

Stabilization of zwitterionic aryltrifluoroborates against hydrolysis

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Supplementary Information

General Considerations. 2-bromothioanisole was purchased from TCI America. KHF_2 was purchased from Alfa Aesar. Solvents were dried by passing through an alumina column (*n*-hexane, CH_2Cl_2) or refluxing under N_2 over Na/K (Et_2O and THF). Air-sensitive compounds were handled under a N_2 atmosphere using standard Schlenk and glovebox techniques. Elemental analyses were performed at Atlantic Microlab (Norcross, GA). NMR spectra were recorded on Varian Unity Inova 400 FT NMR (399.59 MHz for ^1H , 375.99 MHz for ^{19}F , 128.19 MHz for ^{11}B , 100.45 MHz for ^{13}C , 161.75 MHz for ^{31}P) spectrometer at ambient temperature unless otherwise stated. Chemical shifts δ are given in ppm, and are referenced against external Me_4Si (^1H , ^{13}C), $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (^{11}B , ^{19}F) and H_3PO_4 (^{31}P).

Crystallography. Single crystals of **1**- BF_3 were obtained by slow evaporation of a solution of the compound in acetonitrile. Single crystals of **2**- BF_3 and **3**- BF_3 were obtained by slow evaporation of solutions of the compounds in acetonitrile/ H_2O (5/1). The crystallographic measurement of **1**- BF_3 , **2**- BF_3 , and **3**- BF_3 were performed using a Bruker APEX-II CCD area detector diffractometer, with a graphite-monochromated $\text{Mo-K}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). A specimen of suitable size and quality was selected and mounted onto a nylon loop. The structure was solved by direct methods, which successfully located most of the non-hydrogen atoms. Subsequent refinement on F^2 using

the SHELXTL/PC package (version 6.10) allowed location of the remaining non-hydrogen atoms. The crystal data are included in Table S1.

Table S1. Crystal data

Crystal data	1	2	3
Formula	C ₉ H ₁₃ BF ₃ N	C ₁₉ H ₁₇ BF ₃ P	C ₈ H ₁₀ BF ₃ S
Mr	203.02	344.11	206.03
Crystal size/mm	0.20 x 0.20 x 0.16	0.27 x 0.12 x 0.08	0.15 x 0.12 x 0.11
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	P2(1)/c	P-1	P2(1)/n
<i>a</i> /Å	7.0647(2)	11.6184(6)	6.6172(5)
<i>b</i> /Å	13.0809(3)	12.0740(6)	12.6622(9)
<i>c</i> /Å	10.1994(2)	12.6108(7)	11.2891(8)
α /°	90	108.737(3)	90
β /°	95.349(1)	94.921(4)	102.918(1)
γ /°	90	90.944(3)	90
<i>V</i> /Å ³	938.45(4)	1667.30(15)	921.95(12)
<i>Z</i>	4	4	4
ρ_{calc} /g cm ⁻³	1.437	1.371	1.484
μ /mm ⁻¹	0.125	0.192	0.343
F(000)	424	712	424
T/K	110(2)	110(2)	110(2)
Scan mode	ω , ϕ	ω , ϕ	ω , ϕ
<i>hkl</i> Range	-10 → +10 -19 → +18 -15 → +15	-13 → +13 -14 → +14 -14 → +14	-7 → +8 -15 → +15 -13 → +13
Measd reflns	9940	27166	9052
Unique reflns [Rint]	3254 [0.0303]	5847 [0.0758]	1709 [0.0302]
Reflns used for refinement	3254	5847	1709
Refined parameters	127	433	118
GooF	1.000	1.001	1.002
R1, ^a wR2 ^b (all data)	0.0491, 0.0993	0.0981, 0.2021	0.0283, 0.0632
ρ_{fin} (max., min.)/eÅ ⁻³	0.380, -0.220	0.780, -0.611	0.356, -0.2237

^aR1 = $\sum ||F_o| - |F_c|| / \sum |F_o|$; ^bwR2 = $(\sum w(F_o^2 - F_c^2)^2) / (\sum w(F_o^2)^2)^{1/2}$; $w = 1/[\sigma^2(F_o^2) + (ap)^2 + bp]$; $p = (F_o^2 + 2F_c^2)/3$ with $a = 0.0563$ for **1**, 0.0300 for **2**, and 0.0240 for **3**; and $b = 0$ for **1**, 8.5 for **2**, and 0.671 for **3**.

