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Palladium-Catalyzed Cross-Coupling of Arene–Chromium Tricarbonyl Triflate Complexes[1]

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The importance of the recent extension of the Stille cross-coupling reaction[2] to aryl triflates,[3] compounds easily synthesized from phenols, can be seen in its use as a key step in the synthesis of several natural products,[4] natural product analogs,[5] and multifunctional polymers.[6] While this reaction is fairly general with respect to the stannane,[7] the cross-coupling of electron-rich aryl triflates usually fails, presumably due to the reluctance of these compounds to undergo oxidative addition by palladium(0). One solution to this problem involves the use of polar aprotic solvents, but the reaction conditions are extreme (refluxing DMF, 10–15 mol % Pd catalyst).[8] Another solution, which has been previously used with aryl chlorides,[9] would be to activate the aryl triflate to oxidative addition by coordination of an electron-withdrawing $\mathrm{Cr(CO)_3}$ moiety to the arene. These complexes are prepared for the present study by the development of an expedient and general route suggested by our recent methodology for the synthesis of arene–$\mathrm{Cr(CO)_3}$ silyl ether complexes[10] using the benzannulation reaction.[11] In this communication we report the first Stille cross-couplings of arene–$\mathrm{Cr(CO)_3}$ triflate complexes and organostannanes which occur with the retention of the $\mathrm{Cr(CO)_3}$ group under very mild conditions even for highly hindered and electron-rich aryl triflates.

The highly substituted and air-stable[12] arene–$\mathrm{Cr(CO)_3}$ triflate complexes **4**–**6** can be synthesized using a one-pot sequential benzannulation/triflation procedure using triflic anhydride and Hünig's base (Table 1). Other less electrophilic triflating reagents ($\mathrm{PhNTf_2}$ and (5-chloro-2-pyridyl)triflimide[13]) and/or hindered amine bases (2,6-lutidine, 2,6-di-*tert*-butyl-4-methylpyridine, 2,2,6,6-tetramethylpiperidine, and Proton Sponge) give poorer results. Tetrasubstituted triflate complexes **4** and **5** were synthesized in 81% and 66% yields, respectively, from carbene complexes **1**[10] or **2**[10] and 1-pentyne. Pentasubstituted triflate complex **6** was slightly more difficult to obtain but could be prepared in 43% yield from carbene complex **3**[14] and 1-pentyne using a procedure in which the benzannulation and triflation reactions were carried out concurrently.[10] In addition, a 23% yield of 2-*n*-propyl-4-methoxyl-5,6,7,8-tetrahydro-1-naphthol (**8**)[15] was produced due to inefficient triflation and also loss of the $\mathrm{Cr(CO)_3}$ group.[16] Using the sequential procedure to synthesize **6** gave lower yields of both triflate complex **6** (26%) and naphthol **8** (18%). Despite the moderate yield obtained for complex **6**, the benzannulation/triflation procedure can provide good to excellent yields of other aryl triflate complexes and has the advantage over the classical approach of synthesizing arene complexes in that the arene is constructed around the $\mathrm{Cr(CO)_3}$ moiety instead of having to be first synthesized and then appended to it in a thermal reaction with $\mathrm{Cr(CO)_3L_3}$ (L = CO, $\mathrm{CH_3CN}$, naphthalene).[17]

We find that arene-$\mathrm{Cr(CO)_3}$ triflate complexes **4**–**6** undergo Stille cross-coupling reactions with vinyl-, alkynyl-, and alkylstannanes under mild conditions (2 mol % $\mathrm{Pd(Ph_3P)_4}$, 1.05 equiv of stannane, THF, 65 °C) which allow for the isolation of air-stable,[12] cross-coupled arene–$\mathrm{Cr(CO)_3}$ complexes (Table 1). The reaction of tetrasubstituted triflate complex **4** with vinyltributyltin produces the vinylarene complex **9** in 99% yield (entry 1). The corresponding methyl-substituted triflate complex **5** undergoes efficient coupling with vinyltributyltin (91% yield of **10**, entry 2), [(trimethylsilyl)ethynyl]tributyltin (79% yield of **11**, entry 3), and tetramethyltin (46% yield of **12**, entry 4) to give good yields of cross-coupled products. In addition to **11**, a 16% yield of the metal-free cross-coupled product **16**[18] derived from the loss of metal from **11** was also obtained. The more hindered, pentasubstituted triflate complex **6** undergoes efficient cross-coupling reactions with vinyltributyltin (76% yield of **13**, entry 5), tributylstannylpropyne (50% yield of **14**, entry 6), and tetramethyltin (41% yield of **15**, entry 7).

