemistry and Applications*; The Chapel River Press Ltd.: Andover, Hants, England, 1962; pp 99−104. For information regarding toxicology studies of tin reagents, see: (d) Arakawa, Y. In *Chemistry of Tin*, 2nd ed.; Smith, P. J., Ed.; Blackie Academic & Professional: London, 1998; pp 388−428. (e) Smith, P. J. *Ibid*. Smith, P. J., Ed.; Blackie Academic & Professional: London, 1998; pp 429−441. (f) Aldridge, W. N. In *Chemistry and Technology of Silicon and Tin*; Kumar Das, V. G., Weng, N. G., Gielen, M., Eds.; Oxford University Press: New York, 1992; pp 78−92.

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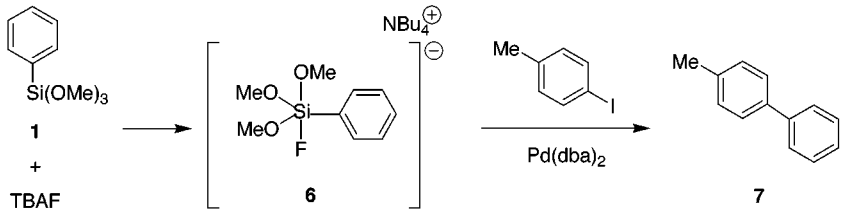
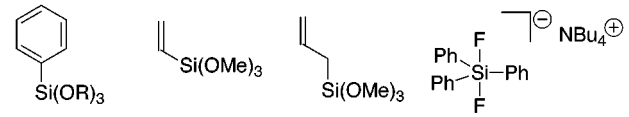
Scheme 2



requirement for the use of hydrolytically unstable and strongly Lewis acidic silyl fluoride derivatives.

In this paper, we report that siloxane derivatives such as **1**−**4** are substrates for Pd(0)-catalyzed coupling reactions with allylic alcohol and aryl derivatives affording cross-coupling products in high yields. Our results complement those of Tamao[8] and Shibata[9] that have been recently reported.



Tamao and co-workers have reported that alkenyl alkoxysilanes serve as effective transmetalation reagents with alkenyl and aryl halides.[8] Interestingly, it was noted that alkenyl trialkoxysilanes were much more reactive than the corresponding alkenyl trifluorosilanes.[8] Shibata investigated the Pd-catalyzed, fluoride promoted cross-coupling of various aryl trimethoxysilanes with aryl bromides for the synthesis of liquid crystalline biaryl derivatives.[9]

Results and Discussion

Recently, studies in our laboratory demonstrated that silicate anions such tetrabutylammonium triphenyldifluorosilicate (TBAT, **5**) underwent condensation with allylic benzoates in the presence of Pd(0) catalysts to afford coupling products.[10] Subsequently, we have also shown that TBAT (**5**) underwent Pd(0)-catalyzed coupling with aryl iodides, bromides, and triflates, affording unsymmetrical biaryls in good to excellent yields.[11] The major limitation of the silicate methodology described above is that only one of the three phenyl groups of TBAT (**5**) is transferred under the coupling conditions.

In an effort to overcome this limitation, the use of silicate derivatives generated in situ was investigated. Treatment of phenyl trimethylsiloxane (**1**) with equimolar amount of tetrabutylammonium fluoride (TBAF) presumably resulted in formation of hypervalent fluorosilicate anion **6** (Scheme 2).[6,7] Silicate **6** coupled with 4-iodotoluene in the presence of a Pd(0) catalyst to afford the unsymmetrical biphenyl **7** in high yield. A survey of the coupling reaction with aryl halide derivatives is summarized in Table 1, and these results indicate that this approach is a viable alternative to the Stille and Suzuki protocols for the synthesis of unsymmetrical biaryls.

