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The palladium-catalysed cross-coupling reaction of lithium polyfluorophenyltrimethoxyborates with 4-fluoroiodobenzene☆

Hermann-Josef Frohn[a,*], Nicolay Yu. Adonin[b], Vadim V. Bardin[b], Vladimir F. Starichenko[b]

[a]*Institute of Chemistry, Inorganic Chemistry, University Duisburg-Essen, Lotharstr. 1, MC 363, D-47048 Duisburg, Germany*
[b]*N.N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, SB RAS, Acad. Lavrentjev Avenue 9, 630090 Novosibirsk, Russia*

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Abstract

$Li[C_6F_5B(OMe)_3]$, $Li[C_6HF_4B(OMe)_3]$ (all three isomers) and $Li[3,4,5\text{-}C_6H_2F_3B(OMe)_3]$ are the first examples of polyfluorophenyltrimethoxyborate salts which have been applied as reagents to Pd-catalysed cross-coupling reactions. A series of polyfluorinated biphenyls $C_6H_{5-n}F_n\text{-}C_6H_4F\text{-}4'$ were obtained from $Li[C_6H_{5-n}F_nB(OMe)_3]$ and the model substrate $4\text{-}FC_6H_4I$ in the presence of Pd catalysts. The influence of the number and the position of fluorine atoms in the polyfluorophenyltrimethoxyborate salts on the reactivity in the coupling reaction was elucidated.

Keywords: Polyfluoroarylborates; Methoxyborates; Cross-coupling; Polyfluorobiphenyls; Palladium catalysis; Silver oxide

1. Introduction

The palladium-catalysed cross-coupling reaction of organic halides with organoboron compounds is a convenient method for synthesising biaryl, ethenylarene, and ethynylarene skeletons, which are useful intermediates, e.g. for biologically active compounds, chiral ligands, liquid crystals, dyes, etc. [2]. The wide use of this synthetic method is favoured for several reasons, as a rule, organoboron compounds are easily accessible, not expensive, not moisture and air sensitive and do not demand special handling conditions. Furthermore, the inorganic by-products of the reaction are non-toxic and can be easily separated from the target products.

The original procedure of Suzuki and co-workers [3] was developed primarily for organodihydroxyboranes (organoboronic acids) and for organodialkoxyboranes and was later modified [4]. Frequently, these reactions are carried out in the presence of aqueous bases. However, aryldihydroxyboranes and aryldialkoxyboranes with electron-withdrawing substituents in the *ortho*-positions often do not give satisfactory results under these conditions or they are consumed in competitive hydrodeboration reactions [5]. Pentafluorophenyldihydroxyborane belongs to this group of reagents. Only recently, two unsuccessful attempts to apply it to cross-coupling reactions have been reported, both under basic conditions [6]. This behaviour is in agreement with our recent results on the reactivity of fluorine-containing aryldihydroxyboranes, $C_6H_{5-n}F_nB(OH)_2$, towards bases which revealed the significant acceleration of hydrodeboration with an increasing number of fluorine atoms from $n = 1$ to 5 [1].

To avoid this property, we used potassium polyfluorophenyltrifluoroborates, $K[C_6H_{5-n}F_nBF_3]$, instead of the corresponding polyfluorophenyldihydroxyboranes and succeeded in the first cross-coupling of polyfluoroorganoboron compounds with arenediazonium tetrafluoroborates as carbon electrophiles [7]. Continuing our efforts in this field, we decided to study the reactivity of the closely related salts $Li[C_6H_{5-n}F_nB(OMe)_3]$ in cross-coupling reactions with 4-fluoroiodobenzene as a model substrate. To our knowledge, only the non-fluorinated salts $M[RB(OMe)_3]$ ($M = Li$, Na) were used previously in cross-coupling reactions with R = alkynyl [8] and hetaryl [9] groups.

2. Results and discussion

The previously unknown salts $Li[Ar_FB(OMe)_3]$ ($Ar_F = C_6F_5$ (**1a**), $2,3,4,5\text{-}C_6HF_4$ (**1b**), $2,3,5,6\text{-}C_6HF_4$ (**1c**), 2,3,4,

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☆ Part 3 in the series "polyfluoroorganoboron oxygen compounds" [1].

