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# Synthesis of *ortho*-modified mercapto- and piperazino-methyl-phenylboronic acid derivatives

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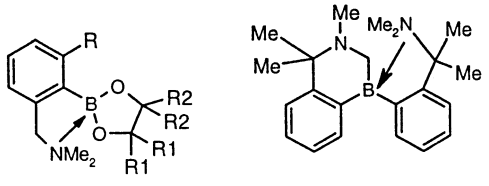
**Abstract**—The synthesis of 2-mercapto- and 2-piperazino- (methyl-phenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolanes **4** and **5**, respectively, is described and their inhibitory activity against serine proteases including thrombin was measured. Some of these compounds were studied in both the solid state and in solution, displaying no S–B coordination and only weak N–B coordination. © 2002 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Arylboronic acids are versatile and readily available compounds, which have applications in areas as diverse as organometallic chemistry[1] and organic synthesis,[2] host–guest chemistry and materials science,[3] separation science[4] and medicinal chemistry.[5] Many *ortho*-substituted arylboronate derivatives, mainly based around the benzylamine framework, have been reported and extensively characterised in both the solid state and in solution, and share the common feature of coordination of the nitrogen atom to the boron centre e.g. **1** and **2** (see Fig. 1).[6]

The stability and unique properties of *ortho*-heteroatom-substituted aryl organometalloid and organometallic derivatives can in many cases be attributed to the coordination of the heteroatom to the metalloid/metal centre.[7] We recently embarked on a programme aimed at synthesising *ortho*-substituted arylboronic derivatives with potential heteroatom coordination or proximity to boron, the aim of such a study being to improve the well-established weak serine protease inhibitory activity of simple phenylboronic acids.[8]




**1a**; R= H, R¹=R² =Me
**1b**; R= $CH_2NMe_2$, R¹=Ph, R²=H

**2**

**Figure 1.**

We report herein a synthetic route to 2-mercapto(methyl-phenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolanes **4** via the nucleophilic substitution of the readily-available 2-(bromomethylphenyl)boronic acid pinacol ester **3** by thiols under basic conditions (Scheme 1). This represents an alternative to the literature route to such derivatives, including **4i**,[9] which is unselective and leads to several products. Moreover, our method was developed as a parallel synthetic route capable of producing a range of electronically and sterically different thioether-containing arylboronates. Additionally, piperazino-(methyl-phenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolanes **5** were made from **3** in basic conditions using an adaptation of known chemistry.[6f,g] Structural studies of **4** and **5**, in both solution and in the solid state, as well as their biological activity are also presented.

## 2. Results

The reaction of **3** with benzylmercaptan was attempted in basic conditions using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[10] or phase-transfer conditions.[11] The product **4c** was obtained in comparable yields in both cases (purity >90%) and the facile DBU method was exploited for the parallel synthesis of the derivatives **4** by merely stirring **3** with the appropriate thiol and DBU in benzene overnight. Reactions were not optimised since our goal was the rapid synthesis of a series of compounds for biological screening without the need for extensive purification.

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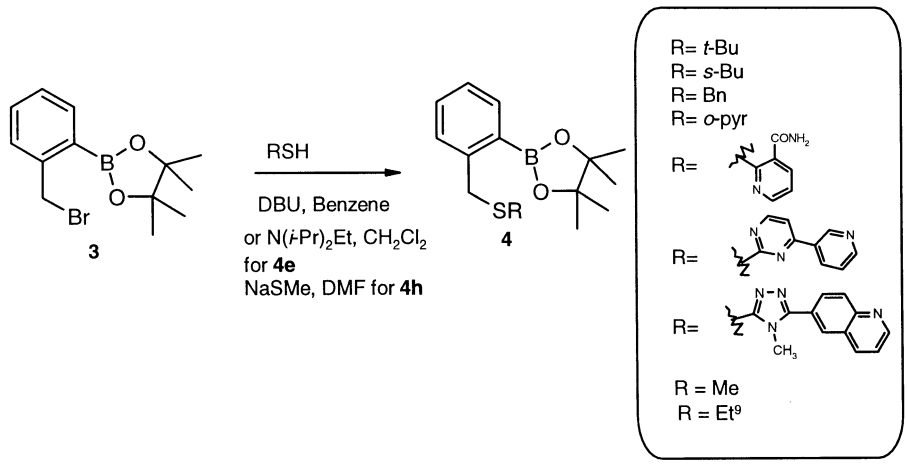
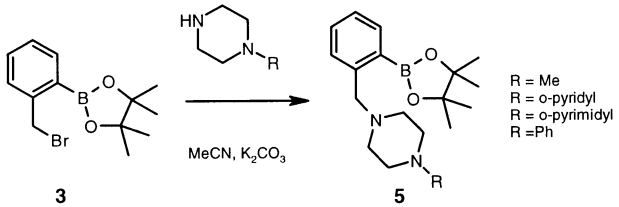



**Scheme 1.**

The poor solubility of the nicotinamide-thiol precursor of **4e** in benzene was overcome by using dichloromethane as solvent, with diisopropylethylamine as base, and the product was obtained and fully characterized, albeit in poor yield. The synthesis of the methylthioether derivative **4h** was performed more conveniently in DMF using sodium thiomethoxide as nucleophile.