Control experiments with 4-iodotoluene and phenyltrimethylsilane (entries 1 and 2) demonstrated that silanes would not participate in the coupling reaction. Equimolar quantities of $PhSiMe_3$ and TBAF yielded only the homocoupled adduct (40%, entry 1).[12] Changing from a silane to siloxane derivative was postulated to favor formation of the hypervalent silicate anion (i.e., **6**) and subsequent transmetalation to palladium would occur.[13] The control experiment employing $PhSi(OMe)_3$ and no TBAF gave only starting material (entry 3). Adding an equimolar amount of TBAF to siloxane **1**, presumably with formation of silicate anion **6** in situ, gave 90% of the heterocoupled product (entry 4).

The cross-coupling reaction of siloxanes appears to be insensitive to the reaction conditions. Changing the catalyst from ($Pd(dba)_2$) to allyl palladium chloride dimer (APC) gave a marginally lower yield (85%, entry 5). Similarly, replacing dimethylformamide (DMF) with tetrahydrofuran (THF) (entry 6) gave a higher yield (94% vs 90%) of the cross-coupling product, but 6% of the homocoupled product, which was not observed in the reactions performed in DMF, was also obtained in the

(6) For recent reviews on organosilicon compounds and cross-coupling reactions, see: (a) Hiyama, T. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley−VCH: Weinhein, Germany, 1998; pp 421−452. (b) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317−1350. (c) Hiyama, T.; Hatanaka, Y. Pure *Appl. Chem.* **1994**, *66*, 1417−1478. (d) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1317−1448. (e) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845−853.

(7) For information about Pd-catalyzed, fluoride promoted cross-coupling reactions of reactions of organohalosilanes with aryl and alkenyl-halides see: (a) Gouda, K.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232−7233. (b) Hatanaka, Y.; Goda, K.; Okahara, Y.; Hiyama, T. *Tetrahedron* **1994,** *50*, 8301−8316. (c) Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Heterocycles* **1990**, *30*, 303−306. (d) Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Chem. Lett.* **1989**, 1711−1714. For information about alkylation of aryl halides with alkyltrifluorosilanes, see: (e) Matsuhashi, H.; Asai, S.; Hirabayashi, K.; Hatanaka, Y.; Mori, A. Hiyama, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 437−444. (f) Matsuhashi, H.; Kuroboshi, M.; Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1994**, *35*, 6507−6510. For information about Pd-catalyzed, NaOH-promoted reactions of organochlorosilanes with aryl chlorides, see: (g) Hagiwara, E.; Gouda, K.; Hatanaka, Y.; Hiyama, T. Tetrahedron *Lett.* **1997**, *38*, 439- 442.

(8) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051−6064 and references cited therein.

(9) Shibata, K.; Miyazawa, K.; Goto, Y. *Chem. Commun.* **1997**, 1309−1310.

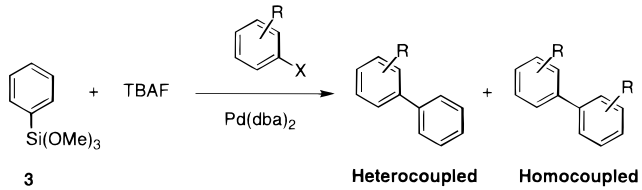
(10) Brescia, M.-R.; DeShong, P. *J. Org. Chem.* **1998**, *63*, 3156−3157. See also ref 7. For other papers relating to the application of hypervalent silicates as reagents, see: (a) Pilcher, A. S.; DeShong, P. *J. Org. Chem.* **1996**, *61*, 6901−6905. (b) Pilcher, A. S.; Ammon, H. L.; DeShong, P. *J. Am. Chem. Soc.* **1995**, *117*, 5166−5167. (c) Pilcher, A. S.; DeShong, P. *J. Org. Chem.* **1993**, *58*, 5130−5134. (d) Pilcher, A. S.; Hill, D. K.; Waltermire, R. E.; Shimshock, S. J.; DeShong, P. *J. Org. Chem.* **1992**, *57*, 2492−2495.

(11) Mowery, M. E.; DeShong, P. Submitted for publication in *J. Org. Chem.*

(12) The mechanism of this remarkable fluoride-induced homocoupling of aryl iodides by Pd is under investigation.

