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Rapid Fluorous Stille Coupling Reactions Conducted under Microwave Irradiation

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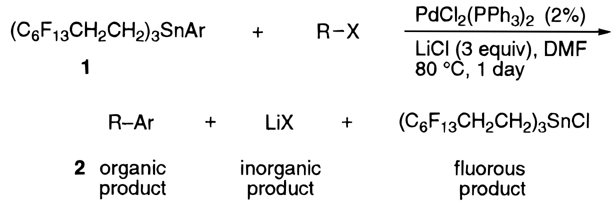
Palladium-catalyzed fluorous Stille cross-coupling reactions with organic halides or triflates require only 90−120 s for completion when conducted under microwave irradiation. Comparable thermal reactions require about 1 day. Fourteen different coupling products were synthesized and isolated in good yields after three-phase extraction (FC-84, dichloromethane, water) and chromatography. The examples extend the scope of the fluorous Stille coupling with respect to both the tin and halide/triflate components. Applications in parallel synthesis are suggested.

Introduction

Among the many examples of microwave-assisted organic reactions that have been disclosed,[1] few are transition-metal-catalyzed transformations.[2] The dramatic acceleration of reactions upon microwave irradiation has been demonstrated in the palladium-catalyzed Heck, Suzuki, and Stille reactions both on solid phase[3] and in solution.[4] Full conversions are achieved in a few minutes, and high yields of isolated coupling products are obtained.

The Heck,[5] Suzuki,[6,7] and Stille[8] reactions constitute robust and general methods for C−C bond formation and have therefore emerged as important reactions in parallel synthesis and combinatorial chemistry.[9] Recently, a modification of the Stille coupling that relies on fluorous tin reactants was introduced.[10ab] Readily available tin reactants **1** bearing 39 fluorine atoms couple with aryl halides, aryl triflates, and benzyl bromides to form products **2** in good yields. The method provides attractive features for preparative organic synthesis and promising options for liquid-phase combinatorial synthesis[11] because the organic, inorganic, and fluorous (tin-containing) products can be separated at the end of the reaction by a simple three-phase extraction with an organic solvent, water, and a fluorocarbon solvent.[10]



$$(C_6F_{13}CH_2CH_2)_3SnAr + R{-}X \xrightarrow[\text{LiCl (3 equiv), DMF, 80 °C, 1 day}]{PdCl_2(PPh_3)_2\ (2\%)} R{-}Ar + LiX + (C_6F_{13}CH_2CH_2)_3SnCl$$

Offsetting the advantages of the fluorous Stille reaction are some detractions. The long reaction times required (about 1 day at 80 °C) are a significant drawback for rapid parallel synthesis applications. More generally, all fluorous methods[10] need to come to grips with the low solubilities of fluorous compounds in many types of organic solvents, and several strategies have already been proposed.[10c,e] The microwave heating technique offers potential solutions to these problems, and we

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[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1997.

[1] (a) Mingos, D. M. P.; Baghurst, D. R. *Chem. Soc. Rev.* **1991**, *20*, 1. (b) Abramovitch, R. A. *Org. Prep. Proc. Int.* **1991**, *23*, 683. (c) Majetich, G.; Hicks, R. *J. Microwave Power Electromag. Energy* **1995**, *30*, 27. (d) Strauss, C. R.; Trainor, R. W. *Aust. J. Chem.* **1995**, *48*, 1665. (e) Caddick, S. *Tetrahedron* **1995**, *51*, 10403. For a theoretical background see also: (f) Neas, E. D.; Collins, M. J. In *Introduction to Microwave Sample Preparation*; Kingston, H. M., Jassie, L. B., Eds.; American Chemical Society: Washington, DC, 1988; p 7. The technique has also found use in the preparation of radiopharmaceuticals. See: (g) Stone-Elander, S.; Elander, N. In *Chemists' Views of Imaging Centers;* Emran, A. M., Ed.; Plenum Press: New York, 1995; p 445 and references therein.