All of these air stable compounds were obtained in high purity without purification and fully characterised. The variety of thioether substituents such as simple alkyl derivatives as in **4a**, **4b** and **4h**, *o*-pyridyl derivatives, such as **4d** and **4e**, and more elaborate substituents, including the pyrimidylpyridine and quinolyltriazole units in **4f** and **4g**, respectively, demonstrates the successful diversity achieved through these synthetic approaches.

Piperazines have numerous applications in medicinal chemistry[12] and, as an extrapolation from the simple well-established simple dialkylamine-containing arylboronate derivatives, we embarked upon the synthesis of arylboronates containing such fragments with potential coordination of nitrogen to boron. Hence, reactions of **3** with piperazines in basic conditions in acetonitrile, were smooth and could be performed in parallel and yielded **5** with purities of >85% (See Scheme 2).




**Scheme 2.**

## 3. Discussion

A recent in vitro screen of selective inhibitors of the serine protease thrombin in our laboratories was carried out; of a series of boronates containing the D-PhePro peptide backbone, the most potent derivative was **6** (Fig. 2), which contains a methoxy group in proximity to the Lewis acid centre in what can be considered to be a pseudo-cyclic structure, with an interaction of the type MeO–B.[13] The specific combination of this peptide sequence with the boron *serine trap* leads to the nanomolar activity of **6** towards thrombin and the neutral (non-guanidino) side chain enables the high enzyme specificity, with over two orders of magnitude selectivity ($Ki_{Try}/Ki_{Thr}$) against trypsin. The added potential influence of intramolecular coordination, or heteroatom proximity to boron, on selectivity of this compound for thrombin aroused our interest in designing easily-accessible boron-containing systems with a predefined and 'tuneable' coordination of a heteroatom to the electrophilic metalloid centre (see Fig. 2). Having achieved the synthesis of **4** and **5**, *vide supra*, a cursory examination of their solution and solid-state structures was undertaken.

The $^1$H NMR spectra of $CDCl_3$ solutions of **4a** and **4f** were unchanged when cooled from room temperature (rt) to −50°C and in particular the benzylic protons situated at around $\delta$ 4.0 and 4.8 ppm, respectively, remained as singlets. This indicates no interaction between the sulphur atom and boron on the NMR time scale. **4i** displayed no S–B coordination in solution at −90°C[9] whereas, in the related thioether-coordinated complexes, $[2\text{-}RSCH_2C_6H_4PdI]_2$ (R=Me, Et, *t*-Bu), the diastereotopic benzylic protons gave rise to an AB system in the $^1$H NMR spectrum at rt.[11a]

$^{11}$B NMR has been extensively used for probing the degree of tetrahedral character in boron containing derivatives[4,14] and accordingly the $^{11}$B NMR spectra of **3**, **4c**, **4h** and **5c** were measured in $CDCl_3$ at room temperature relative to a $BF_3{\cdot}OEt_2$ external standard. For **5c** we observed a broad signal at $\delta$ 21 ppm, which is indicative of weak N–B coordination. For the three other derivatives we observed a broad signal at around $\delta$ 32. These observations point to no S–B coordination in **4c** and **4h** and coupled with the low temperature $^1$H NMR studies for **4a** and **4f** it was quite apparent that S–B coordination would appear to be unfavourable[9] in these derivatives, as was observed for **4i**,

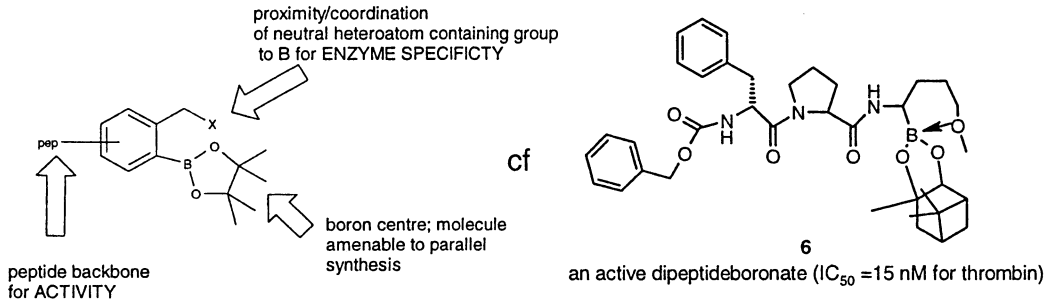



**Figure 2.**

despite the measures taken in varying the electronic and steric properties of the thioether substituents.