(13) The presumed mechanism for these types of cross-coupling reactions is as follows: formation of the hypervalent organosilane, oxidative addition of Pd(0) to the aryl or alkyl halide, followed by transmetalation of the hypervalent organosilane to the organopalladium(II) complex. Reductive elimination then occurs, giving the cross-coupled adduct, Pd(0), and a tetravalent organosilane. The transmetalation adduct using Hiyama-type conditions was recently isolated. For more information, see: Mateo, C.; Fernandez-Rivas, C.; Echavarren, A. M.; Cardenas, D. J. *Organometallics* **1997**, *16*, 1997−1999.

Table 1. Results of Cross Coupling Reactions Using Siloxanes

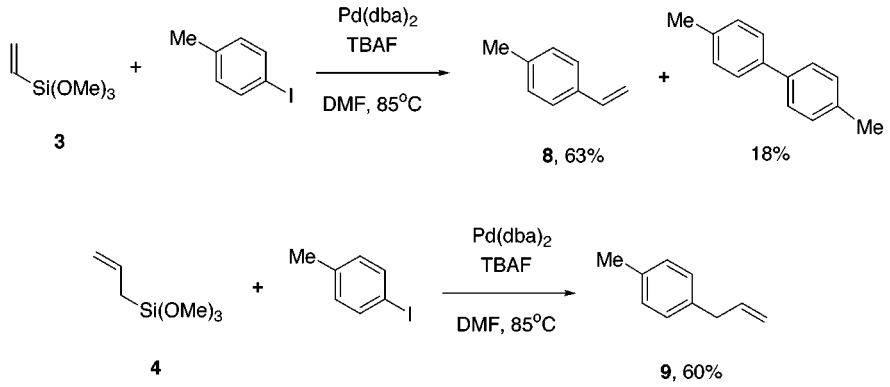


3 Heterocoupled Homocoupled

						yield[a] (%)	
entry	R	X	siloxane (equiv)	TBAF (equiv)	solvent	hetero	homo
1	4-Me	I	$PhSi(Me)_3$ (2.0)	2.0	DMF	0	40
2	4-Me	I	$PhSi(Me)_3$ (2.2)	0	DMF	0[b]	0
3	4-Me	I	$PhSi(OMe)_3$ (2.1)	0	DMF	0[c]	0
4	4-Me	I	$PhSi(OMe)_3$ (2.0)	1.9	DMF	90	trace
5	4-Me[d]	I	$PhSi(OMe)_3$ (2.2)	2.2	DMF	85	0
6	4-Me	I	$PhSi(OMe)_3$ (2.0)	1.9	THF	94	6
7	4-Me	I	$PhSi(OMe)_3$ (1.2)	1.0	DMF	80[e]	0
8	4-Ac	I	$PhSi(OMe)_3$ (2.0)	2.0	DMF	58	0
9	4-OMe	I	$PhSi(OMe)_3$ (2.5)	3.6	DMF	54	0
10	Cl	I	$PhSi(OMe)_3$ (2.2)	2.2	DMF	78	21
11	4-Ac	Br	$PhSi(OMe)_3$ (1.8)	1.8	DMF	78	0
12	4-Me	Br	$PhSi(OMe)_3$ (2.0)	2.0	DMF	0	0
13	4-OMe[f]	Br	$PhSi(OMe)_3$ (2.0)	2.0	DMF	0	34
14	4-Ac	Cl	$PhSi(OMe)_3$ (2.0)	2.0	DMF	0	0
15	4-Me	I	$PhSi(OCH_2CF_3)_3$ (2.0)	2.0	DMF	97	0
16	4-Ac	I	$PhSi(OCH_2CF_3)_3$ (2.3)	2.3	DMF	78	16
17	4-OMe	I	$PhSi(OCH_2CF_3)_3$ (2.0)	1.9	DMF	77	0
18	4-Ac[g]	Br	$PhSi(OCH_2CF_3)_3$ (1.9)	1.9	DMF	56	0

[a] Calculations are corrected for 2 equiv of starting material consumed to make the homocoupled product. Reaction times were not optimized, and most reactions were complete within 1 h or less. [b] Isolated starting material only. [c] 96% of starting material recovered. [d] 18 mol % allyl Pd chloride dimer used. [e] 20% starting material recovered. [f] GC yield; 66% of starting material recovered. [g] 26% of starting material recovered.