[*] Corresponding author. Tel.: +49-203-379-3310; fax: +49-203-379-2231.
E-mail address: frohn@uni-duisburg.de (H.-J. Frohn).

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$$\mathrm{ArH} \xrightarrow{\mathrm{BuLi}} \mathrm{ArLi} \xrightarrow{\mathrm{B(OMe)_3}} \underset{\mathbf{1a-e}}{\mathrm{Li\,[ArB(OMe)_3]}}$$

Scheme 1.

6-C_6HF_4 (**1d**) and 3,4,5-$C_6H_2F_3$ (**1e**)) were prepared by the nucleophilic arylation of $B(OMe)_3$ with ArLi and isolated as white moisture-sensitive solids (see also preliminary communication [10]) (Scheme 1).

We examined the reaction of **1a** with 4-fluoroiodobenzene (**2**) under different conditions (solvent, temperature, catalyst, additives) and monitored these reactions (Eq. (1)) by ^{19}F NMR spectroscopy (Table 1).

$$\underset{\mathbf{1a}}{\mathrm{Li[C_6F_5B(OMe)_3]}} + \underset{\mathbf{2}}{\mathrm{4\text{-}FC_6H_4I}} \overset{\text{catalysts}}{\underset{\text{conditions}}{\rightarrow}} \underset{\mathbf{3a}}{\mathrm{C_6F_5\text{-}C_6H_4F\text{-}4'}} \qquad (1)$$

The reaction of **1a** with **2** in DME at 65–70 °C in the presence of palladium acetate (5 mol%) gave 2,3,4,4′,5,6-hexafluorobiphenyl (**3a**) in 26% yield (40% conversion of substrate **2** within 1 h (entry 1)). The use of toluene instead of DME as solvent under the same conditions yielded 9% of the target product **3a** (21% conversion of **2**) (entry 2). Carrying out the reaction in boiling DME (85 °C) decreased both, the yield of **3a** and the conversion of **2** (entry 3). A similar disadvantageous influence on the reactivity was observed when the cross-coupling was carried out for 12 h at 20 °C (entry 4). The reaction in toluene at 100–110 °C resulted in 50% conversion of substrate **2** after 7 h, but the yield of biphenyl **3a** was only 23% (entry 5). In addition, we studied the influence of DME on the lithium salts and of the amount of catalyst on the effectiveness of the cross-coupling both at the fixed temperature of 80 °C in toluene. The influence of the amount of DME was lower in comparison to that of the amount of catalyst (entries 6–8). In the presence of 10 mol% of palladium acetate, the yield of the target biphenyl was 50% (entry 6). When the reaction was carried out in toluene at 100 °C without addition of DME, 2,3,4,4′,5,6-hexafluorobiphenyl (**3a**) was obtained in 25% yield only (26% conversion of **2** (entry 9)). Carrying out the reaction in DME in the presence of the ligand P(*o*-Tol)$_3$ resulted in lower yields of **3a** (entry 10). The addition of the Lewis acid $B(OMe)_3$ (entry 11) or of the hard base KF (entry 12) gave no satisfactory results. In all reactions with $Pd(OAc)_2$ as catalyst (entries 1–12) beside signals due to expected biphenyls, a C_6F_5-Pd species was observed in the ^{19}F NMR spectra. The highest yield of **3a** was achieved when $[Pd(PPh_3)_4]$ was used as catalyst, being 60% (90% conversion of **2** (entry 13)).

Table 1
Reactions of lithium polyfluorophenyltrimethoxyborates Li[Ar$_F$B(OMe)$_3$] (**1a**–**1e**) with 4-fluoroiodobenzene (**2**)

