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Highly efficient cross-coupling reactions with the perfluoroorganotrifluoroborate salts K [R_FBF_3] ($R_F = C_6F_5$, $CF_2{=}CF$)†

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Abstract—Potassium pentafluorophenyl- and trifluorovinyltrifluoroborates, both containing electron-poor organo groups, reacted with iodobenzene and *p*-substituted iodobenzenes in the presence of palladium compounds and stoichiometric amounts of silveroxide to the fluorinated cross-coupling products in very good yields. Substituted bromobenzenes were less efficient substrates.

The palladium-catalysed cross-coupling of organic electrophiles with organoboron compounds is a very convenient and widely used tool for the carbon–carbon bond formation.[1] Boronic acids [organo(dihydroxy)boranes] and their esters commonly are used as organoboron compounds in the presence of bases.[1] However, polyfluorophenyl- and perfluoroalkenylboronic acids or their esters are not stable under basic conditions.[2]

Recently, the air, moisture, and thermally stable organotrifluoroborate salts were offered as an alternative to boronic acids and their esters.[3–6] Genet has previously reported Pd-catalysed cross-coupling reactions of potassium organotrifluoroborates with arenediazonium tetrafluoroborates.[3] Additionally, he showed that substrates with halogen functionalities were too unreactive electrophiles.[3,7] Positive results were obtained by Chen with the strong electrophilic diaryliodonium substrates.[4] Molander published the cross-coupling of potassium alkyl-, alkenyl-, and aryltrifluoroborates with organic halides and triflates.[5] Batey reacted tetraalkylammonium organotrifluoroborates with aryl- and alkenylhalides efficiently in cross-coupling reactions.[6] In contrast to these well established hydrocarbon organoboron reagents, the reactivity of polyfluorinated organoboron compounds in cross-coupling processes was practically unstudied. It is well known, that the chemical properties of poly- and especially perfluorinated organic and organoelement compounds differ significantly from that of their hydrocarbon or the less-fluorinated analogues, and the quantitative distinguishes cannot be described merely as an additive effect of the number of fluorine atoms (see fundamental survey[8]). In the case of perfluoroorganotrifluoroborates, the organo group takes over a part of the negative net-charge of the borate anion. This charge is mainly distributed to the carbon-bonded fluorine atoms. Consequently, the nucleophilicity at C(1) is low in comparison to the hydrocarbon analogues and the reactivity of the polyfluorinated organotrifluoroborate salts in cross-couplings is diminished. This circumstance impedes the use perfluoroorganotrifluoroborates in Suzuki type cross-coupling reactions. Recently, we have found that polyfluorinated phenyl- and ethenyltrifluoroborate salts are principally able to undergo Pd-catalysed cross-coupling with strong electrophilic substrates, like benzenediazonium salts.[9]

In this paper, we studied the conditions for the efficient interaction of potassium pentafluorophenyl- and trifluorovinyltrifluoroborates with *p*-I-C_6H_4R [R = H, F, CH_3, NO_2, C(O)OEt] and *p*-Br-C_6H_4R [R = F, OCH_3, NO_2] as model partners.

Keywords: perfluorophenyltrifluoroborate salt; perfluoroethenyltrifluoroborate salt; cross-coupling; palladium; silveroxide.

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Table 1 summarises the investigated reactions of K [$C_6F_5BF_3$] (**1**) with *p*-I-C_6H_4F (**2a**) (Scheme 1).

First, we want to demonstrate the fundamental differences between perfluorophenyl- and phenyltrifluoroborates by applying the same conditions reported by Molander for hydrocarbon trifluoroborate salts to the perfluorinated one.[5b] Different to K [$C_6H_5BF_3$], K [$C_6F_5BF_3$] does not undergo a transformation of the BF_3 group (^{19}F NMR) when refluxed in MeOH in the presence of 3 equiv. of the base K_2CO_3 and catalytic amounts of $Pd(OAc)_2$ (Table 1, entry 1). In this attempted cross-coupling no reaction proceeded. **1** remained unchanged and no hydrodeboration could be observed, whereas in the absence of K_2CO_3 traces of hexafluorobiphenyl (**3a**) were obtained and **1** underwent a nearly complete hydrodeboration. The replacement of protic MeOH by the polar and basic solvents DME or DMF suppressed the hydrodeboration, but no cross-coupled products were detected.[9]

