

# Homocoupling of Aryl Halides Promoted by Tetrabutylammonium Fluoride

Domenico Albanese,\* Dario Landini, Michele Penso, Silvia Petricci

Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università, via Venezian 21, I-20133 Milano, Italy

E-mail: domenico@iumchz.chimorg.unimi.it

Received 1 December 1998

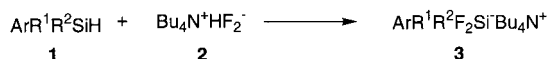
**Abstract:** The palladium-catalysed homocoupling of aryl halides takes place in the presence of anhydrous, *in situ* generated, tetrabutylammonium fluoride (TBAF).

**Key words:** homocoupling, aryl halides, tetrabutylammonium fluoride, palladium

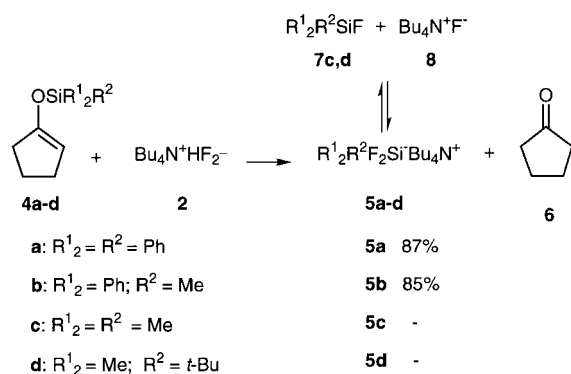
Symmetrical biaryls have been prepared by the classic Ullmann-copper mediated synthesis,<sup>1</sup> whereas modern methodologies take advantage of arylstannanes,<sup>2</sup> arylboronic acids<sup>3</sup> and arylzinc<sup>4</sup> derivatives. These methods are efficient even though they suffer from the drawbacks related to the use of stoichiometric amounts of organometallic species.

Recently, the homocoupling of aryl halides using Pd(OAc)<sub>2</sub> and Bu<sub>4</sub>NBr<sup>5</sup> has been reported therefore prompting us to present our results in this field.

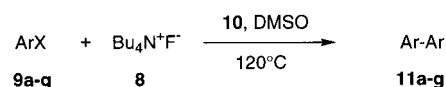
In a previous paper<sup>6</sup> we described a new synthesis of pentacoordinated tetraalkylammonium (difluoro)silicates **3** by reaction of a trisubstituted silane **1**, containing at least one aryl group, and a quaternary onium hydrogendifluoride, *e.g.* tetrabutylammonium hydrogendifluoride (**2**) (TBABF) (Scheme 1). Since trialkylsilanes did not react



Scheme 1



Scheme 2



Scheme 3

with **2** under these reaction conditions, we developed an alternative procedure to generate trialkyl(difluoro)silicates **5** through the reaction of TBABF with a silyl enol ether **4** (Scheme 2). The reaction of **2** with (cyclopentenyl-oxy)triphenylsilane (**4a**) or (cyclopentenyl-oxy)diphenylmethylsilane (**4b**) generated the known crystalline quaternary (difluoro)silicates **5a,b**<sup>7</sup> in good yields (85-87%) confirming the effectiveness of the procedure. However, in the case of trimethyl- and *t*-butyldimethylsilyl enol ethers **4c,d**, the corresponding trialkyl(difluoro)silicates **5c,d** could not be isolated as a consequence of their low stability.<sup>8</sup> On the contrary, after trapping of the transient ammonium enolate by **2**, the short lived pentacoordinate anion silicon intermediate **5** generated the fluorosilane **7**, cyclopentanone **6** and tetrabutylammonium fluoride (**8**) (TBAF). Indeed, after treatment at 0.01 mmHg at 20°C, examination of the reaction mixture by <sup>1</sup>H and <sup>19</sup>F NMR spectroscopy indicates that the residual brown syrupy oil basically consists of TBAF (**8**) in a low hydration state.<sup>9</sup> This highly reactive form of TBAF, although relatively stable at room temperature, promotes a fast palladium catalysed homocoupling of aryl halides. The reaction of 1-iodo-4-nitrobenzene (**9b**) in dimethylsulfoxide (DMSO) at 120°C in the presence of **8**, generated *in situ* according to Scheme 2,<sup>10</sup> and 2.5 mol % of allylpalladium chloride dimer [PdCl(π-C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>] **10** afforded 77% of 4,4'-dinitrophenyl (**11b**) after only 1.5 hours (Table 1, entry 2). The water content of TBAF is crucial for the good outcome of the reaction since **11b** was generated in a 10% yield only after 24 hours by using commercially available TBAF·3H<sub>2</sub>O (entry 1).

Table 1. Homocoupling of 1-iodo-4-nitrobenzene (**9b**)<sup>a</sup>

entry	catalyst	additive	t (h)	<b>11b</b> (%) <sup>b</sup>
1	<b>10</b>	TBAF·3H <sub>2</sub> O	24	10
2	<b>10</b>	[ <b>4c</b> + TBABF] ( <b>8</b> )	1.5	77
3	<b>10</b>	[ <b>4d</b> + TBABF] ( <b>8</b> )	1	71
4	<b>10</b>	TBAF·0.5H <sub>2</sub> O	20	68
5	<b>10</b>	TBABF	7	55 <sup>c</sup>
6	<b>10</b>	Bu <sub>3</sub> N	24	38
7	Pd(OAc) <sub>2</sub>	Bu <sub>3</sub> N	24	46
8	Pd(OAc) <sub>2</sub>	[ <b>4c</b> + TBABF] ( <b>8</b> )	24	34 <sup>c</sup>

<sup>a</sup> The reaction was carried out at 120°C in DMSO (3ml) using 0.35 mmol of **9b** in the presence of 0.0082 mmol of the catalyst and 0.7 mmol of additive. <sup>b</sup> Isolated yields. <sup>c</sup> 80% conversion.