Scheme 3



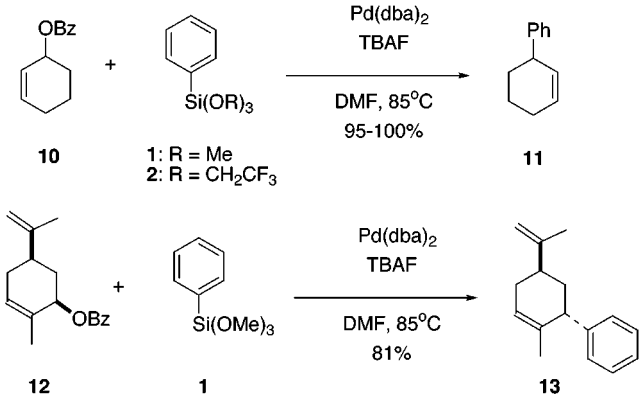
THF reactions. Finally, if siloxane **1** and TBAF were used in equimolar concentration with the iodide (entry 7), the yield of unsymmetrical biaryl decreased to 80%, with 20% of the starting material recovered.

The electronic characteristics of the aromatic substituent on the ring do not have a significant impact on the cross-coupling reactions with siloxane derivatives. As noted in entries 8−10, siloxane **1** underwent Pd-catalyzed coupling with aryl iodide derivatives bearing strongly electron-withdrawing and electron-donating substituents in yields of 58, 54, and 78%, respectively. The major difference noted in this series of reactions was that a significant quantity of the homocoupled product was obtained with the chloro analog (entry 10). A rationalization for this result is not apparent at this time but is under investigation.[12]

Aryl bromides and chlorides were less reactive than iodides in the coupling, in analogy with trends generally observed with Stille and Suzuki coupling.[1−4] Surprisingly, 4-bromoacetophenone underwent coupling with the siloxane to give the unsymmetrical biaryl even *more* efficiently than the iodo analog (entry 11). On the other hand, neither 4-bromotoluene nor 4-bromoanisole gave heterocoupled adducts in the reaction with siloxane **1** (entries 12 and 13, respectively). Last, 4-chloroacetophenone failed to react with siloxane **1** (entry 14) to give the desired heterocoupled adduct, and none of the homocoupled adduct was isolated.

Having demonstrated that phenyl trimethylsiloxane (**1**) serves as the aryl donor for cross-coupling reactions, we chose to determine whether the ether substituent of the siloxane could be employed to modulate the reaction. On the basis of the presumed intermediacy of hypervalent species **6**, an electron-withdrawing substituent was anticipated to facilitate formation of the hypervalent intermediate. Accordingly, coupling reactions of phenyl tris(2,2,2-trifluoroethyl)siloxane ($PhSi(OCH_2CF_3)_3$, **2**) were investigated. Fluoride-induced coupling of siloxane **2** with

Scheme 4



4-iodotoluene increased the yield of the heterocoupled adduct to 97% (entry 15). Similar to the results noted above, a variety of substituents on the aryl ring were tolerated by the fluorosiloxane reagent, and good to excellent yields of unsymmetrical biphenyls were obtained as summarized in entries 16−18.

The in situ generation of silicate anion (i.e., **6**) is not limited to aryl transfer. Under these conditions, vinyl trimethylsiloxane (**3**) gave 63% of the heterocoupled adduct, 4-methylstyrene (**8**), on treatment with 4-iodotoluene (Scheme 3). Also, allyl trimethylsiloxane (**4**) and 4-iodotoluene coupled to afford allyl adduct **9** in good yield.

