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Synthesis of Unsymmetrical Diarylmethanes by Cross-Coupling between Aryl Triflates and Tetrabutylammonium Difluorotribenzylstannate[†]

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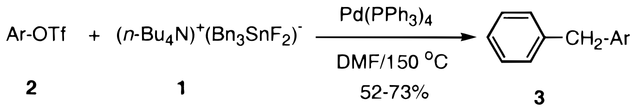
ABSTRACT



The benzylation of aryl triflates can be achieved by cross-coupling between aryl triflates and the new hypervalent tin reagent (n-$Bu_4N)^+(Bn_3SnF_2)^-$.

Diarylmethanes are frequently used as subunits in the design of supramolecular structures such as macrocycles, catenanes, and rotaxanes.[1] Besides this, some diarylmethane derivatives have been shown to possess interesting biological and medicinal properties.[2,3]

The best procedures for the synthesis of the title compounds are the transition metal-catalyzed cross-coupling between either aryl nucleophiles and benzylic halides[3] or aryl halides and benzylic nucleophiles.[4] However, the required nucleophiles are organomagnesium or organozinc halides, which are incompatible with a variety of functional groups. Therefore, the reactions must be carried out using such mild reaction conditions that global yields obtained are quite low.[4]

The palladium-catalyzed cross-coupling of organotin reagents (Stille reaction) is a widely used method for carbon−carbon bond formation.[5] However, the Stille reaction fails in the case of cross-coupling between aryl triflates and substituted benzyltributyltin (highest reported yield: 21%).[3,5] Very recently, the Suzuki−Miyaura palladium-catalyzed cross-coupling reaction has been extended to achieve diarylmethanes.[6] However, this methodology is also limited by the availability of boronic acid derivatives.[7]

Since our preliminary work on the phenylation of alkenyl triflates with tetrabutylammonium difluorotriphenylstannate,[8] a hypervalent tin reagent,[9] other hypervalent tin[10−12] and

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[†] Affectionately dedicated to Prof. José Luis Soto on the occasion of his 70th birthday.

(1) (a) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303. (b) Jäfer, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930.

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(10) (a) Fouquet, E.; Pereyre, M.; Rodriguez, A. L. *J. Org. Chem.* **1997**, *62*, 5242. (b) Fouquet, E.; Rodriguez, A. L. *Synlett* **1998**, 1323.

(11) Fugami, K.; Ohnuma, S.; Kameyama, M.; Saotome, T.; Kosugi, M. *Synlett* **1999**, 63.

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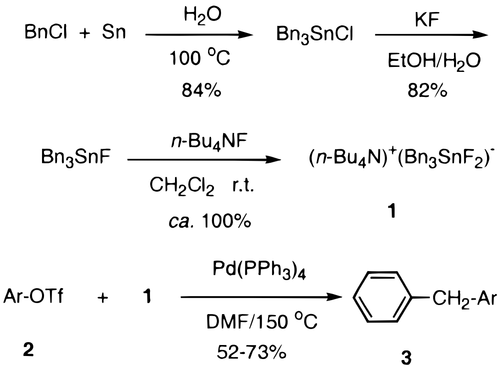
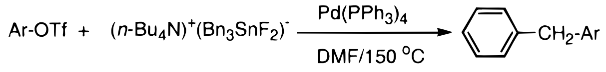
silicon[13] reagents have been employed with success in several coupling reactions. In this paper we report that tetrabutylammonium difluorotribenzylstannate $[(n\text{-Bu}_4\text{N})^+(\text{Bn}_3\text{SnF}_2)^-]$ **1** can be used as an effective transmetalation reagent[14] in $\text{Pd(PPh}_3)_4$-catalyzed cross-coupling reactions with aryl triflates **2** (Scheme 1).

Scheme 1. Preparation of Unsymmetrical Diarylmethanes (**3**)

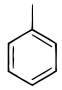
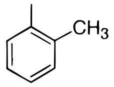
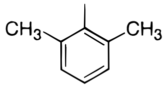
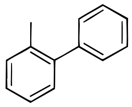
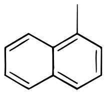
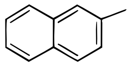


The hypervalent tin reagent **1** was easily prepared from benzyl chloride according to Scheme 1.[9] The coupling reaction between **1** and aryl triflates **2**, prepared from the corresponding phenols,[5c,15] takes place easily in DMF as solvent at 150 °C. The optimized reaction times for each triflate are given in Table 1, as well as the yields in isolated arylphenylmethanes.[16] It should be noted that reaction times in this procedure are very short (1 min−2 h). On the other hand, no coupling reaction was observed by us when trying to obtain **3** following the method reported in the literature based on the use of activated monoorganotins and aryl triflates.[10]

Table 1. Reaction of Aryl Triflates with $(n\text{-Bu}_4\text{N})^+(\text{Bn}_3\text{SnF}_2)^-$



2 **1** **3**

Entry	Ar-	Time	Yield(%)
1		1 min	68
2		1.5 h	52
3		2 h	73
4		5 min	63
5		3 min	60
6		3 min	63

As byproducts, small amounts (<10%) of homocoupled compounds (Ar−Ar and 1,2-diphenylethane) were detected by GLC. In entries 2 and 4, a small amount (ca. 10%) of products proceeding from the arylation of the aryl triflates was also detected. These compounds are formed in the reactions by a transmetalation process involving triphenylphosphine.[5b]

In summary, hypervalent reagent **1** is a highly effective transmetalation reagent for the Pd(0)-catalyzed cross-coupling benzylation of aryl triflates. Furthermore, the hypervalent reagents used do not have the toxicity and purification drawbacks encountered when using tetraorganotins.[17] The scope and limitations of this methodology will be reported in due course.

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[14] For the mechanism of the Stille reaction, see: Casado, A. L.; Espinet, P. *J. Am. Chem. Soc.* **1998**, *120*, 8978.

[15] García Martínez, A.; Subramanian, L. R.; Hanack, M. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley: Chichester, 1995; Vol. 7.

[16] A solution of 1.3 mmol of aryl triflate **2**, 1.31 g (1.95 mmol) of **1**, and 0.13 mmol of $\text{Pd(Ph}_3\text{P)}_4$ in 6 mL of DMF was introduced, under an argon atmosphere, in an oil bath heated at 150 °C. After the reaction time indicated in Table 1, the reaction mixture was poured into water (50 mL) and extracted with Cl_2CH_2 (3 × 25 mL). The organic solution was washed with water and a saturated NaHCO_3 solution and dried over MgSO_4. Evaporation of the solvent and purification of the residue by flash chromatography (silica gel, hexane) yielded the corresponding arylphenylmethanes **3**. All compounds were characterized by ^{1}H and ^{13}C NMR and MS.

[17] For toxicology of tin reagents, see: Aldridge, W. N. In *Chemistry and Technology of Silicon and Tin*; Kurnar Das, V. G., Weng, N. G., Gielen, M., Eds.; Oxford University Press: New York, 1992; pp 78−92.