The trenchant role of the chromium tricarbonyl group in activating these coupling reactions is evident from the information outlined in Scheme 1. As a comparison to the coupling reactions of triflate complexes **5** and **6** with vinyltributyltin, the cross-coupling reactions of metal-free triflates **17** and **18** were examined. Whereas the triflate complex **6** will undergo the coupling reaction to give a 76% yield of **13**, the corresponding metal-free triflate **18** is recovered in 80 % yield after exposure to the more forcing conditions developed by Stille.[3] Likewise, the triflate complex **5** will give a 91% yield of the coupling product **10** under the normal conditions indicated in Table 1, but the coupling of the metal-free triflate **17** completely fails, even under the recently reported forcing conditions developed by Farina[7a,19] shown in Scheme 1 (83% recovery).[20] In both reactions, no cross-coupled

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[4] (a) Micrococcinic acid: Kelly, T. R.; Jagoe, C. T.; Gu, Z. *Tetrahedron Lett.* **1991,** *32,* 4263. (b) (±)-Pterocarpin, (±)-homopterocarpin, and (±)-9-*O*-benzyl-3-*O*-methylsophoropterocarpan A: Engler, T. A.; Reddy, J. P.; Combrink, K. D.; Velde, D. V. *J. Org. Chem.* **1990,** *55,* 1248. (c) Hyellazole: Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990,** *112,* 3093. (d) Amphimedine: Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988,** *110,* 4051.

[5] (a) Streptonigrin and lavendamycin analogs: Godard, A.; Rocca, P.; Fourquez, J.-M.; Rovera, J.-C.; Marsais, F. Quéguimer, G. *Tetrahedron Lett.* **1993,** *34,* 7919. (b) Isoascididemin: Gómez-Bengoa, E.; Echavarren, A. M. *J. Org. Chem.* **1991,** *56,* 3497.

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[7] For recent improvements in the cross-couplings of aryl- and alkylstannanes, see: (a) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993,** *58,* 5434. (b) Vedejs, E.; Haight, A. R.; Moss, W. O. *J. Am. Chem. Soc.* **1992,** *114,* 6556.

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[9] The initial observations in the cross-coupling of chloroarene–$\mathrm{Cr(CO)_3}$ complexes are (a) Cross-couplings with terminal acetylenes: Villemin, D.; Schigeko, E. *J. Organomet. Chem.* **1985,** *293,* C10. (b) Stille cross-couplings with organostannanes: Scott, W. J. *J. Chem. Soc., Chem. Commun.* **1987,** 1755. For recent citations to the literature, see refs 23 and 27.

[10] Chamberlin, S.; Wulff, W. D.; Bax, B. *Tetrahedron* **1993,** *49,* 5531. A single example of an arene–$\mathrm{Cr(CO)_3}$ triflate complex was reported in this work.

[11] For a recent review on the benzannulation reaction, see: Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 5, p 1065.

[12] Arene–$\mathrm{Cr(CO)_3}$ triflate complexes **4**–**6** and arene–$\mathrm{Cr(CO)_3}$ complexes **9**–**15** are stable in air at room temperature for up to 1 h. They may be stored for months under Ar at −20 °C without any noticeable decomposition.

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[16] Subjecting complex **6** to triflation conditions ($\mathrm{Tf_2O}$, *i*-$\mathrm{Pr_2NEt}$, $\mathrm{CH_2Cl_2}$, 50 °C, 18 h) failed to produce any naphthol **8** due to solvolysis of the triflate moiety under the reaction conditions.

[17] For a review of the classical syntheses of arene–$\mathrm{Cr(CO)_3}$ complexes, see: Davis, R.; Kane-Maguire, L. A. P. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, U.K., 1982; Vol. 3, p 953.

[18] Arene **16** could be separately prepared by stirring arene complex **11** with 10 equiv of $\mathrm{(FeCl_3)_2DMF_3}$ in THF/$\mathrm{H_2O}$ (1:1) at room temperature for 15 min.

[19] Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991,** *113,* 9585.

[20] These reactions also fail in THF with the conditions in Table 1.

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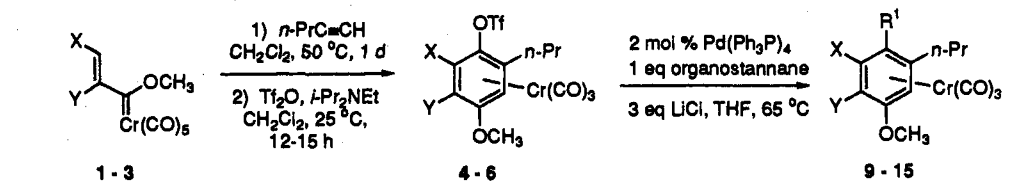
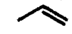
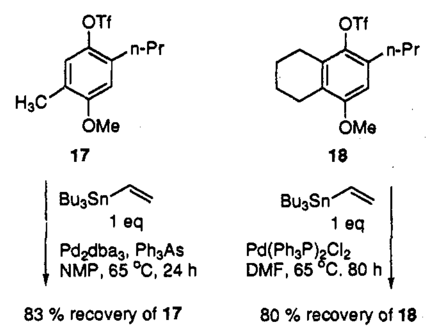
Table 1. Cross-Coupling of Arene–Cr(CO)$_3$ Complexes **4**–**6** with Organostannanes