Preparation of *ortho*-(Me₃N)C₆H₄(BF₃) (1)

A solution of boronic acid *ortho*-(Me₂N)C₆H₄(B(OH)₂)¹ (0.725 g, 4.39 mmol) and pinacol (0.570 g, 4.83 mmol) in CH₂Cl₂ (10 mL) was stirred for 3 hrs over anhydrous MgSO₄. The solution was filtered and the solvent removed *in vacuo* to yield the pinacol borane *o*-(Me₂N)C₆H₄(BPin₂) in 79 % yield (0.860 g). ¹H NMR (399.9 MHz, CDCl₃): δ 1.35 (s, 12H, pinacol-CH₃), 2.86 (s, 6H, N-CH₃), 6.80-6.85 (m, 2H, Ph-CH), 7.30 (ddd, 1H, Ph-CH, ³J_{H-H} = 8.24, 7.14 Hz, ⁴J_{H-H} = 1.83 Hz), 7.63 (dd, 1H, Ph-CH, ³J_{H-H} = 7.33 Hz, ⁴J_{H-H} = 1.83 Hz). ¹¹B NMR (128.2 MHz, CDCl₃): δ 32.4. The reaction of *o*-(Me₂N)C₆H₄(BPin₂) (0.284 g, 1.15 mmol) with 2 eq. of methyl triflate (0.26 mL) in Et₂O (10 mL) led to the immediate precipitation of a white solid, which was filtered and washed with 3 × 5 mL Et₂O to yield the ammonium triflate [*o*-(Me₂N)C₆H₄(BPin₂)]OTf in 65% yield (0.308 g). ¹H NMR (399.9 MHz, CDCl₃): δ 1.38 (s, 12H, pinacol-CH₃), 3.83 (s, 9H, N-CH₃), 7.50 (t, 1H, Ph-CH, ³J_{H-H} = 7.33 Hz), 7.67 (t, 1H, Ph-CH, ³J_{H-H} = 8.43 Hz), 7.85 (d, 1H, Ph-CH, ³J_{H-H} = 8.43 Hz), 7.98 (d, 1H, Ph-CH, ³J_{H-H} = 7.33 Hz). ¹³C NMR (100.5 MHz, CDCl₃): δ 24.61, 57.54, 85.89, 119.72, 122.27, 129.88, 133.30, 139.14, 150.60. ¹¹B NMR (128.2 MHz, CDCl₃): δ 31.50. Anal. Calcd for C₁₆H₂₅BNO₅F₃S: C, 46.73; H, 6.31; N, 3.41. Found: C, 47.00; H, 6.03; N, 3.45. A solution of the ammonium triflate [*o*-(Me₂N)C₆H₄(BPin₂)]OTf in MeOH (1 mL) was treated with KHF₂ (0.038 g, 0.48 mmol) in H₂O (1 mL). The solution was sonicated for 15 minutes and the precipitate collected by filtration. The solid was then extracted with 5 mL hot acetonitrile, the solution was filtered over Celite, and the solvent removed *in vacuo* to yield 0.023 g (93 % yield) of *ortho*-(Me₃N)C₆H₄(BF₃). ¹H NMR (399.9 MHz, CD₃CN): δ 3.63 (s, 9H, N-CH₃), 7.33 (ddd, 1H, Ph-CH, ³J_{H-H} = 8.35 Hz, 7.17 Hz, ⁴J_{H-H} =

2.04 Hz), 7.39 (t, 1H, Ph-CH, $^3J_{\text{H-H}} = 7.16$ Hz), 7.55 (d, 1H, Ph-CH, $^3J_{\text{H-H}} = 8.31$ Hz), 7.97 (d, 1H, Ph-CH, $^3J_{\text{H-H}} = 5.31$ Hz). ^{13}C NMR (100.5 MHz, CD_3CN): δ 57.8 q, (pseudo-q, $^3J_{\text{H-F}} = 3.90$ Hz), 128.46, 129.62, 139.72 (q, $^3J_{\text{H-F}} = 4.32$ Hz), 151.17. ^{11}B NMR (128.2 MHz, CD_3CN): δ 3.2 (q, $^1J_{\text{B-F}} = 45.5$ Hz). ^{19}F NMR (375.97 MHz, CD_3CN): δ -131.5 (q, $^1J_{\text{B-F}} = 45.5$ Hz). Anal. Calcd for $\text{C}_9\text{H}_{13}\text{BNF}_3$: C, 53.25; H, 6.45; N, 6.90. Found: C, 53.18; H, 6.59; N, 6.90.