Entry	Ar$_F$	**1a**–**1e** (mmol)	**2** (mmol)	Catalyst (mmol)	Solvent (ml) and additives (mmol)	Temperature (°C)	Time (h)	Conversion of **2** (%)	Yield of **3** (%)[a]
1	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.027)	DME (1)	65–70	1	40	26 (66)
2	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.027)	Toluene (1)	65–70	1	21	9 (43)
3	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.027)	DME (1)	~85 (reflux)	1	13	7 (51)
4	C_6F_5 (**1a**)	0.67	0.5	$Pd(OAc)_2$ (0.027)	DME (1)	20	~12	23	6 (28)
5	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.027)	Toluene (1)	100–110	7	50	23 (46)
6	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.054)	Toluene (1) + DME (0.078)	80	3	ND	50
7	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.027)	Toluene (1) + DME (0.078)	80	3	ND	18
8	C_6F_5 (**1a**)	0.86	0.5	$Pd(OAc)_2$ (0.027)	Toluene (1) + DME (0.16)	80	3	ND	19
9	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.054)	Toluene (1)	100	4	26	25 (96)
10	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.060)	DME (1) + P(*o*-Tol)$_3$ (0.12)	80	1	10	9 (95)
11	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.031)	DME (1) + $B(OMe)_3$ (0.028)	80	3	ND	20
12	C_6F_5 (**1a**)	0.75	0.5	$Pd(OAc)_2$ (0.050)	DME (1) + KF (1.5)	65	1	20	17 (83)
13	C_6F_5 (**1a**)	0.75	0.5	$[Pd(PPh_3)_4]$ (0.050)	Toluene (1)	100	2.5	98	60 (63)
14	2,3,4,5-F_4C_6H (**1b**)	0.89	0.5	$[Pd(PPh_3)_4]$ (0.050)	Toluene (1)	100	3	60	8 (13)
15	2,3,4,5-F_4C_6H (**1b**)	0.89	0.5	$Pd(OAc)_2$ (0.050)	DME (1)	80	3	73	70 (96)[b]
16	2,3,5,6-F_4C_6H (**1c**)	0.9	0.5	$[Pd(PPh_3)_4]$ (0.050)	Toluene (1)	100	3	82	34 (42)
17	2,3,5,6-F_4C_6H (**1c**)	0.9	0.5	$Pd(OAc)_2$ (0.050)	DME (1)	80	3	42	40 (95)
18	2,3,4,6-F_4C_6H (**1d**)	0.92	0.5	$[Pd(PPh_3)_4]$ (0.050)	Toluene (1)	100	3	63	22 (35)
19	2,3,4,6-F_4C_6H (**1d**)	0.85	0.5	$Pd(OAc)_2$ (0.050)	DME (1)	80	3	35	32 (91)
20	3,4,5-$F_3C_6H_2$ (**1e**)	0.8	0.5	$[Pd(PPh_3)_4]$ (0.050)	Toluene (1)	100	3	60	3 (5)
21	3,4,5-$F_3C_6H_2$ (**1e**)	0.8	0.5	$Pd(OAc)_2$ (0.050)	DME (1)	80	3	45	32 (98)[c]

[a] Based on initial 4-FC_6H_4I (on reacted 4-FC_6H_4I).

[b] Biphenyl **4** (11% yield) was obtained beside **3b**.

[c] Biphenyl **5** (22% yield) was obtained beside **3e**.

Thus, the conversion of substrate **2** and the yield of the target biphenyl **3a** depend on different factors. The most essential seems to be the stability of the reagent, lithium pentafluorophenyltrimethoxyborate (**1a**), in the solvent used. Apparently, in DME at 65–70 °C, there is an optimal ratio of the cross-coupling reaction rate over the rate of decomposition of **1a** and, consequently, the best yield (entry 1). Salt **1a** is nearly insoluble in toluene (^{19}F NMR). The addition of stoichiometric amounts of DME increased the reactivity of the reagent by higher solubility in toluene on one hand, but on the other hand the rate of destruction of **1a** was raised also (entries 6–8).

The nature and quantity of the catalyst were important factors which determined the out come of the coupling reaction. With palladium acetate as catalyst, formation of a C_6F_5Pd-containing compound was observed [11]. Probably, the concurrent formation of a C_6F_5Pd compound was the main reason why only moderate yields of **3a** were achieved in entries 1–12. With $[Pd(PPh_3)_4]$ as catalyst we observed no C_6F_5Pd compound and obtained biphenyl **3a** in a reasonable yield (entry 13).