This methodology has been extended to cross-coupling reactions between siloxanes and allylic alcohol derivatives as outlined in Scheme 4. Coupling of benzoate **10** gave a quantitative yield of 3-phenylcyclohexene (**11**) when treated with $PhSi(OMe)_3$ (**1**) and TBAF. Substituting fluorosiloxane **2** gave an equally high yield of adduct **11**. Finally, when (*R*,*R*)-*cis*-carveol benzoate (**12**) was coupled with $PhSi(OMe)_3$ and TBAF, 81% of phenylated adduct **13** was obtained (Scheme 4). As was observed with preformed silicate derivatives,[10] the cross-coupling reaction occurred with complete inversion of configuration.

Conclusion

These results summarized above conclusively demonstrate that siloxane derivatives such as **1**−**4** are versatile transmetalation reagents for Pd(0)-catalyzed cross-coupling reactions using aryl halides and allylic alcohol derivatives in moderate to excellent yield. In addition, the reaction conditions are compatible with a variety of functional groups. The scope and limitations of this methodology for the synthesis of natural products will be reported in due course.

Experimental Section

General Methods. All ^1H and ^{13}C NMR spectra were recorded on a 400 MHz instrument in $CDCl_3$ unless otherwise indicated. Coupling constants (*J*) are given in Hz. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl. Pyridine and methylene chloride (CH_2Cl_2) were distilled from calcium hydride. Dimethyl formamide (DMF) was distilled from molecular sieves. Methanol (MeOH) was dried and stored over molecular sieves. Glassware used in the reactions was dried overnight in an oven at 120 °C. All reactions were performed under an atmosphere of nitrogen unless noted otherwise.

Allyl palladium chloride dimer, allyl trimethoxysilane (**4**), phenyl trimethoxysilane (**1**), vinyl trimethoxysilane (**3**), benzoyl chloride (BzCl), (*R*)-(−)-carvone, cerium chloride heptahydrate ($CeCl_3 \cdot 7H_2O$), sodium borohydride ($NaBH_4$), all aryl iodides, all aryl bromides, and all aryl chlorides were purchased from Aldrich and used as received. Bis(dibenzylideneacetone)palladium ($Pd(dba)_2$) was purchased from Acros. Tetrabutylammonium fluoride (TBAF) was used as a 1.0 M solution in THF and is commercially available from Acros and Aldrich. Phenyl tris(trifluoroethoxy)silane (**2**) was prepared according to the literature procedure.[14] All compounds were determined to be >95% pure by GC and ^1H NMR unless otherwise noted.

Preparation of Phenyl Tris(trifluoroethoxy)silane (2). The siloxane was prepared according to the procedure of Swamy et al.:[14] bp 112−116.5 °C/20 mmHg; IR (CCl_4) 3078 (m), 3057 (m), 2957 (s), 2896 (m), 1594 (s), 1574 (s), 1533 (s), 1151 (s), 867 (s), 808 (s); ^1H NMR ($CDCl_3$) δ 4.52 (q, J = 8.1, 6H), 7.40−7.65 (m, 5H). The ^1H NMR matched spectral data found in ref 14. ^{19}F NMR and elemental analysis results are also available in ref 14.

General Procedure for the Cross-Coupling Reactions Utilizing Aryl Iodides, Bromides, and Chlorides. Entry 1. To a solution of 0.104 g (0.477 mmol) of 4-iodotoluene and 0.159 g (1.058 mmol) of phenyl trimethylsilane in 10 mL of DMF was added 25 mg (0.043 mmol) of $Pd(dba)_2$. Then 1.10 mL (1.10 mmol) of TBAF was added to the reaction mixture via syringe. The reaction mixture was degassed to remove oxygen via one freeze−pump−thaw cycle. The brown reaction was heated at 95 °C for 2 h. The resulting brown mixture was quenched by the addition of 50 mL of water; the aqueous layer was then extracted with 4 × 50 mL of Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 16 cm, pentane) gave 17 mg (40%) of 4,4′-dimethylbiphenyl. This matched an authentic sample (purchased from Aldrich) by GC and TLC.