Preparation of *ortho*-(Ph₂MeP)C₆H₄(BF₃) (2)

The pinacol borane *ortho*-(Ph₂P)C₆H₄(Bpin)² (0.175 g, 0.451 mmol) was treated with 2 eq. of MeOTf (0.10 mL) in Et₂O (5 mL) leading to the immediate precipitation of a white solid. This white solid was filtered and washed with 3 × 5 mL of Et₂O. Recrystallization by slow diffusion of Et₂O into a CH₂Cl₂ solution (3 mL) yielded [*o*-(Ph₂MeP)C₆H₄(Bpin)]OTf (0.180 g, 72%). ^1H NMR (399.9 MHz, CDCl_3): δ 0.96 (s, 12H, pinacol-CH₃), 3.06 (d, 3H, P-CH₃, $^1J_{\text{H-P}} = 13.92$ Hz), 7.11 (dd, 1H, Ph-CH, $^3J_{\text{H-P}} = 15.7$ Hz, $^3J_{\text{H-H}} = 7.80$ Hz), 7.54-7.67 (m, 9H, Ph-CH), 7.74 (t, 3H, Ph-CH, $^3J_{\text{H-H}} = 7.51$ Hz) 8.22 (dd, 1H, Ph-CH, $^3J_{\text{H-P}} = 7.50$ Hz, $^3J_{\text{H-H}} = 6.87$ Hz). ^{13}C NMR (100.5 MHz, CDCl_3): δ 9.88 (d, P-CH₃, $^1J_{\text{C-P}} = 57.22$ Hz), 24.24 (pinacol-CH₃), 85.28 (pinacol-C-O), 121.07 (d, $J_{\text{C-P}} = 88.5$ Hz), 123.95 (d, $J_{\text{C-P}} = 84.7$ Hz), 130.32 (d, $J_{\text{C-P}} = 13.0$ Hz), 132.13 (d, $J_{\text{C-P}} = 13.73$ Hz), 132.7 (d, $J_{\text{C-P}} = 9.9$ Hz), 133.88 (d, $J_{\text{C-P}} = 3.0$ Hz), 134.55 (d, $J_{\text{C-P}} = 2.3$ Hz), 136.84 (d, $J_{\text{C-P}} = 13.0$ Hz), 139.27 ((d, $J_{\text{C-P}} = 13.7$ Hz), (ipso C for phenylene-C-B not observed). ^{11}B NMR (128.2 MHz, CDCl_3): δ 29.72. ^{31}P NMR (161.75 MHz, CDCl_3): δ 25.64. Anal. Calcd for $\text{C}_{26}\text{H}_{29}\text{BO}_5\text{F}_3\text{PS}$: C, 56.54; H, 5.29. Found: C, 56.29; H, 5.26. The phosphonium triflate [*o*-(Ph₂MeP)C₆H₄(Bpin)]OTf (0.050 g, 0.09 mmol) in 1