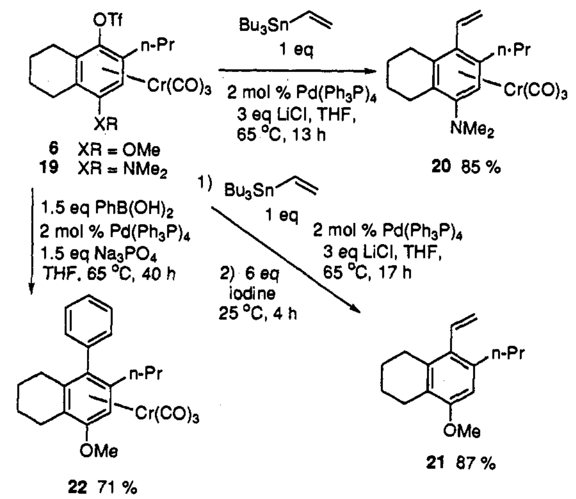
entry	carbene complex	X	Y	Arene Complex (% Yield)		Organo-stannane	Time (h)	Product (% Yield)		R^1
1	1	H	SiMe$_3$	4	81 %	Bu$_3$Sn 	24	9	99 %	
2	2	H	CH$_3$	5^a	66 %	Bu$_3$Sn 	16	10	91 %	
3		H	CH$_3$			Bu$_3$Sn—≡—SiMe$_3$	37	11	79 %^{b}	—≡—SiMe$_3$
4		H	CH$_3$			Me$_4$Sn	37	12	46 %	CH$_3$
5	3	-- (CH$_2$)$_4$–		6^c	43 %	Bu$_3$Sn 	15	13	76 %^{d}	
6		-- (CH$_2$)$_4$--				Bu$_3$Sn—≡—CH$_3$	83	14	50 %	—≡—CH$_3$
7		-- (CH$_2$)$_4$–				Me$_4$Sn	132	15	41 %	CH$_3$

^{a} Triflation time is 24 h. ^{b} A 16% yield of **16**, the decomplexed form of **11**, was also obtained. ^{c} A 23% yield of phenol **8** corresponding to **6** was also obtained. Benzannulation and triflation performed concurrently. ^{d} 2 mol % of Pd(Ph$_3$P)$_2$Cl$_2$ was used as catalyst.

Scheme 1



Scheme 2



products are formed, presumably due to failure of Pd(0) to undergo oxidative addition into the C–OTf bond.

The efficacy of the chromium tricarbonyl group in promoting cross-coupling with electron-rich aryl triflates was more severely tested with the *p*-(dimethylamino)-substituted triflate complex **19**.[21] This complex undergoes cross-coupling with vinyltributyltin under the standard conditions (Table 1) to give an 85% yield of arene–chromium tricarbonyl complex **20** (Scheme 2). Metal-free, cross-coupled products may be obtained by oxidizing the reaction mixture with excess iodine. For example, performing the cross-coupling reaction in entry 5 of Table 1 and oxidizing with 6 equiv of iodine at room temperature for 4 h gave an 87% yield of **21** (76% for **13**). All attempts to cross-couple triflate complexes **5** and **6** with phenylstannanes (PhSnMe$_3$, PhSnBu$_3$, and Ph$_4$Sn), allyltributyltin, and tributyltin hydride give inseparable and complicated reaction mixtures, most likely due to nonselective substituent transfer from tin and/or demetalation of the starting triflate complexes and coupled products. However, we have found that phenylboronic acid undergoes Suzuki-type cross-coupling[22] with triflate complex **6** to give a 71% yield of the interesting biphenylarene complex **22** (Scheme 2).[23]

These results demonstrate another example[24] of the powerful electron-withdrawing effect that a Cr(CO)$_3$ creates when bound to an arene, the same effect that leads to increased acidity of arene and benzylic protons[25] and the more facile nucleophilic aromatic substitution reactions in arene-Cr(CO)$_3$ complexes.[26] The synthetic applications of the cross-coupling reactions of hindered, electron-rich arene–Cr(CO)$_3$ triflate complexes with organostannanes will be reported in due course.

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Supplementary Material Available: Experimental procedures and characterization data for compounds **4**–**6**, **9**–**16**, and **20**–**22** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered form the ACS; see any current masthead page for ordering information.

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