[2] For examples of microwave-assisted transition-metal-catalyzed reactions: (a) Adámek, F.; Hájek, M. *Tetrahedron Lett.* **1992**, *33*, 2039. (b) Bose, A. K.; Banik, B. K.; Barakat, K. J.; Manhas, M. S. *Synlett* **1993**, 575. (c) Gordon, E. M.; Gaba, D. C.; Jebber, K. A.; Zacharias, D. M. *Organometallics* **1993**, *12*, 5020. (d) Leskovsek, S.; Smidovnik, A.; Koloini, T. *J. Org. Chem.* **1994**, *59*, 7433. (e) Jiang, Y.-L.; Hu, Y.-Q.; Feng, S.-Q.; Wu, J.-S.; Wu, Z.-W.; Yuan, Y.-C.; Liu, J.-M.; Hao, Q.-S.; Li, D.-P. *Synth. Commun.* **1996**, *26*, 161. (f) Kabza, K. G.; Gestwicki, J. E.; McGrath, J. L.; Petrassi, H. M. *J. Org. Chem.* **1996**, *61*, 9599.

[3] Larhed, M.; Lindeberg, G.; Hallberg, A. *Tetrahedron Lett.* **1996**, *37,* 8219.

[4] Larhed, M.; Hallberg, A. *J. Org. Chem.* **1996**, 61, 9582.

[5] For recent reviews on the Heck reaction see: (a) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. (b) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (c) Jeffery, T. *Advances in Metal−Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc: Greenwich, 1996; Vol. 5, p 153.

[6] For reviews on the Suzuki reaction see: (a) Martin, A. R.; Yang, Y. *Acta Chem. Scand.* **1993**, *47*, 221. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

[7] Very fast Suzuki coupling reactions with iodonium salts under conventional heating were recently reported: Kang, S.-K.; Lee, H.-W.; Jang, S.-B.; Ho, P.-S. *J. Org. Chem.* **1996**, 61, 4720.

[8] For reviews on the Stille reaction see: (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Michell, T. N. *Synthesis* **1992**, 803. (c) Ritter, K. *Synthesis* **1993**, 735. (d) Farina, V.; Roth, G. P. In *Advances in Metal−Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc: Greenwich, 1996; Vol. 5, p 1.

[9] (a) Thompson, L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555. (b) Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. *Tetrahedron* **1996**, *52*, 4527. (c) Balkenhohl, F.; von dem Bussche-Hünnefeld, C.; Lansky, A.; Zechel, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2289.

[10] (a) Curran, D. P.; Hoshino, M. *J. Org. Chem.* **1996**, *61*, 6480. (b) Curran, D. P.; Hoshino, M. Submitted for publication. (c) Studer, A.; Hadida, S.; Feritto, R.; Kim, S.-Y.; Jeger, P.; Wipf, P.; Curran, D. P. *Science* **1997**, 275, 823. (d) Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72. (e) Curran, D. P.; Hadida, S. *J. Am. Chem. Soc.* **1996**, *118*, 2531. (f) Curran, D. P. *Chemtracts−Org. Chem.* **1996**, *9*, 75.

[11] Recent publications in the field of liquid-phase combinatorial chemistry: (a) Han, H.; Janda, K. D. *J. Am. Chem. Soc.* **1996**, *118*, 2539. (b) Cheng, S.; Comer, D. D.; Williams, J. P.; Myers, P. L.; Boger, D. L. *J. Am. Chem. Soc.* **1996**, *118*, 2567. (c) Park, W. K. C.; Auer, M.; Jaksche, H.; Wong, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 10150. (d) Hogan, L. C. *Nature* **1996**, *384*, Suppl. 7, Nov 17. (e) Pinilla, C.; Appel, J.; Dooley, C.; Blondelle, S.; Eichler, J.; Dorner, B.; Ostresh, J.; Houghten, R. A. In *Combinatorial Peptide and Non-Peptide Libraries*; Jung, G., Ed.; VCH: Weinheim, 1996; p 139.

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decided to undertake a study of microwave-promoted fluorous Stille coupling reactions to evaluate the effectiveness of microwave irradiation on a prototypical fluorous reaction.