It was interesting to study the influence of one or two hydrogen atoms in the polyfluorinated phenyl group on the effectiveness of cross-coupling. Therefore, we compared the reactivity of lithium 2,3,4,5-tetrafluorophenyltrimethoxyborate (**1b**), 2,3,5,6-tetrafluorophenyltrimethoxyborate (**1c**), 2,3,4,6-tetrafluorophenyltrimethoxyborate (**1d**) and 3,4,5-trifluorophenyltrimethoxyborate (**1e**) with that of borate **1a** (Eq. (2)).

$$\underset{\mathbf{1b-1e}}{Li[C_6H_{5-n}F_nB(OMe)_3]} + \underset{\mathbf{2}}{4\text{-}FC_6H_4I} \xrightarrow[\text{conditions}]{\text{catalysts}} \underset{\mathbf{3b-3e}}{C_6H_{5-n}F_n\text{-}C_6H_4F\text{-}4'} \quad (n=1-4) \qquad (2)$$

Lithium polyfluorophenyltrimethoxyborates (**1b**–**1e**) reacted easily in DME with 4-fluoroiodobenzene (**2**) in the presence of palladium acetate, forming the cross-coupling products **3b**–**3e** in satisfactory to good yields (entries 15, 17, 19 and 21). The tetrakis(triphenylphosphine)palladium(0) catalysed reactions in toluene delivered the target biphenyls **3b**–**3e** in significant lower yields (entries 14, 16, 18 and 20).

For lithium 2,3,4,5-tetrafluorotrimethoxyborate and 3,4,5-trifluorotrimethoxyborate, both with H-atoms in the *ortho*-position(s), the formation of the corresponding symmetrical biphenyls (2,2′,3,3′,4,4′,5,5′-octafluorobiphenyl and 3,3′,4,4′,5,5′-hexafluorobiphenyl) was observed in addition to the cross-coupling products **3b** and **3e**.

The comparison of the results presented here with the data obtained in the cross-coupling of $K[C_6H_{5-n}F_nBF_3]$ [7] revealed the higher reactivity of the salts $Li[C_6H_{5-n}F_n\text{-}B(OMe)_3]$. Indeed, salt **1a** forms biphenyl **3a** when reacted with **2** while the related salt $K[C_6F_5BF_3]$ did not react with **2** under the same conditions [7]. Less differentiated reactivity of both classes was found in the presence of the additive Ag_2O. We were able to improve significantly the yield of **3a** in the cross-coupling of **1a** with **2** by using the additive Ag_2O. This behaviour is quite similar to the recently published results with salts $K[C_6H_{5-n}F_nBF_3]$ [12].

$$\underset{\mathbf{1a}}{Li[C_6F_5B(OMe)_3]} + \underset{\mathbf{2}}{4\text{-}FC_6H_4I} \xrightarrow[Ag_2O,\ \text{toluene},\ 100\,^{\circ}C, 3\,h]{[Pd(PPh_3)_4]} \underset{\mathbf{3a}}{C_6F_5\text{-}C_6H_4F\text{-}4'}\ (90\%) \qquad (3)$$

Further investigations of polyfluoroorganoboron compounds in cross-coupling reactions are in progress.

3. Conclusion

For the first time lithium salts of polyfluorophenyltrimethoxyborates were used as polyfluorophenylating reagents in Pd-catalysed cross-coupling reactions. Generally, salts of polyfluoroorgano alkoxyborates should be suitable fluoroorgano reagents in coupling reactions under aprotic conditions.

4. Experimental

The ^{1}H and ^{19}F NMR spectra were recorded on BRUKER WP 80 SY (^{1}H at 80.13 MHz and ^{19}F at 75.39 MHz at 32 °C) and BRUKER AVANCE 300 (^{1}H at 300.13 MHz, ^{7}Li at 116.64 MHz, ^{11}B at 96.29 MHz and ^{19}F at 282.40 MHz at 24 °C) spectrometers. The chemical shifts are referenced to TMS (^{1}H), 1.0 M LiBr in D_2O (^{7}Li), 15 vol.% $BF_3{\cdot}OEt_2$ in $CDCl_3$ (^{11}B) and $CFCl_3$ (^{19}F, with C_6F_6 as secondary reference (−162.9 ppm)). Raman spectra were recorded on a BRUKER RFS 100/S FT spectrometer. For measuring the infrared spectra (BRUKER IFS 66 FT spectrometer) of salts **1a** and **1c**, the samples were deposited on a polished silicon disc in a glove box. High resolution mass spectra were recorded on an AMD 604 spectrometer (EI mode, 70 eV).