Entry 4. 4-Methylbiphenyl (7): TLC R_f = 0.47 (10% Et_2O/pentane); mp 44.5−46.5 °C (lit.[15] mp 49 °C (EtOH)); IR (CCl_4) 3081 (w), 3063 (w), 3038 (w), 2925 (w), 2863 (w), 1556 (s), 1531 (s); ^1H NMR ($CDCl_3$) δ 2.38 (s, 3H), 7.23 (m, 2H), 7.30 (t, J = 7.6, 1H), 7.41 (t, J = 7.6, 2H), 7.48 (d, J = 8.1, 2H), 7.58 (d, J = 7.3, 2H); ^{13}C NMR ($CDCl_3$) δ 21.1, 127.0, 128.7, 129.5, 137.0, 138.4, 141.2; LRMS (EI) 169 ((M + 1), 19), 168 ((M^+), 100), 167 (63), 90 (21); HRMS (EI) calcd for $C_{13}H_{12}$ 168.0939 (M^+), found 168.0945. The IR and ^1H NMR matched spectral data found in ref 15.

Entry 8. 4-Acetylbiphenyl: TLC R_f = 0.29 (10% EtOAc/hexane); mp 119−119.5 °C (lit.[2c] mp 119−120 °C (EtOH)); IR (CCl_4) 3081 (w), 3038 (w), 3000 (w), 2931 (m), 2850 (w), 1691 (m), 1569 (s), 1538 (s); ^1H NMR ($CDCl_3$) δ 2.63 (s, 3H), 7.38 (t, J = 7.3, 1H), 7.46 (t, J = 7.4, 2H), 7.61 (d, J = 7.2, 2H), 7.67 (A of AB quartet, J_{AB} = 8.4, 2H), 8.02 (B of AB quartet, J_{AB} = 8.4, 2H); ^{13}C NMR ($CDCl_3$) δ 26.6, 127.2, 128.9, 135.9, 139.0, 145.8, 197.7; LRMS (EI) 197 ((M + 1), 10), 196 ((M^+), 59), 181 (100), 153 (35); HRMS (EI) calcd for $C_{14}H_{12}O$ 196.0888 (M^+), found 196.0883. The IR and ^1H NMR matched spectral data found in ref 2c.

Entry 9. 4-Methoxybiphenyl: TLC R_f = 0.46 (10% EtOAc/hexane); mp 83.5−85.5 °C (lit.[16] mp 90 °C (EtOH)); IR (CCl_4) 3081 (w), 3047 (w), 3006 (w), 2931 (w), 2856 (w), 2838 (w), 1563 (s), 1512 (s), 1250 (s), 1006 (m); ^1H NMR ($CDCl_3$) δ 3.83 (s, 3H), 6.95−6.97 (m, 2H), 7.40 (t, J = 7.7, 2H), 7.50−7.54 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 55.4, 114.2, 126.6, 126.7, 128.2, 128.7, 135.2; LRMS (EI) 185 ((M + 1), 15), 184 ((M^+), 100), 169 (39); HRMS (EI) calculated for $C_{13}H_{12}O$ 184.0888 (M^+), found 184.0885. The IR and ^1H NMR matched spectral data found in ref 17.

Entry 10. 4-Chlorobiphenyl: TLC R_f = 0.56 (pentane);

(14) Swamy, K. C. K.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 2341−2348.
(15) Rao, M. S. C.; Rao, G. S. K. *Synthesis* **1987**, 231−233.
(16) Neeman, M.; Caserio, M. C.; Roberts, J. D.; Johnson, W. S. *Tetrahedron* **1959**, *6*, 36−47.
(17) Lipshutz, B. H.; Siegmann, K.; Garcia, E.; Kayser, F. *J. Am. Chem. Soc.* **1993**, *115*, 9276- 9282.

mp 75−77 °C (lit.[18] mp 77−77.5 °C (MeOH/H_2O)); IR (CCl_4) 3112 (w), 3089 (w), 3032 (w), 1584 (s), 1526 (s), 1479 (s), 836 (s); ^{1}H NMR ($CDCl_3$) δ 7.33−7.56 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 127.0, 127.6, 128.4, 128.9, 139.7, 140.0; LRMS (EI) 190 ((M + 2), 32), 189 ((M + 1), 13), 188 ((M^+), 100), 152 (28); HRMS (EI) calcd for $C_{12}H_9Cl$ 188.0393 (M^+), found 188.0386. The IR and LRMS matched spectral data found in ref 18.