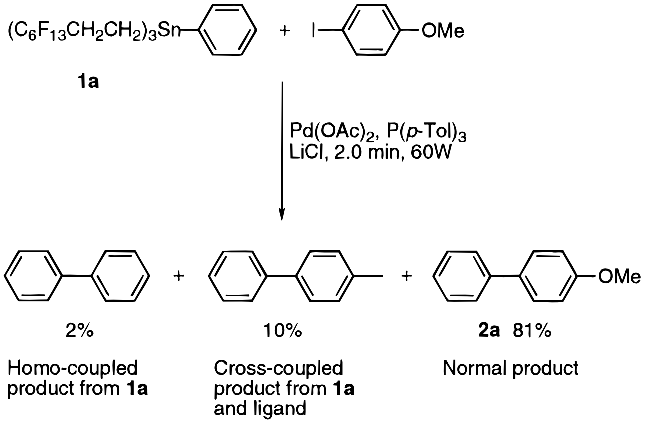
Results and Discussion

A series of fluorinated aryltin, heteroaryltin, and allyltin reactants **1a**−**e** (1.2 equiv) were reacted with a variety of organic halides and triflates (0.20 mmol, 1.0 equiv) in the presence of lithium chloride (3.0 equiv)[10b] and a catalytic amount of bis(triphenylphosphine)palladium(II) chloride[12] (0.02 equiv) in DMF, a microwave-active solvent.[13] The reactions were performed under an atmosphere of nitrogen in sealed Pyrex vessels,[14] and a commercially available single mode cavity producing continuous irradiation was used.[15] All reactions were completed in less than 2 min with microwave dielectric heating and a microwave power of 50−70 W.

The preparative results are summarized in Table 1. All reactions provided fair to good yields of isolated products after workup by three-phase extraction (perfluoroheptanes (FC-84),[16] dichloromethane, water) and subsequent chromatography (Table 1, entries 1−16). The three-phase extraction procedure was also applied prior to GC−MS injections (for monitoring of the reactions) to ensure removal of tin compounds, which are deleterious for the GC columns. The results in Table 1 illustrate that not only aryl halides, aryl triflates, and 3-chlorobenzyl bromide but also vinyl triflates (Table 1, entries 10 and 12) are suitable coupling partners. Furthermore, we learned that the previously unreported fluorous allyl tin reactant **1e** reacts smoothly to give the desired product **2n** with no traces of the conjugated isomer (Table 1, entry 16).

A low chemoselectivity was encountered with 4-bromoiodobenzene (Table 1, entry 5). This reaction produced the doubly coupled product **2d** in 39% yield along with a considerable amount of 4-bromobiphenyl (15%). Apparently, there is only a small preference for the aryl−iodide bond, compared to the aryl−bromide bond, to undergo oxidative addition under the heating conditions employed. In common with both the normal Stille coupling[17a] and the thermal version of the fluorous Stille coupling,[10a,b] we observed that coupling with the pyridyltin compound **1d** resulted in an unsatisfactory mixture of products. But this problem was circumvented by substitution of LiCl for CuO,[17] which delivered the coupled pyridyl compound **2m** with high selectivity and in good isolated yield (Table 1, entry 15).

The thermal fluorous Stille coupling provided significant amounts (5−10%) of symmetrical biaryl side products.[10a,b] We were therefore surprised to find that only a very minor amount of symmetrical biaryls were formed in the microwave-promoted reactions with aryl halides or aryl triflates (<3%, estimated by GC−MS). The reactions with electron-rich aryl halides (Table 1, entries 1, 2, and 6) were exceptions to this generalization, producing up to 10−15% of biphenyl as a side product. A control experiment where tri-*p*-tolylphosphine and palladium acetate were substituted for bis(triphenylphosphine)palladium(II)chloride strongly suggested that the biphenyl (in Table 1, entries 1, 2, and 6), to a large extent, was not derived from homocoupling of the tin reactants. Instead, the major formation of biphenyl, under microwave conditions (Table 1), presumably arises from coupling between the tin reactant and the oxidative addition complex $PhPd(PArPh_2)(PPh_3)X$ formed after aryl migration from $ArPd(PPh_3)_2X$.[18]



The high heating rate associated with microwave irradiation has been postulated to be useful for control of product formation.[1d,19] We presume that the higher Stille product/homocoupled biaryl ratio[20] observed under microwave irradiation originates from a predominance of Stille coupling as compared to the competing homocoupling at high temperatures.

Macroscopic dielectric loss heating effects associated with the solvent (DMF) are likely to be responsible for the startling acceleration of reaction rates, and contributions from specific molecular absorption effects should be less significant.[1,21] Since the reaction tubes are made

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(12) Bis(triphenylphosphine)palladium(II) chloride acts as a precatalyst and is rapidly reduced to active Pd(0) species under typical Stille conditions. Baker, S. R.; Roth, G. P.; Sapino, C. *Synth. Commun.* **1990**, *20*, 2185. See also ref 8d.