Single crystals of **4f** and **5c** suitable for X-ray diffraction were obtained by the slow diffusion of hexane into dichloromethane solutions. The resulting crystal structures are depicted in Figs. 3 and 4. The arylboronic acid pinacol group shows variations in its conformation between **4f** and **5c** as the mean B–O bond length of 1.357(5) Å within **4f** is significantly longer than the corresponding mean of 1.345(4) Å observed in **5c**. The variations within this ligand[15] in the two structures are further reflected with the B–C (phenyl) bond length of 1.589(7) Å in **5c** being significantly longer than the corresponding length of 1.537(8) Å observed in **4f**. The observed variations in bond lengths within the arylboronic acid pinacol group between the two structures may be a result of N(1) in **5c** showing a weak coordination to the boron atom with a resulting contact distance of 2.98 Å, which is shorter than the contact distance of 3.3 Å observed between the sulphur and boron in **4f**. The weak coordination between N(1) and B in **5c** is also signified with the angle B–C(1)–C(6) of 123.1(5) Å being smaller than the corresponding angle of 125.4(5) Å in **4f**. It is envisaged for **5c** that steric factors, arising from the axial H atoms of C(11) and C(12) within the piperazine ring interacting with the hydrogen atoms from pinacol groups C(81) and C(91), may be preventing the N(1) from formally coordinating to the boron atom.

## 4. Biological Activity of 4 and 5

Despite the absence of: (i) significant S–B or N–B coordination or (ii) a peptide-backbone, the derivatives **4** and **5** were tested for their in vitro activity against thrombin, an important enzyme in the coagulation cascade.[16] **1a** and the pinacol ester of phenylboronic acid (PhBOPin) were made for comparative purposes since the former displays strong N–B coordination, satisfying part of our model system (Fig. 2), and the latter is a good reference point for assessing the effect of an *ortho* $CH_2X$ group (where X=SR or $NR_2$) on biological activity in the phenylboronic acid series. Results are listed in Table 1 and demonstrate that these compounds exhibit varying degrees of potency towards the enzyme. Solubility issues precluded the assaying of other derivatives **4** and **5**.