4-Methylstyrene (8): TLC R_f = 0.70 (pentane); IR (CCl_4) 3089 (m), 3048 (m), 3009 (s), 2962 (s), 2926 (s), 2855 (s), 1628 (m), 1570 (s), 1513 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.59 (d, J = 10.9, 1H), 2.56 (d, J = 17.6, 1H), 6.67 (dd, J = 17.5, 10.9, 1H), 7.12 (d, J = 8.0, 2H), 7.29 (d, J = 8.1, 2H); ^{13}C NMR ($CDCl_3$) δ 21.2, 112.8, 126.1, 129.2, 134.8, 136.7, 137.6; LRMS (EI) 119 ((M + 1), 11), 118 ((M^+), 100), 117 (68), 91 (42); HRMS (EI) calcd for C_9H_{10} 118.0783 (M^+), found 118.0777. The IR and ^{1}H NMR matched spectral data found in ref 19.

4-Allyltoluene (9): TLC R_f = 0.55 (pentane); IR (CCl_4) 3126 (w), 3082 (m), 3049 (s), 3005 (s), 2980 (s), 2923 (s), 2853 (m), 1639 (s), 1576 (s), 1514 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.34 (d, J = 6.7, 2H), 5.01 (t, J = 1.4, 1H), 5.06−5.10 (m, 1H), 5.88−6.02 (m, 1H), 7.04−7.20 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.0, 39.8, 115.5, 126.8, 128.4, 129.1, 135.5, 137.8; LRMS (EI) 132 ((M^+), 12), 131 (13), 117 (81), 91 (100); HRMS (EI) calcd for $C_{10}H_{12}$ 132.0939 (M^+), found 132.0940. The ^{1}H NMR matched spectral data found in ref 20.

Preparation of Allylic Alcohol Derivatives. 3-Benzoylcyclohexene (10). To a solution of 0.320 g (3.26 mmol) of 2-cyclohexen-1-ol and 0.76 mL (9.40 mmol) of pyridine in 20 mL of CH_2Cl_2 was added 1.04 mL (8.96 mmol) of benzoyl chloride via syringe. The reaction mixture was yellow with a white precipitate. The reaction was stirred at room temperature for 17 h. The reaction was quenched by the addition of 50 mL of H_2O; the aqueous layer was washed with 4 × 50 mL of Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (35 mm, 20 cm, 10% CH_2Cl_2/hexane) gave 0.635 g (99%) of 3-benzoylcyclohexene as a pale yellow oil: TLC R_f = 0.35 (10% CH_2Cl_2/hexane); IR (CCl_4) 3100 (w), 3081 (w), 3038 (w), 2931 (s), 1725 (s), 1550 (s); ^{1}H NMR ($CDCl_3$) δ 1.66−2.12 (m, 6H), 5.49 (bs, 1H), 5.79−5.83 (m, 1H), 5.97−6.01 (m, 1H), 7.41 (t, J = 7.7, 2H), 7.52 (t, J = 7.4, 1H), 8.02−8.04 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 19.0, 25.0, 28.4, 68.6, 125.8, 128.3, 129.6, 130.9, 132.7, 132.8, 166.2; LRMS (EI) 203 ((M + 1), 3), 202 ((M^+), 20), 105 (100); HRMS (EI) calcd for $C_{13}H_{14}O_2$ 202.0994 (M^+), found 202.1003. The IR, ^{1}H NMR, and ^{13}C NMR matched spectral data found in ref 21.