In DME or DMF instead of protic MeOH and in the presence of Ag[BF_4] in a comparable amount to the Pd-catalyst and stoichiometric amounts of AgF as fluoro-base for removing the acidic cross-coupling co-product BF_3, borate **1** reacted with **2a** even at 20°C, but with unsatisfactory conversions and yields (Table 1, entries 2–4). The increase of the reaction temperature did not influence the result positively (Table 1, entry 5). A quantitative conversion of **2a** occurred when the cross-coupling reaction was carried out in toluene (100°C) in the presence of the bases Ag_2O (1 equiv.) and K_2CO_3 (2 equiv.).[10] The reaction was catalysed by $Pd(OAc)_2$/2 P(*o*-Tol)$_3$ (Table 1, entry 6). In the absence of the phosphane ligand the reaction did not proceed (Table 1, entry 7). The use of the individual complex $Pd_2(\mu\text{-}OAc)_2(P(o\text{-}Tol)_2C_6H_4CH_2)_2$ which was assumed to be formed under the reaction conditions[11] gave biphenyl **3a** only in 5% yield (20% conversion of **2a**, Table 1, entry 8). The increase of Ag_2O to 1.2 equiv. improved the yield of 2,3,4,4′,5,6-hexafluorobiphenyl (**3a**) to 89% (Table 1, entry 9). It should be noted that K_2CO_3 does not take part directly in the reaction, but it avoids traces of toluene soluble pentafluorophenyl-containing impurities formed during the reaction. In the absence of Ag_2O there proceeded no formation of **3a** (Table 1, entry 10). The variation of the catalyst from [$Pd(PPh_3)_4$] to $Pd(OAc)_2$/2 PPh_3 increased the yield of the target product **3a** from 71% to 92% (Table 1, entries 11 and 12). $Pd(OAc)_2$/2 P(*o*-Tol)$_3$ showed a comparable good yield of 89%, even in the absence of K_2CO_3 (Table 1, entry 9). Without a Pd-catalyst there was no reaction.

The optimised conditions presented in entry 12 (Table 1) was used for the following investigations of **1** with iodobenzene and the *p*-substituted iodo- and bromobenzenes **2b**–**h**, respectively (Scheme 2, Table 2).

Table 1. The cross-coupling of K [$C_6F_5BF_3$] **1** with *p*-I-C_6H_4F **2a**[a]

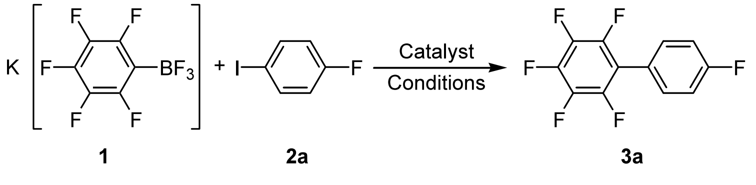
Entry	Catalyst	Conditions	Conversion of **2a** (%)	Yield of **3a** (%)
1	$Pd(OAc)_2$	**A**, MeOH, reflux	No reaction	–
2	[$Pd(PPh_3)_4$]	**B**, DME, 20°C[b]	38	22
3	[$Pd(PPh_3)_4$]	**B**, DMF, 20°C[c]	23	10
4	$Pd(OAc)_2$/2 P(*o*-Tol)$_3$	**B**, DME, 20°C[c]	22	21
5	[$Pd(PPh_3)_4$]	**B**, DMF, 100°C	3	Traces
6	$Pd(OAc)_2$/2 P(*o*-Tol)$_3$	**C**, toluene, 100°C	100	67
7	$Pd(OAc)_2$	**C**, toluene, 100°C	No reaction	–
8	[d]	**C**, toluene, 100°C	20	5
9	$Pd(OAc)_2$/2 P(*o*-Tol)$_3$	**D**, toluene, 100°C	100	89
10	$Pd(OAc)_2$/2 P(*o*-Tol)$_3$	**A**, toluene, 100°C	No reaction	–
11	[$Pd(PPh_3)_4$]	**C**, toluene, 100°C	100	71
12	$Pd(OAc)_2$/2 PPh_3	**C**, toluene, 100°C	100	92
13	None	**C**, toluene, 100°C	No reaction	–

[a] **General procedure**: **1** (0.6 mmol), catalyst (0.1 equiv.), additives [**A**: K_2CO_3 (2–3 equiv.); **B**: Ag[BF_4] (0.12 equiv.)+AgF (1 equiv.); **C**: Ag_2O (1.2 equiv.)+K_2CO_3 (2 equiv.); **D**: Ag_2O (1.2 equiv.)] were placed into the flask under an atmosphere of dry argon. **2a** (0.5 mmol) and the degassed solvent were added and the reaction mixture was stirred for 3 h. After cooling to 20°C (if necessary) $C_6H_5CF_3$ (quant. stand., 5 µl, 0.041 mmol) was added and the composition of reaction mixture was analysed by ^{19}F NMR.