mL of MeOH was then treated with a solution of KHF_2 (0.028 g, 0.36 mmol) in 1 mL H_2O . The resulting solution was sonicated for 15 minutes and the precipitate collected by filtration. The solid was washed with H_2O (3×1 mL) and dried *in vacuo* to yield 0.026 g (97 % yield) of *ortho*-(Ph_2MeP) $\text{C}_6\text{H}_4(\text{BF}_3)$ (**2**). ^1H NMR (399.9 MHz, CDCl_3): δ 2.89, (d, 3H, P- CH_3 , $^2J_{\text{H-P}} = 13.9$ Hz), 6.81 (dd, 1H, $^3J_{\text{H-P}} = 15.1$ Hz, $^3J_{\text{H-H}} = 7.8$ Hz), 7.19 (tdd, 1H, $J = 7.69, 3.45, 1.33$ Hz), 7.41 (dd, 4H, *m*-phenyl- CH , $J = 12.96, 7.88$ Hz), 7.55 (td, 4H, *o*-phenyl- CH , $J = 8.13, 3.17$ Hz), 7.59 (td, 1H, phenyl- CH , $J = 7.58, 1.87$ Hz), 7.68 (tq, 1H, phenyl- CH , $J = 7.58, 1.68$ Hz), 8.15 (dd, 1H, phenyl- CH , $J = 6.40, 7.58$ Hz). ^{13}C NMR (100.5 MHz, CDCl_3): δ 11.50 (d, $^1J_{\text{P-C}} = 58.85$ Hz), 119.05 (d $J_{\text{P-C}} = 86.98$ Hz), 123.62 (d $J_{\text{P-C}} = 88.50$ Hz), 126.67 (d $J_{\text{P-C}} = 14.49$ Hz), 129.63 (d $J_{\text{P-C}} = 12.97$ Hz), 132.62 (d $J_{\text{P-C}} = 9.91$ Hz), 133.43 (d $J_{\text{P-C}} = 3.38$ Hz), 133.64 (d $J_{\text{P-C}} = 3.03$ Hz), 134.16 (d $J_{\text{P-C}} = 15.26$ Hz), 135.84 (dq $^1J_{\text{P-C}} = 16.77$ Hz, $^3J_{\text{F-C}} = 3.02$ Hz). ^{11}B NMR (128.2 MHz, CDCl_3): δ 3.68. ^{19}F NMR (375.97 MHz, CDCl_3): δ -139.0. ^{31}P NMR (161.75 MHz, CDCl_3): δ 26.23. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{BF}_3\text{P}$: C, 66.32; H, 4.98. Found: C, 65.62; H, 4.83.

Preparation of *ortho*-(Me_2S) $\text{C}_6\text{H}_4(\text{BF}_3)$ (**3**)

To 2-bromothioanisole (2.0 g, 9.8 mmol) in diethyl ether (20 mL) was added *n*-BuLi (3.4 mL, 11.7 mmol, 2.9M in *n*-hexane) at 0 °C. After stirring the mixture for 1h at 0 °C, trimethylborate (1.32 mL, 11.8 mmol) was added dropwise to the lithiated compound at -78 °C. The mixture was allowed to warm to room temperature and stirred for 3 hours. The mixture was quenched with 3 M HCl (16 mL) and extracted with ethyl acetate (50 ml \times 3). The organic layer was separated, dried over MgSO_4 and filtered. The volatiles were removed *in vacuo* to give a white solid which was washed with hexanes

(20 mL) to afford 1.2 g of the crude boronic acid. The boronic acid *o*-(MeS)C₆H₄(B(OH)₂) (0.2 g, 1.19 mmol) was treated with MeOTf (0.23 mL, 2.05 mmol) in dichloromethane (15 mL) at room temperature. The mixture was refluxed overnight and cooled to room temperature. The solvent was removed *in vacuo* yielding an off-white solid that was washed with diethyl ether to afford the sulfonium triflate [*o*-(Me₂S)C₆H₄(B(OH)₂)]OTf (0.28 g, yield 74%). ¹H-NMR (400 MHz, CD₃CN): δ 3.10 (s, 6H, S-CH₃), 7.71-7.80 (m, 2H, Ph-CH), 7.90 (d, 1H, Ph-CH, ³J_{H-H} = 8.0 Hz), 7.99 (d, 1H, Ph-CH, J = 7.2 Hz). ¹¹B-NMR (128 MHz, CD₃CN): δ + 28.7. A solution of the sulfonium triflate [*ortho*-(Me₂S)C₆H₄(B(OH)₂)]OTf (0.20 g, 0.6 mmol) in acetonitrile (5 mL) was treated with solid KHF₂ (0.19 g, 2.4 mmol) and the mixture was stirred for 1 hour at room temperature. After filtration, the solvent was removed *in vacuo* to yield a white solid. The solid was washed with ethanol (40 ml) to afford *ortho*-(Me₂S)C₆H₄(BF₃) (0.078 g, yield 63%). ¹H-NMR (400 MHz, CD₃CN): δ 3.04 (s, 6H, S-CH₃), 7.50-7.56 (m, 2H, Ph-CH), 7.74 (d, 2H, Ph-CH, ³J_{H-H} = 8.0 Hz). ¹³C NMR (100.5 MHz, CD₃CN): 27.85, 125.16, 128.73, 132.01, 133.92. ¹¹B-NMR (128 MHz, CD₃CN): δ + 3.14 (q, ¹J_{B-F} = 43.7 Hz). ¹⁹F NMR (375.97 MHz, CD₃CN): δ -136.58 (q, ¹J_{B-F} = 43.7 Hz). Anal. Calcd for C₈H₁₀BF₃S: C, 46.64; H, 4.89; F, 27.66. Found: C, 46.46; H, 4.90; F, 27.46.

