Preparation of functionalized biaryl compounds *via* cross-coupling reactions of aryltrialkoxysilanes with aryl bromides

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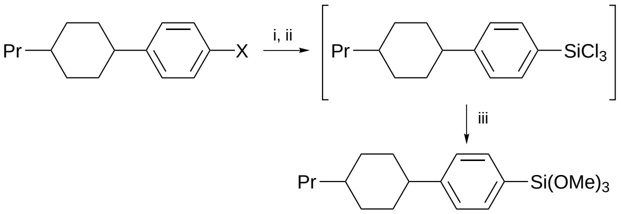
Aryltrimethoxysilanes react with aryl bromides in the presence of fluoride ion and palladium catalysts to give the corresponding biaryl compounds in good yields with high chemoselectivity.

Many functional organic materials and natural bioactive organic compounds contain biaryl units in their structures. In particular, the proportion of biaryl compounds in liquid crystalline compounds is high, and many biaryl-type liquid crystalline compounds have been developed.[1] In recent years, considerable interest in the construction of functionalized biaryl components *via* aryl–aryl coupling reactions has been aroused.[2]

Arylboronic acids are known to undergo cross-coupling reactions with aryl halides.[3] Recently, pentacoordinate aryl silicates activated by fluoride ion have been shown to exhibit high reactivity in coupling reactions, and different kinds of pentacoordinate aryl silicates have been used for aryl–aryl cross-coupling reactions.[2c,2f,4]



1a 64% (X = Br)
66% (X = I)

Scheme 1 *Reagents and conditions*: i (X = Br) Mg (1.1 equiv.), THF, 50 °C, 2 h; (X = I) BuLi (1.0 equiv.), hexane, −70 °C, 2 h; ii (X = Br) $SiCl_4$ (1.5 equiv.), 0 °C to room temp., 17 h; (X = I) $SiCl_4$ (2 equiv.), −70 °C to room temp., 17 h; iii, MeOH (8.0 equiv.), pyridine (8.0 equiv.), 0 °C, 30 min

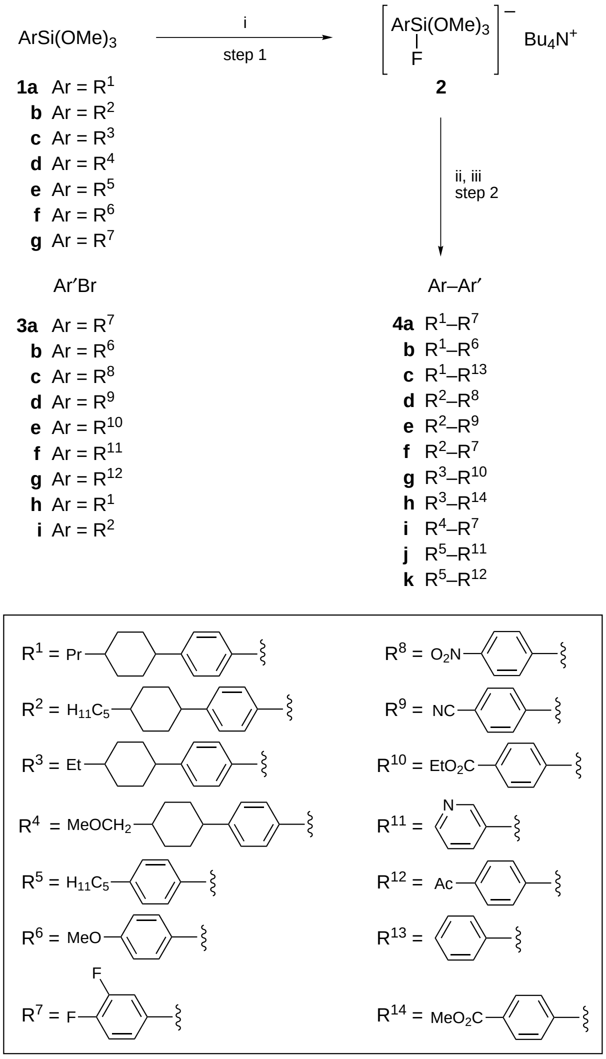
Table 1 Preparation of biphenyl **4a** from **1a** and **3a**[a]

		Step 2		
Entry	Catalyst (mol%)	Solvent	*t*/h	Yield of **4a** (%)
1[b]	$Pd(OAc)_2$ (5)	DMF	3	2
2	$Pd(OAc)_2$ (10)	THF–DMF	3	49
3	$Pd(Ph_3P)_4$ (5)	THF–DMF	3	71
4[c]	$Pd(Ph_3P)_4$ (5)	THF-Toluene	10	91
5	$Pd(Ph_3P)_4$ (5)	THF	3	19
6	$Pd(Ph_3P)_4$ (5)	Toluene[d]	3	94
7	$Pd(OAc)_2$ (5)	Toluene[d]	3	46
8	$Pd(OAc)_2$ (5)–Ph_3P (5)	Toluene[d]	3	83
9	$Pd(OAc)_2$ (5)–Ph_3P (10)	Toluene[d]	3	89
10	$Pd(OAc)_2$ (5)–Ph_3P (15)	Toluene[d]	3	90
11	$Pd(OAc)_2$ (5)–Ph_3P (20)	Toluene[d]	3	80

[a] TBAF (1.05 equiv.) was used as a fluoride ion source, and Step 1 was carried out in THF for 30 min at room temperature, unless otherwise noted. [b] Step 1: KF (5 equiv.) was used instead of TBAF and the reaction was carried out for 3 h at 100 °C in DMF; Step 2: Reaction was carried out for 3 h at 120 °C. [c] Reaction time of Step 2 was 10 h. [d] Before Step 2, THF was removed under reduced pressure.