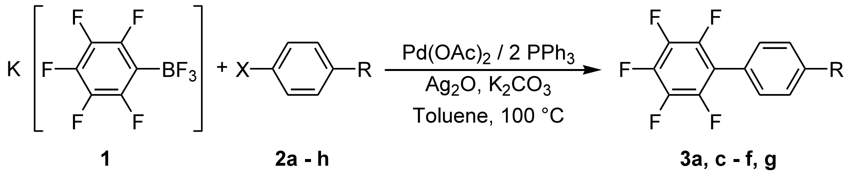
[b] Reaction time 18 h.

[c] Reaction time 14 h.

[d] $Pd_2(\mu\text{-}OAc)_2[P(o\text{-}Tol)_2C_6H_4CH_2]_2$ (0.05 equiv.).



Scheme 1.



X = Br, I; R = NO_2, $C(O)OC_2H_5$, F, H, CH_3, OCH_3

Scheme 2.

Table 2. The cross-coupling of K [$C_6F_5BF_3$] **1** with *p*-X-C_6H_4R **2a**–**h**[a]

Entry	R	X	Conversion of **2** (%)	Yield of **3** (%)[b,c]
1	F (**2a**)	I	100	92 (76)
2	F (**2b**)	Br	30	28
3	NO_2 (**2c**)	I	100	>98 (81)
4	H (**2d**)	I	100	>98 (90)
5	CH_3 (**2e**)	I	100	98 (93)
6	CH_3O (**2f**)[d]	Br	nd	25
7	NO_2 (**2g**)[e]	Br	nd	36
8	NO_2 (**2g**)[d]	Br	nd	62
9	C(O)OEt (**2h**)	I	100	>98 (82)

[a] **General procedure**: **1** (165 mg, 0.6 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), PPh_3 (26 mg, 0.1 mmol), Ag_2O (140 mg, 0.6 mmol), and K_2CO_3 (138 mg, 1 mmol) were placed into the flask under an atmosphere of dry argon. **2a**–**h** (0.5 mmol) and degassed toluene (2 ml) were added and the reaction mixture was stirred at 100°C for 3 h. After cooling to 20°C, $C_6H_5CF_3$ (5 µl, 0.041 mmol) was added and the motherliquor was analysed by ^{19}F NMR. For isolation of the product the mixture was diluted with pentane and filtrated. After removing of the solvent practically pure products were received. The ^{1}H and ^{19}F NMR spectra of the obtained fluorinated biphenyls coincided with the published spectra of the known compounds.[9,12,13]

[b] Determined by ^{19}F NMR.

[c] Preparative yields are given in brackets.

[d] Reaction time 24 h.

[e] Reaction time 5 h.

All iodobenzenes **2a**, **2c**–**e**, and **2h** readily react with potassium pentafluorophenyltrifluoroborate giving the corresponding biphenyls in very high yields (Table 2). The *p*-substituted bromobenzenes are less reactive. Thus, only 30% conversion and 28% yield were achieved for *p*-fluorobromobenzene (Table 2, entry 2) within 3 h, whereas *p*-bromoanisole needed 25 h to form the corresponding biphenyl **3f** in 25% only (Table 2, entry 6). *p*-Nitrobromobenzene reacted with potassium pentafluorophenyltrifluoroborate to yield 36% **3g** within 5 h (Table 2, entry 7) and 62% within 24 h (Table 2, entry 8).

It was a challenge to extend this investigation on cross-coupling to a prototype of perfluorinated alkenyltrifluoroborates (Scheme 3). In potassium trifluorovinyltrifluoroborate (**4**) C(1) is less nucleophilic than in **1** caused by the directly bonded fluorine atom. Indeed, salt **4** was less reactive than the pentafluorophenyl analogue **1**. Thus **4** reacted with **2a** to the corresponding tetrafluorostyrene **5** with 63% conversion of **2a** within 3 h and 54% yield. When the reaction time was increased to 8 h the conversion of **2a** reached 100% and the yield 76%.

Acknowledgements

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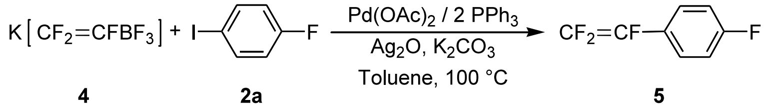

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