(13) Polar solvents absorb microwave energy efficently. The rate of rise of temperature is controlled by the dielectric loss, specific heat capacity and emissivity of the reaction mixture, as well as the geometry and volume of the sample, and the strength of the applied microwave field. Stone-Elander, S.; Elander, N. *Appl. Radiat. Isot.* **1991**, *42*, 885. See also ref 1a.

(14) The Pyrex tube permits the use of higher-boiling solvents than those that may be used with a Teflon vessel. Baghurst, D. R.; Mingos, D. M. P. *J. Chem. Soc., Dalton Trans.* **1992**, 1151.

(15) The use of a single mode microwave cavity (focused microwaves) allows the sample to be exposed to a well-defined microwave field (to avoid local heating effects) during the entire reaction. This is essential for high reproducibility and makes it possible to optimize both the reaction times and the intensities. Carrillo-Munoz, J.-R.; Bouvet, D.; Guibé-Jampel, E.; Loupy, A.; Petit, A. *J. Org. Chem.* **1996**, *61,* 7746 and references therein. See also ref 1g.

(16) FC-84 is a commercially available (3M) nontoxic, nonflammable perfluorinated liquid with a typical boiling point of 80 °C and an average molecular weight of 388 g/mol. It consists mostly of isomers of perfluoroheptane.

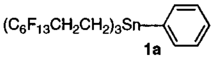
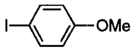
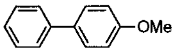
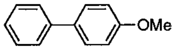
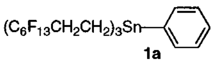
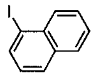
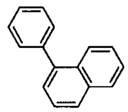
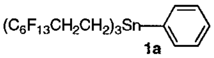
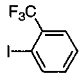
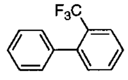
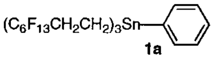
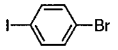
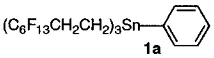
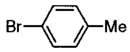
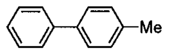
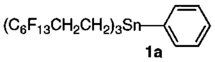
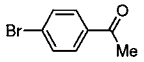
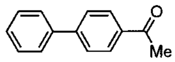
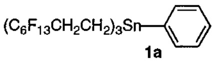
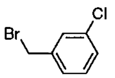
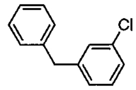
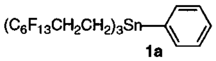
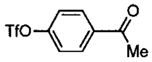
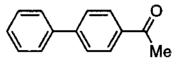
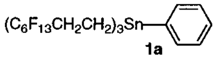
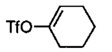
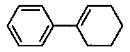
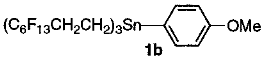
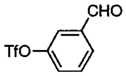
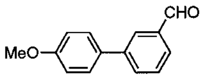
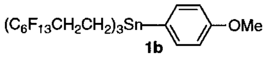
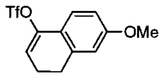
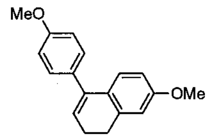
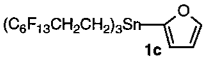
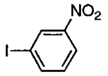
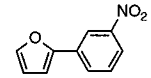
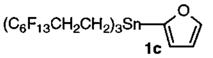
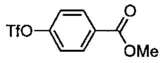
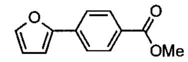
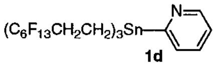
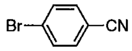
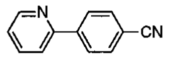
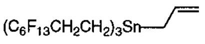
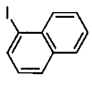
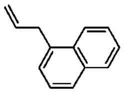
(17) (a) Gronowitz, S.; Björk, P.; Malm, J.; Hörnfeldt, A.-B. *J. Organomet. Chem.* **1993**, *460,* 127. For additional examples of beneficial effects of copper additives on the Stille coupling reaction see: (b) Liebeskind, L. S.; Fengl, R. W. *J. Org. Chem.* **1990**, *55*, 5359. (c) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W. *Tetrahedron Lett.* **1992**, *33,* 919. (d) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905. (e) Hodgson, D. M.; Witherington, J.; Moloney, B. A.; Richards, I. C.; Brayer, J.-L. *Synlett* **1995**, 32. (f) Gibbs, R. A.; Krishnan, U.; Dolence, J. M.; Poulter, C. D. *J. Org. Chem.* **1995**, *60*, 7821.