(+)-(*R*,*R*)-*cis*-Carveolbenzoate (12). To a solution of (*R*)-(−)-carvone and 19.269 g (51.72 mmol) of $CeCl_3 \cdot 7H_2O$ in 97 mL of anhydrous MeOH was added 2.026 g (53.56 mmol) of $NaBH_4$ via a solid addition funnel. The $NaBH_4$ was slowly added over a period of 10 min. The reaction was stirred at room temperature for 1.5 h. The reaction was quenched by the addition of 200 mL of H_2O; the aqueous layer was washed with 4 × 250 mL of Et_2O, and the combined organics were washed with 3 × 200 mL of saturated NaCl and 1 × 200 mL of H_2O. The reaction was dried over $MgSO_4$ and concentrated in vacuo. The crude product was >95% pure by GC and indicated a 32.9:1 ratio of cis/trans alcohols was present. The yield was 6.16 g (87%) of a clear oil. The ^{1}H NMR (200 MHz) matched spectral data in ref 22, so further characterization was not performed. IR and elemental analysis results are located in ref 22.

To a solution of 1.859 g (12.21 mmol) of carveol and 3.98 mL (32.26 mmol) of pyridine in 145 mL of CH_2Cl_2 was added 4.60 mL (37.00 mmol) of benzoyl chloride via syringe. The yellow reaction was stirred at room temperature for 24 h. The reaction was quenched by the addition of 200 mL of H_2O; the aqueous layer was washed with 1 × 100 mL of each of the following: 10% HCl, 10% $NaHCO_3$, saturated NaCl, and H_2O, and the extracts were dried with $MgSO_4$ and concentrated in vacuo. Purification of a 1.004 g portion of the crude material by flash chromatography (50 mm, 17 cm, 10% EtOAc/hexane) gave 0.441 g (44%) of pure (+)-(*R*,*R*)-*cis*-carveolbenzoate: TLC R_f = 0.43; $[\alpha]^{27}_D$ = +17.0 (c = 3.70, EtOH) (lit.[23b] $[\alpha]^{22}_D$ = 13.3 (c = 1.25, EtOH)). The IR and ^{1}H NMR spectra were identical to spectral data located in ref 23, so further characterization was not performed.

Cross-Coupling Reactions Utilizing Allylic Alcohol Derivatives. 3-Phenylcyclohexene (11): TLC R_f = 0.67 (10% CH_2Cl_2/hexane); IR (CCl_4) 3088 (m), 3063 (m), 3025 (s), 2938 (s), 2863 (s), 2838 (s), 1656 (w), 1606 (m), 1543 (m); ^{1}H NMR ($CDCl_3$) δ 0.85−2.09 (m, 6H), 3.38 (bs, 1H), 5.70 (dd, J = 10.0, 2.1, 1H), 5.86−5.88 (m, 1H), 7.16−7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.2, 22.7, 32.6, 41.8, 125.9, 127.7, 128.2, 128.3, 130.2, 146.6; LRMS (EI) 159 ((M + 1), 15), 158 ((M^+), 100), 143 (43), 129 (79); HRMS (EI) calcd for $C_{12}H_{14}$ 158.1096 (M^+), found 158.1098. The IR, ^{1}H NMR, ^{13}C NMR, and MS matched spectral data found in ref 24.

(*R*,*S*)-*trans*-2-Methyl-3-phenyl-5-isopropenyl-1-cyclohexene (13): TLC R_f = 0.43 (10% CH_2Cl_2/hexane). The ^{1}H NMR spectrum (200 MHz) matched spectral data from compounds made previously in the DeShong laborabory and the data are published as part of the Supporting Information in ref 10 so further characterization was not necessary.

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(18) Chikasawa, K.; Uyeta, M. *Chem. Pharm. Bull.* **1980**, *28*, 57−61.
(19) Hollywood, F.; Suschitzsky, H. *Synthesis* **1982**, 662−665.
(20) Fueno, T.; Kajimoto, O.; Izawa, K.; Masago, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1418−1421.
(21) Akermark, B.; Larsson, E. M.; Oslob, J. D. *J. Org. Chem.* **1994**, *59*, 5729−5733.
(22) Nonoshita, K.; Marvoka, K.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2241−2243.
(23) (a) Ravindranath, B.; Srinivas, P. *Ind. J. Chem.* **1984**, *23B*, 666−667. (b) Utagawa, A.; Hirota, H.; Ohno, S.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1207−212.
(24) Arnold, D. R.; Mines, S. A. *Can. J. Chem.* **1989**, *67*, 689−698.