Here we report the reactivity of a new type of pentacoordinate aryl silicate, aryl(fluoro)trimethoxosilicate(1−) **2**, which was easily obtained from aryltrimethoxysilane **1** and a fluoride ion source. At the outset, preparation of **1a** was attempted in several ways, and reactions using tetrachlorosilane gave **1a** in acceptable yields after distillation (Scheme 1).[4] Other arylsilanes **1b**–**g** were also prepared using this method and they were so stable that no decomposition occurred during ordinary aqueous work-up. Although direct reaction of the aryl Grignard or lithium reagent with tetramethoxysilane could afford **1a**, its yield was low (*ca.* 35%).[5] The main product of the reaction was diaryl(dimethoxy)silane.

4-(*trans*-4-*n*-Propylcyclohexyl)-3′,4′-difluorobiphenyl **4a**, which is used in active matrix liquid crystal displays, was



Scheme 2 *Reagents and conditions*: i, Bu_4NF (1.05 equiv.); ii, Ar'Br (**3a**–**i**) (1.2 equiv.); iii, Pd catalyst, reflux

chosen as a model compound, and cross-coupling reactions of 4-(*trans*-4-*n*-propylcyclohexyl)phenyltrimethoxysilane **1a** with 1-bromo-3,4-difluorobenzene **3a** were attempted.[6] Arylsilane **1a** was stirred with KF in DMF and then the reaction mixture was reacted with **3a** for 3 h at 120 °C in the presence of a catalytic amount of palladium(II) acetate [Pd(OAc)$_2$]. However, the yield of the desired product **4a** was only 2% (Table 1, entry 1). When the fluoride ion source and the solvent were changed to tetrabutylammonium fluoride (TBAF)† and THF–DMF mixed solvents, respectively, the yield of **4a** increased to 49% (entry 2). In addition, changing of the catalyst to tetrakis-(triphenylphosphine)palladium(0) [(Ph$_3$P)$_4$Pd] gave **4a** in 71% yield (entry 3). Under theses conditions, reactions were carried out in several solvents (entries 4–6), and toluene was found to be the best solvent (entry 6).

Although the yield of **4a** was 46% when Pd(OAc)$_2$ was used as a catalyst, the addition of Ph$_3$P had a remarkable effect (entries 8–11). The best molar ratio of Pd(OAc)$_2$ and Ph$_3$P was 1 : 3, which gave **4a** in 90% yield (entry 10). From the above results, it can be seen that (Ph$_3$P)$_4$Pd and Pd(OAc)$_2$–Ph$_3$P are good catalysts for the reaction. Taking the price, stability and simplicity of handling into account, Pd(OAc)$_2$–Ph$_3$P is the more practical.

The reactions of several arylsilanes **1** with aryl bromides were investigated next under the conditions used in Table 1, entry 10 (Scheme 2). They proceeded with high chemoselectivity and the results are summarized in Table 2.

All reactions gave the desired biaryl derivatives in good yields except entry 2. In particular, when **3a** was used, **4a**, **4f**, and **4i** were obtained in more than 82% yield within 10 h (entries 1, 5 and 7). In general, as liquid crystalline compounds having fluorine atoms on their aromatic rings are known to exhibit good properties, the present reaction is very useful for the preparation of fluorinated liquid crystalline compounds.[6,7]

Table 2 Preparation of a variety of biaryl compounds[a] **4**

Entry	1	3	*t*/h	Product (% yield)
1[b]	**1a**	**3a**	3	**4a** (90)
2	**1a**	**3b**	10	**4b** (61), **4c** (29)
3	**1b**	**3c**	25	**4d** (74)
4	**1b**	**3d**	30	**4e** (87)
5	**1b**	**3a**	10	**4f** (92)
6	**1c**	**3e**	30	**4g** (84), **4h** (4)
7	**1d**	**3a**	30	**4i** (82)
8	**1e**	**3f**	30	**4j** (72)
9	**1e**	**3g**	30	**4k** (84)
10	**1f**	**3h**	30	**4b** (75)
11	**1g**	**3i**	30	**4f** (78)

[a] Pd(OAc)$_2$ (5 mol%)-Ph$_3$P (15 mol%) was used as catalyst and the reactions were carried out in toluene. [b] The same data as shown in Table 1, entry 10.

The reaction of 4-bromoanisole **3b** with **1a** gave not only the desired **4b** (61%) but also the demethoxylated product **4c** (29%; entry 2). Although the mechanism of demethoxylation has not been elucidated, it is most probable that demethoxylation occurs before the formation of the new sp^2–sp^2 bond because the reaction of the reverse combination of entry 2 showed no formation of **4c** (entry 10).

In these reactions, homo-coupling products were not detected and other byproducts were also very rare, which made purification of the products straightforward. Another advantage of this reaction system is that **1** is very resistant to hydrolysis, and thus can be stored for a long time without special precautions to exclude moisture.

Footnotes

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† TBAF containing 5 mass% water was purchased from Aldrich and used after drying with molecular sieves 4 Å.

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