Toluene, ether and $B(OMe)_3$ were distilled over sodium. Dichloromethane was distilled over P_4O_{10} and stored over molecular sieve (4 Å). DME was distilled over $Li[AlH_4]$ and stored under an atmosphere of dry argon. $Pd(OAc)_2$, $P(o\text{-}Tol)_3$, 2.5 M butyllithium in hexanes (all Aldrich) and KF (spray-dried) (Morita, Japan) were used as supplied. Tetrakis(triphenylphosphine)palladium(0) was prepared using the literature method [13]. All manipulations with lithium polyfluorophenyltrimethoxyborates were performed under an atmosphere of dry argon. Biphenyls **3a**–**3e** were identified by ^{19}F NMR spectroscopy [7].

4.1. Preparation of lithium polyfluorophenyltrimethoxyborates *1a*–*1e*

4.1.1. Lithium pentafluorophenyltrimethoxyborate (*1a*)

Pentafluorobenzene (7.6 g, 45 mmol) was dissolved in dry ether (40 ml) and cooled to −78 °C. Butyllithium (2.5 M) in hexane (16 ml) was added within 30 min, and after 2 h, a white suspension had been formed which was slowly added to the cold solution (−78 °C) of $B(OMe)_3$ (6.21 g, 59.8 mmol) in pentane (100 ml). The reaction mixture was stirred at −78 °C for 0.5 h, than warmed up to −40 °C slowly, stirred at this temperature for 5–10 min, before it was cooled down to −78 °C and kept without stirring for 30 min for phase separation. The upper layer was decanted and the residue was washed with pentane ($3\times$ 60 ml) with stirring at 0–20 °C. After each washing, the flask was cooled to −78 °C, kept without stirring for 15 min, before the upper layer was decanted. Finally, all volatile products were removed from the solid residue in high vacuum for 3 h yielding 8.36 g (75%) of $Li[C_6F_5B(OMe)_3]$ (white solid, mp (capillary) 110–115 °C (dec.).

Because of the hygroscopicity of salts **1a**–**1e**, we were not able to obtain correct analytical results (C, H, F) using standard analytical procedures in air. For instance, after 10–15 min exposure of **1a** (~10 mg) to air, the analysis gave C 28.06%, H 6.82% and F 2.39% (cf. with calculated values for $Li[B(OCH_3)_3OH]$: C 28.18% and H 7.88%).

^{1}H NMR (CD_2Cl_2) $\delta = 3.21$ (OCH_3). ^{19}F NMR (CD_2Cl_2) $\delta = -143.89$ (2F, $F^{2,6}$), -158.83 (1F, F^4), -163.87 (2F, $F^{3,5}$) and additional resonances at -144.64, -159.16 and -163.87 (2:1:2) (ca. 7%). ^{11}B NMR (CD_2Cl_2) $\delta = 4.23$ (s, $\tau_{1/2} =$ 36 Hz). ^{7}Li NMR (CD_2Cl_2) $\delta = -0.25$ (s, $\tau_{1/2} = 21$ Hz).

IR (powder on Si) $\bar{\upsilon}$, cm^{-1}: 2946 (w), 2913 (w), 2834 (w) (C–H), 1648 (w), 1534 (m), 1518 (m), 1464 (s), 1386 (w), 1280 (m), 1198 (m), 1180 (m), 1133 (m), 1086 (m), 1046 (s), 955 (s), 779 (m), 751 (w), 718 (w), 708 (w), 627 (w), 584 (w), 556 (w), 530 (w).

Raman (glass capillary) $\bar{\upsilon}$, cm^{-1}: 2947, 2837 (C–H), 1648, 1460, 1359, 1133, 1046, 938, 787, 665, 582, 492, 450, 401, 248.

*4.1.2. Lithium 2,3,4,5-tetrafluorophenyltrimethoxyborate (**1b**)*

2,3,4,5-Tetrafluorophenyllithium was prepared from 1,2,3,4-tetrafluorobenzene (3.40 g, 22.7 mmol) and 2.5 M BuLi in hexane (8 ml, 20 mmol) in ether (40 ml) at −78 °C (3 h) and added to the cold solution (−78 °C) of $B(OMe)_3$ (3.24 g, 31.3 mmol) in pentane (50 ml). After working up (see above), salt **1b** (2.40 g, 46%) was obtained.