NMR Spectroscopic Kinetic Analyses

Samples of **1** (5 mg), **2** (8.5 mg), and **3** (5 mg) were each dissolved in 0.2 mL CD₃CN and 1.0 mL D₂O phosphate buffer (pH 7.5, 500 mM). All of the resulting mixtures were filtered over glass wool to remove any precipitated solids. The ¹⁹F NMR spectrum of each sample was collected periodically. Decomposition of the aryltrifluoroborate species was monitored by integration of the decreasing aryltrifluoroborate signal in conjunction with the increasing signal corresponding to free F⁻ using VNMRJ Version 2.2 NMR processing software. The rate constants, k_{obs} , were calculated using a method reported in the literature.³ The data used for these calculations is given in Table S2-S5.

Table S2: Kinetic data for the hydrolysis of 1

		<u>Data for 1</u>		
				k=6.30E-05
			exp. ratio	calc. ratio
<u>Time</u> <u>(min)</u>	<u>[F-]</u>	<u>[BF3]</u>	<u>[BF3]/([BF3]+[F])</u>	<u>[BF3]/([BF3]+[F])</u>
0	0	100	1.000	1.000
255	2.82	100	0.973	0.984
450	3.47	100	0.966	0.972
595	4.86	100	0.954	0.963
740	5.94	100	0.944	0.954
1330	10.14	100	0.908	0.920
1660	12.57	100	0.888	0.901
2790	21.51	100	0.823	0.839
4350	31.28	100	0.762	0.760
5700	44.78	100	0.691	0.698
10155	84.44	100	0.542	0.527
14460	137.25	100	0.421	0.402
20000				0.284
30000				0.151
40000				0.080
50000				0.043

Table S3: Kinetic data for the hydrolysis of 2

		<u>Data for 2</u>		
				k=3.40E-06
				exp. ratio
				calc. ratio
<u>Time</u> <u>(min)</u>	<u>[F-]</u>	<u>[BF3]</u>	<u>[BF3]/([BF3]+[F])</u>	<u>[BF3]/([BF3]+[F])</u>
0	0	100	1	1
1100	0.25	100	0.997506234	0.996266985
2560	0.81	100	0.991965083	0.99133377
4170	1.21	100	0.98804466	0.985922035
5520	2.67	100	0.973994351	0.981407022
9975	4.46	100	0.957304231	0.966653667
14250	5.3	100	0.949667616	0.952704973
19920	7.24	100	0.932487878	0.934514627
24300	7.97	100	0.926183199	0.920700947
40110	13.77	100	0.878966336	0.87251625
50000				0.843664817

Table S4: Kinetic data for the hydrolysis of 3

		<u>Data for 3</u>		
				k=1.20E-04
				exp. ratio
				calc. ratio
<u>Time</u> <u>(min)</u>	<u>[F-]</u>	<u>[BF3]</u>	<u>[BF3]/([BF3]+[F])</u>	<u>[BF3]/([BF3]+[F])</u>
0	0	100	1.000	1.000
212	2.88	100	0.972	0.975
308	3.07	100	0.970	0.964
523	6.12	100	0.942	0.939
688	7.96	100	0.926	0.921
1430	17.75	100	0.849	0.842
1650	19.99	100	0.833	0.820
2857	36.89	100	0.731	0.710
6000				0.487
9000				0.340
12000				0.237
15805	607.15	100	0.141	0.150
20000				0.091
30000				0.027
40000				0.008
50000				0.002

Table S4: Kinetic data for the hydrolysis of PhBF_3^-

		Data for $\text{K}[\text{C}_6\text{H}_5\text{BF}_3]$		
				k = 0.0245
				exp. ratio
				calc. ratio
Time (min)	[F ⁻]	[BF ₃]	$[\text{BF}_3]/([\text{BF}_3]+[\text{F}^-])$	$[\text{BF}_3]/([\text{BF}_3]+[\text{F}^-])$
0	0	100	1.000	1.000
15	44	100	0.694	0.692
30	105	100	0.488	0.480
45	197	100	0.337	0.332
60	335	100	0.230	0.230
75	531	100	0.158	0.159
90	841	100	0.106	0.110

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