In a control experiment TBAF·3H<sub>2</sub>O was dehydrated by gently heating for 31 hours under sonication and high vacuum.<sup>11</sup> TBAF·0.5H<sub>2</sub>O thus obtained generated the homocoupled product **11b** in 68% yield in 20 h (entry 4). It seems likely that the slower reaction can be ascribed to a partial decomposition to the less reactive TBABF (**2**) taking place during dehydration of the commercial salt.<sup>11</sup> In fact under the same reaction conditions TBABF afforded 55% of **11b** in 7 hours without complete conversion of **9b** (entry 5). The use of tributylamine (**12**) instead of **8** or Pd(OAc)<sub>2</sub> as a substitute for **10** gave lower yields (entries 6-8).

A representative list of aryl halides **9a-g** bearing various functionalities were converted into the corresponding biaryl derivatives **11a-g** in moderate to good yield (Table 2). Iodo- and bromoaryls can be successfully used. 4-Bromoacetophenone (**9f**) generated 4,4'-diacetylbiaryl (**11f**) in a 75% yield, whereas the homocoupling of 2-bromoacetophenone (**9g**) did not take place indicating that the reaction is sensitive to steric hindrance.

**Table 2.** Palladium Catalysed Homocoupling of Aryl Halides **9a-g**<sup>a</sup>

substrate <b>9</b>	t (h)	product <b>11a-g</b>	yield (%) <sup>b</sup>
<b>a</b> PhI	4.5		82
<b>b</b> 4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -I	1.5		77
<b>c</b>	3		58
<b>d</b>	15		48
<b>e</b> 3-F-C <sub>6</sub> H <sub>4</sub> -I	2.5		68
<b>f</b> CH <sub>3</sub> CO-C <sub>6</sub> H <sub>4</sub> -Br	7.0		75
<b>g</b>	15	-	-

<sup>a</sup> The reaction was carried out at 120°C in DMSO (3 ml) using 0.35 mmol of substrate **9** in the presence of 0.0082 mmol of the catalyst **10** and 0.7 mmol of TBAF (**8**). <sup>b</sup> Isolated yields.

In conclusion we developed a simple procedure for the phosphine-free palladium catalysed homocoupling of aryl halides. Further work is under way in order to determine the exact nature of the process and will be reported in due course.

### Acknowledgement

Financial support by CNR and MURST is gratefully acknowledged.

### References and Notes

- (1) Semmelhack, M. F.; Helouit, P. M.; Jones, L. D. *J. Am. Chem. Soc.* **1971**, *93*, 5308.
- (2) Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73.
- (3) Miyauro, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
- (4) Negishi, E.; *Acc. Chem. Res.* **1982**, *15*, 340.
- (5) Penalva, V.; Hassan, J.; Lavenot, L.; Gozzi, C.; Lemaire, M. *Tetrahedron Lett.* **1998**, *39*, 2559.
- (6) Albanese, D.; Landini, D.; Penso, M. *Tetrahedron Lett.* **1995**, *36*, 8865.
- (7) A solution of **4b** (280 mg, 1 mmol) in benzene (1 ml) is added dropwise to **2** (281 mg, 1 mmol) dissolved in 1 ml of benzene. After stirring under nitrogen at 20°C for 20 h the solvent is evaporated and the residue treated with hexane/benzene 3/1 (3 x 2 ml) and decanted. The solid residue is then filtered affording 406 mg (yield 85%) of **5b**, mp 68-69°C (lit. ref. 7, 70°C). The same procedure afforded 470 mg of **5a** (yield 87%), mp 150°C, by direct filtration of the reaction mixture followed by washing the solid with 1 ml of benzene.
- (8) Christe, K. O.; Wilson, W. W.; Wilson, R. D.; Bau, R.; Feng, J. *J. Am. Chem. Soc.* **1990**, *112*, 7619.
- (9) Karl-Fischer titration of different batches of TBAF·*n*H<sub>2</sub>O indicated a hydration range *n* = 0.6-0.7.
- (10) **2** (1.13 g, 4 mmol) is dissolved in 2 ml of THF and added dropwise to a THF (2 ml) solution of **4c** (625 mg, 4 mmol). After stirring under nitrogen for 1h at 20°C the mixture was evaporated affording 1.04 g of TBAF (95%). This material was used for the homocoupling reaction. [PdCl(π-C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>] **10** (3 mg, 0.0082 mmol) and the aryl halide (0.35 mmol) are added to a DMSO (3 ml) solution of TBAF (**8**) (192 mg, 0.70 mmol). After stirring under nitrogen at 120°C for the time indicated in Table 2, the mixture is cooled to room temperature, treated with brine and extracted with Et<sub>2</sub>O (3 x 5 ml). The organic layer is washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The residue is purified by silica-gel chromatography affording biaryls **11a-f** whose physical and spectroscopic data match those reported in the literature.
- (11) Albanese, D.; Landini, D.; Penso, M. *J. Org. Chem.* in press.