(18) For recent articles concerning exchange of metal- and phosphine-bound organic moieties in the oxidative addition complex see: (a) Kong, K.-C.; Cheng, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 6313. (b) Segelstein, B. E.; Butler, T. W.; Chenard, B. L. *J. Org. Chem.* **1995**, *60*, 12. (c) Morita, D. K.; Stille, J. K.; Norton, J. R. *J. Am. Chem. Soc.* **1995**, *117*, 8576 and references cited therein.

(19) Stuerga, D.; Gonon, K.; Lallemant, M. *Tetrahedron* **1993,** *49*, 6229.

(20) It has been reported that stannane homocoupling does not proceed when careful precautions are taken to exclude atmospheric oxygen. Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*, 5434.

Table 1. Fast Stille Couplings with Fluorous Tin Reactants under Microwave Irradiation[a]

entry	tin reactant	organic halide or organic triflate	time and microwave power[b]	product		isolated yield[c]
1	 **1a**		2.0 min 60 W		**2a**	77%
2			1.5 min 70 W		**2a**	76%
3	 **1a**		1.5 min 70 W		**2b**	96%
4	 **1a**		2.0 min 60 W		**2c**	47%
5	 **1a**		2.0 min 60 W		**2d**	39%[d]
6	 **1a**		2.0 min 60 W		**2e**	51%
7	 **1a**		2.0 min 60 W		**2f**	71%
8	 **1a**		2.0 min 50 W		**2g**	90%
9	 **1a**		2.0 min 60 W		**2f**	92%
10	 **1a**		2.0 min 50 W		**2h**	51%
11	 **1b**		2.0 min 60 W		**2i**	83%
12	 **1b**		2.0 min 50 W		**2j**	49%
13	 **1c**		1.5 min 70W		**2k**	87%
14	 **1c**		2.0 min 60 W		**2l**	63%
15	 **1d**		2.0 min 60 W		**2m**	79%[e]
16	 **1e**		2.0 min 60 W		**2n**	54%

[a] Reactions were conducted under continuous microwave irradiation (2450 MHz) in sealed Pyrex tubes under an atmosphere of nitrogen. The organic halide or organic triflate (0.20 mmol, 1.0 equiv) was reacted with the tin reactants (1.2 equiv) in the presence of $PdCl_2(PPh_3)_2$ (0.02 equiv) and LiCl (3.0 equiv) in DMF (1.0 mL). After cooling, a small sample was partitioned between FC-84, dichloromethane, and water, and the organic phase was analyzed by GC−MS. [b] The microwave power and the irradiation time were selected to allow >95% conversion in all cases. [c] Based on the organic halide or organic triflate. >95% purity by GC−MS. [d] 15% 4-bromobiphenyl was also isolated. [e] CuO (1.0 equiv) was added instead of LiCl.

of Pyrex, conductivity heat losses are small[22] and the irradiation energy, with very high energy density, is absorbed by the reaction mixture directly, an effect that within a short time leads to a "pressure cooker effect" in the sealed tubes. Wall effects are largely eliminated, and the whole of the reaction medium is heated simultaneously without local heating effects.[1d,21e] This methodology provides a rapid and convenient way of synthesizing compounds that are thermally stable but are the final products of kinetically slow reactions.[14]

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(22) Pyrex is almost transparent to microwave energy and is a poor conductor of heat. Stone-Elander, S. A.; Elander, N.; Thorell, J.-O.; Solås, G.; Svennebrink, J. *J. Labelled Cmpds. Radiopharm.* **1994**, *10*, 949. See also ref 1f.

Conclusions

The microwave variant of the fluorous Stille reaction is an expedient procedure that couples the facile workup and separation features associated with the fluorous Stille reactants and the rapid reaction time associated with microwave methods. An unexpected benefit of the microwave method is the reduced amount homocoupled byproduct that is formed in many reactions. Additional work will be needed to ascertain if the application of microwave radiation provides a mild and general method to promote reactions between organic and fluorous reaction components. But even at this early stage, it appears as if the combination of these two techniques holds significant potential for parallel synthesis applications to make combinatorial libraries in the solution phase because time and effort are minimized at both the reaction and the separation stages.