^{1}H NMR (CD_2Cl_2) $\delta = 7.00$ (1H, H^6), 3.18 (9H, OCH_3). ^{19}F NMR (CD_2Cl_2) $\delta = -140.83$ (1F, F^5), -148.21 (1F, F^2), -158.86 (1F, F^4), -160.24 (1F, F^3). ^{11}B NMR (CD_2Cl_2) $\delta = 4.44$ (s, $\tau_{1/2} = 113$ Hz). ^{7}Li NMR (CD_2Cl_2) $\delta = -0.15$ (s, $\tau_{1/2} = 16$ Hz).

Raman (glass capillary) $\bar{\upsilon}$, cm^{-1}: 3067 (C_{Ar}–H), 2944, 2836 (C–H), 1650, 1459, 1326, 1189, 1158, 1138, 1132, 1088, 1059, 706, 685, 657, 525, 505, 467, 453, 414, 361, 332, 312, 304, 290, 276, 249, 234.

*4.1.3. Lithium 2,3,4,6-tetrafluorophenyltrimethoxyborate (**1d**)*

2,3,4,6-Tetrafluorophenyllithium was prepared from 1,2,3,5-tetrafluorobenzene (6.75 g, 45 mmol) and 2.5 M BuLi in hexane (16 ml, 40 mmol) in ether (60 ml) at −78 °C and added to the cold solution (−78 °C) of $B(OMe)_3$ (6.50 g, 62.5 mmol) in pentane (150 ml). After the procedure above for working up, salt **1d** (4.54 g, 44%) was obtained (mp (capillary) 115–125 °C (dec.).

^{1}H NMR (CD_2Cl_2) $\delta = 6.75$ (1H, H^5), 3.20 (9H, OCH_3). ^{19}F NMR (CD_2Cl_2) $\delta = -119.31$ (1F, F^6), -135.00 (1F, F^2), -137.74 (1F, F^4), -168.01 (1F, F^3) and additional resonances at -119.72, -136.15, -138.31 and -168.01 (1:1:1:1) (ca. 5%). ^{11}B NMR (CD_2Cl_2) $\delta = 4.18$ (s, $\tau_{1/2} = 42$ Hz). ^{7}Li NMR (CD_2Cl_2) $\delta = -0.21$ (s, $\tau_{1/2} = 18$ Hz).

IR (powder on Si) $\bar{\upsilon}$, cm^{-1}: 2933 (w), 2890 (w), 2824 (w) (C–H), 1633 (m), 1606 (m), 1500 (m), 1488 (m), 1416 (s), 1275 (w), 1230 (w), 1195 (w), 1136 (w), 1080 (s), 1046 (m), 1014 (m), 968 (m), 936 (m), 825 (m), 809 (m), 728 (w).

Raman (glass capillary) $\bar{\upsilon}$, cm^{-1}: 3082 (C_{Ar}–H), 2969, 2965, 2958, 2906, 2832 (C–H), 1609, 1600, 1471, 1197, 1031, 833, 684, 580, 566, 458, 410, 398, 389, 368, 343, 290, 284, 256, 221,171, 164.

*4.1.4. Lithium 2,3,5,6-tetrafluorophenyltrimethoxyborate (**1c**)*

2,3,5,6-Tetrafluorophenyllithium was prepared from 1,2,4,5-tetrafluorobenzene (6.75 g, 45 mmol) and 2.5 M BuLi in hexane (16 ml, 40 mmol) in ether (40 ml) at −78 °C (2 h) and added to the cold solution (−78 °C) of $B(OMe)_3$ (6.50 g, 62.5 mmol) in pentane (100 ml). After working up (see the procedure above), salt **1c** (8.80 g, 85%) was obtained (mp (capillary) 125–130 °C (dec.).

^{1}H NMR (CD_2Cl_2) $\delta = 6.96$ (1H, H^4), 3.20 (9H, OCH_3). ^{19}F NMR (CD_2Cl_2) $\delta = -144.66$ (2F, $F^{2,6}$), -141.14 (2F, $F^{3,5}$) and additional resonances at -145.15 and -141.36 (1:1) (ca. 6%). ^{11}B NMR (CD_2Cl_2) $\delta = 4.27$ (s, $\tau_{1/2} =$ 42 Hz). ^{7}Li NMR (CD_2Cl_2) $\delta = -0.17$ (s, $\tau_{1/2} = 19$ Hz).

