

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

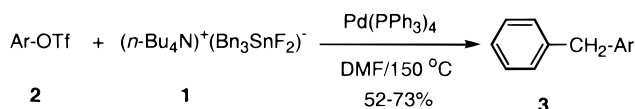
Antonio García Martínez,* José Osío Barcina,
María del Rosario Colorado Heras, and Álvaro de Fresno Cerezo

Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad
Complutense de Madrid, Ciudad Universitaria, 28040 Madrid, Spain

josio@eucmos.sim.ucm.es

Received February 14, 2000

ABSTRACT



The benzylation of aryl triflates can be achieved by cross-coupling between aryl triflates and the new hypervalent tin reagent $(n\text{-Bu}_4\text{N})^+(\text{Bn}_3\text{SnF}_2)^-$.

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 halides³ 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

[†] 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.

(2) (a) Rische, T.; Eilbracht, P. *Tetrahedron* **1999**, 55, 1915. (b) Prat, L.; Mojovic, L.; Levacher, V.; Dupas, G.; Quéguines, G.; Bourguignon, J. *Tetrahedron: Asymmetry* **1998**, 9, 2509. (c) Ku, Y.-Y.; Patel, R. P.; Sawick, D. P. *Tetrahedron Lett.* **1996**, 37, 1949.

(3) de Lang, R.-J.; van Hooijdonk, M. J. C. M.; Brandsma, L.; Kramer, H.; Seinen, W. *Tetrahedron* **1998**, 54, 2953 and references therein.

(4) Rottländer, M.; Knochel, P. *Tetrahedron Lett.* **1997**, 38, 1749 and references therein.

(5) For reviews, see: (a) Stanforth, S. P. *Tetrahedron* **1998**, 54, 263. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Organic Reactions*; Wiley: New York, 1997; Vol. 50. (c) Ritter, K. *Synthesis* **1993**, 735.

(6) Chowdhury, S.; Georgiou, P. E. *Tetrahedron Lett.* **1999**, 40, 7599.

(7) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, 95, 2457.

(8) García Martínez, A.; Osío Barcina, J.; de Fresno Cerezo, A.; Subramanian, L. R. *Synlett* **1994**, 1047.

(9) Gingras, M. *Tetrahedron* **1991**, 32, 7381.

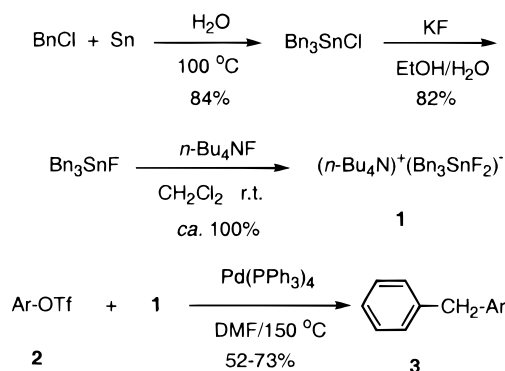
(10) (a) Fouquet, E.; Pereyre, M.; Rodriguez, A. L. *J. Org. Chem.* **1997**, 62, 5242. (b) Fouquet, E.; Rodriguez, A. L. *Synlett* **1998**, 1323.

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

(12) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, 38, 2411.

silicon¹³ reagents have been employed with success in several coupling reactions. In this paper we report that tetrabutylammonium difluorotribenzylstannate [(*n*-Bu₄N)⁺(Bn₃SnF₂)⁻] **1** can be used as an effective transmetalation reagent¹⁴ in Pd(PPh₃)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 monoorganotin and aryl triflates.¹⁰

As byproducts, small amounts (<10%) of homocoupled compounds (Ar–Ar and 1,2-diphenylethane) were detected

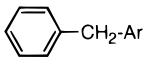

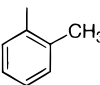
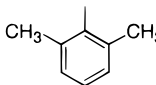
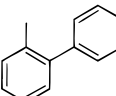
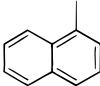
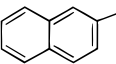
(13) (a) Mowery, M. E.; DeShong, P. J. *Org. Chem.* **1999**, *64*, 1684. (b) Mowery, M. E.; DeShong, P. J. *Org. Chem.* **1999**, *64*, 3266.

(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 Pd(PPh₃)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 Cl₂CH₂ (3 × 25 mL). The organic solution was washed with water and a saturated NaHCO₃ solution and dried over MgSO₄. 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 ¹H and ¹³C NMR and MS.

Table 1. Reaction of Aryl Triflates with (n-Bu₄N)⁺(Bn₃SnF₂)⁻

Ar-OTf + (n-Bu ₄ N) ⁺ (Bn ₃ SnF ₂) ⁻ $\xrightarrow[\text{DMF/150 } ^\circ\text{C}]{\text{Pd(PPh}_3)_4}$ 			
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

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 tetraorganotin.¹⁷ The scope and limitations of this methodology will be reported in due course.

Acknowledgment. We thank the DGICYT, Spain (Grant PB-97-0268-C02), for financial support.

OL005666C

(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.