Experimental Section

Procedures. Reactions were performed in a MicroWell 10 single-mode microwave cavity[22] producing continuous irradiation (2450 MHz) from Labwell AB, SE-753 19 Uppsala, Sweden. The reactions were performed under nitrogen in heavy-walled Pyrex tubes (8 mL, $l = 150$ mm) sealed with a silicon septum. In the event of overpressurization, this septum was distorted. Silicone septa (110.623-18) and screwcaps with aperture (110.627-18) were purchased from KEBO Lab AB, SE-163 94 Spånga, Sweden. The reaction volume occupied not more than 1/5th of the total volume of the tube, thereby allowing head space for pressure buildup during the microwave treatment. To ensure a satisfactory antenna function of the reaction liquid, the height of the liquid column was >2.5 cm. All couplings were conducted in the absence of stirring. After irradiation, small samples were removed and partitioned between FC-84, dichloromethane, and water, and the dichloromethane phase was analyzed by GC−MS. ^{1}H NMR spectra of the coupling products were measured at 270 MHz in $CDCl_3$ solution. In the ^{119}Sn NMR spectra, chemical shifts are relative to tetramethyltin. Mass spectra were determined at 70 eV (EI). IR spectra were recorded on a FTIR spectrometer. Column chromatography was performed on silica using Kieselgel S (0.032−0.063 mm, Riedel-de Haen). Elemental analyses were carried out by Mikro Kemi AB, Uppsala, Sweden.

Materials. Organo halides, lithium chloride, copper(II) oxide, tri-*p*-tolylphosphine, DMF, and allylmagnesium bromide (1 M in diethyl ether) were purchased from commercial suppliers and were used directly as received. Bis(triphenylphosphine)palladium(II)chloride was obtained from Acros and used without further purification. FC-84 was obtained from 3M. The aryl triflates were synthesized from the corresponding phenols using an excess of triflic anhydride and 2,4,6-trimethylpyridine, essentially following a literature procedure.[23] 4-Acetylphenyl trifluoromethanesulfonate,[24] 3-formylphenyl trifluoromethanesulfonate,[25] and methyl 4-[[(trifluoromethyl)sulfonyl]oxy]benzoate[26] are known compounds. The vinyl triflates 1-cyclohexenyl trifluoromethanesulfonate[27] and 6-methoxy-3,4-dihydro-1-naphthyl trifluoromethanesulfonate[28] were prepared according to the method described by Stang.[29] Tris[2-(perfluorohexyl)ethyl]phenyltin (**1a**), tris[2-(perfluorohexyl)ethyl](4′-methoxyphenyl)tin (**1b**), tris[2-(perfluorohexyl)ethyl](2′-furyl)tin (**1c**), and tris[2-(perfluorohexyl)ethyl](2′-pyridyl)tin (**1d**) were prepared as described previously.[10a,b,e] Structure and purity of isolated coupling products were determined by ^{1}H NMR and GC−MS (>95% purity). Products **2g**,[30] **2i**,[31] **2j**,[32] **2k**,[33] **2l**,[34] **2m**,[35] and **2n**[36,37] have been synthesized and fully characterized before. Compounds **2a**,**b**,**d**,**e**,**f**,**h** are commercially available, and the structures were determined by comparison with an authentic sample (**2d**,**f**,**h**) or by comparison of their spectroscopic data with the reported values (**2a**,**b**,**e**).[37,38] The biaryl **2c** was previously reported but not characterized.[39]

Caution! The microwave-assisted reactions described in this paper should not be repeated in closed vessels unless an appropriate septum is used as a pressure relief device since this could result in an explosion.[40]

Tris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)allyltin (Tris[2-(perfluorohexyl)ethyl]allyltin) (1e). Allylmagnesium bromide (1.0 mL, 1.0 mmol) 1 M in diethyl ether was added to a solution of tris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)tin bromide (1.0 g, 0.80 mmol) in diethyl ether (10 mL). The mixture was heated at reflux for 2 h with stirring. To the reaction cooled at 0 °C were added a saturated solution of amonium chloride (8 mL) and diethyl ether (5 mL). The two phases were separated, and the aqueous phase was extracted twice with diethyl ether (2 × 10 mL). The combined ether extracts were dried over $MgSO_4$, evaporated, and purified by column chromathography on neutral alumina (hexanes), yielding **1e** as a colorless oil (770 mg, 80%): MS m/z (relative intensity, 70 eV) 1201 (M^+, 12), 1161 (100), 855 (25); ^{1}H NMR ($CDCl_3$) δ 5.95 (m, 1H), 5.0−4.8 (m, 2H), 2.30 (m, 6H), 1.95 (d, $J = 9$ Hz, $^2J(^{119}Sn{-}H) = 66$ Hz, 2H), 1.20 (t, $J = 8.3$ Hz, $^2J(^{119}Sn{-}H) = 59$ Hz, 6H); ^{119}Sn NMR ($CF_3C_6H_5/C_6D_6$) −9.76 ppm; IR (thin film) 2884, 2872, 1627, 1442, 1351, 1317, 1236, 1204, 1144, 1119, 1063, 843, 699 cm^{-1}.