Raman (glass capillary) $\bar{\upsilon}$, cm^{-1}: 3101 (C_{Ar}–H), 2939, 2848, 2829 (C–H), 1641, 1462, 1451, 1427, 1351, 1167, 1136, 1102, 1047, 981, 956, 796, 723, 707, 672, 586, 495, 453, 442, 421, 383, 360, 336, 306, 241, 163.

*4.1.5. Lithium 3,4,5-trifluorophenyltrimethoxyborate (**1e**)*

3,4,5-Trifluorophenyllithium was prepared from 1-bromo-3,4,5-trifluorobenzene (9 g, 42.7 mmol) and 2.5 M BuLi in hexane (16 ml, 40 mmol) in ether (40 ml) at −78 °C (2 h) and added to the cold solution (−78 °C) of $B(OMe)_3$ (6.50 g, 62.5 mmol) in pentane (100 ml). After working up (see above), salt **1e** (9.60 g, 99%) was obtained (mp (capillary) 105–110 °C (dec.).

^{1}H NMR (CD_2Cl_2) $\delta = 7.07$ (2H, $H^{2,6}$), 3.25 (9H, OCH_3). ^{19}F NMR (CD_2Cl_2) $\delta = -138.33$ (2F, $F^{3,5}$), -165.67 (1F, F^4) and additional resonances at -139.16 and -167.46 (2:1) (ca. 8%). ^{11}B NMR (CD_2Cl_2) $\delta = 5.92$ (s, $\tau_{1/2} = 204$ Hz). ^{7}Li NMR (CD_2Cl_2) $\delta = -0.22$ (s, $\tau_{1/2} = 12$ Hz).

Raman (glass capillary) $\bar{\upsilon}$, cm^{-1}: 3058 (C_{Ar}–H), 2980, 2943, 2893, 2873, 2835 (C–H), 1621, 1608, 1520, 1471, 1453, 1281, 1131, 1110, 1050, 1026, 1012, 998, 916, 838, 730, 643, 610, 567, 542, 502, 445, 377, 309, 268, 141.

4.2. The cross-coupling reaction of lithium polyfluorophenyltrimethoxyborates (**1a**–**1e**) with 4-FC_6H_4I (**2**) (general procedure)

Lithium polyfluorophenyltrimethoxyborate and the palladium catalyst (see Table 1) were placed in a flask under an atmosphere of dry argon. 4-Fluoroiodobenzene and the degassed solvent were added and the reaction mixture was stirred under the described reaction conditions (Table 1). After cooling to 20 °C, $CF_3C(O)OCH_3$ (quantitative standard) (10 µl, 0.1 mmol) was added and the solution was analysed by ^{19}F NMR spectroscopy.

4.3. The isolation and identification of the cross-coupling products (**3a**–**3e**) and biphenyls (**4** and **5**)

The reaction mixture was diluted with pentane (5 ml), filtered through silica gel (60 µm). The silica gel was washed with pentane (5 ml) and the solvent was removed from the combined pentane solutions. The hetero-coupling products **3a**, **3c** and **3d** were obtained as individual compounds and their purity was proved by MS, ^1H and ^{19}F NMR spectroscopy [7]. The coupling products of **1b** and **1e** (Table 1, entries 15 and 21) gave mixtures of the hetero- and homocoupling product **3b/4** and **3e/5**, respectively (MS, ^1H, ^{19}F) [7].

4.4. The cross-coupling of lithium pentafluorophenyltrimethoxyborate (**1a**) with 4-FC_6H_4I (**2**) in the presence of Ag_2O

1a (0.5 mmol), $[Pd(PPh_3)_4]$ (0.05 mmol) and Ag_2O (0.6 mmol) were placed in a flask under an atmosphere of dry argon. **2** (0.5 mmol) and degassed toluene (2 ml) were added. The reaction mixture was stirred for 3 h at 100 °C and cooled to 20 °C. The ^{19}F NMR spectrum showed the presence of biphenyl **3a** (0.45 mmol, 90%), C_6F_5H (0.04 mmol) and C_6H_5F (0.05 mmol).

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