General Procedure for Coupling Reactions (Table 1). In a screw-capped Pyrex tube were placed tris[2-(perfluorohexyl)ethyl]organotin (0.24 mmol), organic halide or organic triflate (0.20 mmol), bis(triphenylphosphine)palladium(II) chloride (0.004 mmol, 2.8 mg), lithium chloride (0.60 mmol, 25.4 mg), and DMF (1.0 mL). The tube was capped, and the suspension was purged with nitrogen. The contents of the tube were mixed with a whirlimixer and thereafter rapidly heated by the application of microwave power (see Table 1 for details concerning reaction times and microwave power). The microwave power was adjusted to give full conversion in less than 2.0 min. After the reaction mixture was cooled to room temperature, toluene (2 mL) was added, and most of the DMF was azeotropically evaporated under reduced pressure at 50−

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70 °C. The residue was then partitioned in a three-phase extraction between water (10 mL, top), dichloromethane (20 mL, middle), and FC-84 (10 mL, bottom). The three layers were separated, and the dichloromethane layer was washed three additional times with water (3 × 10 mL) and FC-84 (3 × 10 mL) and evaporated under reduced pressure.[41] The resulting crude product was purified by chromatography (silica column)[42] to afford pure coupling product (see Table 1, >95% pure by GC−MS). No attempt was made to recover the fluorous tin chloride from the FC-84 phase.[10a,b]

2-(Trifluoromethyl)biphenyl (2c):[39] pale red oil, 0.021 g (47%); eluent isohexane: MS *m/z* (relative intensity, 70 eV) 222 (M^+, 100), 201 (30), 183 (8), 152 (10); ^{1}H NMR ($CDCl_3$) δ 7.28−7.49 (m, 7H), 7.54 (br t, $J = 7.6$ Hz, 1H), 7.73 (br d, $J = 7.6$ Hz, 1H). Anal. Calcd for $C_{13}H_9F_3$: C, 70.3; H, 4.1. Found: C, 70.2; H, 4.3.

Procedure for the Control Experiment. A mixture of tris[2-(perfluorohexyl)ethyl]phenyltin (**1a**) (0.24 mmol, 297 mg), 4-iodoanisole (0.20 mmol, 46.8 mg), palladium(II) acetate (0.004 mmol, 0.90 mg), tri-*p*-tolylphosphine (0.008 mmol, 2.4 mg), lithium chloride (0.60 mmol, 25.4 mg), and DMF (1.0 mL) was treated with microwaves (2.0 min, 60 W) under nitrogen. The reaction was repeated twice (to increase the amount of products). All three reaction mixtures were then cooled, combined, and purified by three-phase extraction and column chromatography (silica, isohexane) to afford 81% (89.8 mg) of 4-methoxybiphenyl (based on 4-iodoanisole, expected product, **2a**), 10% (10.4 mg) of 4-methylbiphenyl[37,38] (based on 4-iodoanisole, from aryl interchange in the oxidative addition complex), and 2% (2.5 mg) biphenyl[37,38] (based on **1a**, from stannane homocoupling). This product distribution is in accordance with yields estimated by GC−MS.

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(41) In most cases small amounts of fluoroalkyl transfer products were detected (GC−MS) in the dichloromethane layer after the FC-84/water wash.

(42) Eluents; **2a** isohexane/diethyl ether (9/1), **2b** isohexane/ethyl acetate (19/1), **2d** isohexane, **2e** isohexane, **2f** pentane/ethyl acetate (9/1), **2g** isohexane/diethyl ether (99/1), **2h** isohexane, **2i** isohexane/ethyl acetate (7/1), **2j** isohexane/ethyl acetate (99/1), **2k** isohexane/ethyl acetate (19/1), **2l** isohexane/ethyl acetate (7/1), **2m** isohexane/ethyl acetate (2/1), **2n** isohexane.