In comparison to PhBOPin, the compounds **4h** and the

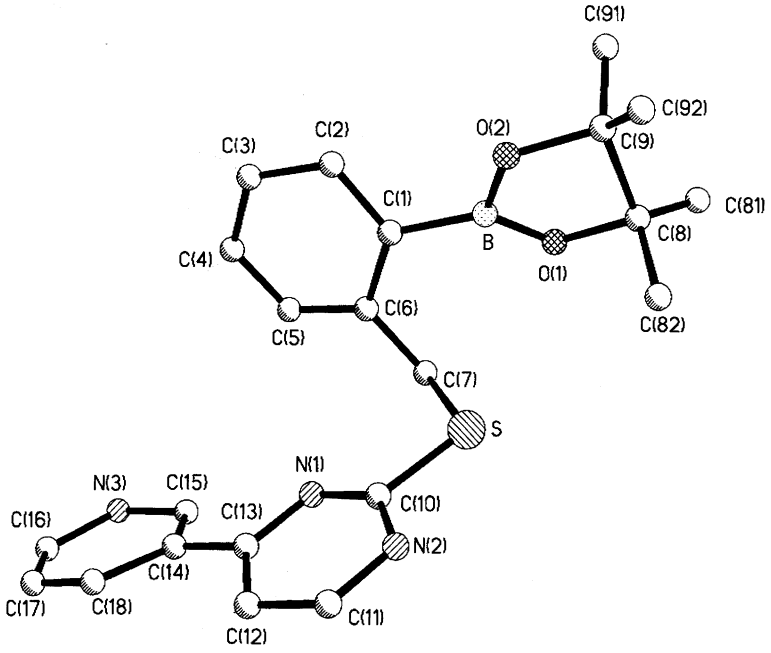



**Figure 3.** ORTEP diagram of **4f** using the adopted numbering scheme.

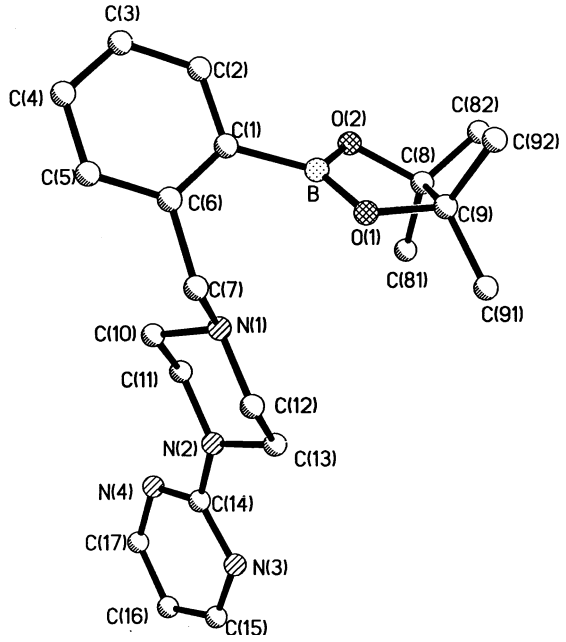



**Figure 4.** ORTEP diagram of **5c** using the adopted numbering scheme.

**Table 1.** Biological activity of arylboronates against thrombin

| Compound | Relative activity vs thrombin |
|---|---|
| PhBOPin | 1 |
| **1a** | 1 |
| **4e** | 500 |
| **4h** | 130 |
| **5c** | 1 |
| **5d** | 0 |
| **6** | 500,000 |

aminocarbonylpyridyl-substituted methylthioether derivative **4e** exhibit ca. 100 and 500 times more potency towards thrombin, respectively. **1a**, with N–B coordination, and **5c** are virtually equipotent with PhBOPin. **6** ($IC_{50}$=ca. 15 nM), with the D-Phe-Pro backbone, is a further thousand fold more potent than **4e**, translating for the latter to an $IC_{50}$ of ca. 20 μM. None of the derivatives tested had significant activity towards either FXa or Trypsin, militating once again for a neutral side chain in order to achieve thrombin selectivity, as predicted in Fig. 2.

In the simple arylboronate series, **4** and **5**, there would indeed appear to be a marked increase in potency towards thrombin on the *ortho*-modification of PhBOPin by certain mercaptomethyl substituents, whereas the aminomethyl substituents studied herein have a much less pronounced effect. Present studies addressing this effect as well as the incorporation of a peptide backbone into these aryl systems, in order to increase their potency towards thrombin, will be reported in due course.

## 5. Conclusion

2-Mercaptomethyl- and 2-piperazino-(methylphenyl)boronic acid derivatives **4** and **5** have been rapidly synthesized and some of these derivatives were studied in both solution and solid state, displaying no S–B coordination and only weak N–B coordination. Current studies are aimed at the exploitation of **4** and **5** in synthetic processes, including biaryl coupling reactions,[17] as well as further structure–activity relationships in these molecules with regard to thrombin.

## 6. Experimental

### 6.1. General

Anhydrous benzene (Aldrich Sure/Seal™) and other reagents were used as obtained. Compound **3** was purchased from Combi-Blocks, USA and $PhB(OH)_2$ was obtained from Fluka and the thiols were purchased from Aldrich or Maybridge, UK. Routine $^1H$ (400.13 MHz) and $^{13}C$ (100.6 MHz) were recorded on a Bruker Avance spectrometer. $^{11}B$ NMR were carried out at 128.4 MHz relative to $BF_3{\cdot}OEt_2$ as external standard at 0 ppm. Chemical shifts are given in ppm and coupling constants ($J$) are given in Hertz. Elemental analyses and FAB mass spectra were carried out at the Analytical Department of the University of North London, UK. The EPSRC Service, Swansea, carried out accurate mass determinations.

Compounds **4** were synthesised in parallel, typically on a 0.5 mmol scale, starting from **3** and the appropriate thiol, RSH.

**6.1.1. 2-[2-(Benzylsulfanylmethyl)phenyl]-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane 4c.** This synthesis is given as a representative example. **3** (150 mg, 0.50 mmol), benzyl mercaptan (68 mg, 0.54 mmol) and DBU (80 mg, 0.52 mmol) in benzene (2 ml) were stirred overnight at rt in a small vial. After dilution with benzene (8 ml), filtration, to remove the DBU·HBr precipitate, the filtrate was washed with a ca. 1N solution of NaOH and dried over $mgSO_4$. Filtration and concentration afforded orange oil that solidified on standing (115 mg, 68%) to give pale orange plates. (Found: C, 70.54; H, 7.55. $C_{20}H_{25}BO_2S$ requires C, 70.59, H, 7.41). $^1H$ NMR ($CDCl_3$) $\delta$ 1.34 (s, 12H), 3.58 (s, 2H), 3.95 (s, 2H), 7.0–7.4 (m, 8H), 7.78 (d, 1H, $J$=8 Hz). $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.9, 35.4 (2 equiv. $CH_2$), 83.6, 126.1, 126.7, 128.4, 128.7, 128.9, 129.3,130.5, 136.2, 138.6, 145.1. $^{11}B$ NMR ($CDCl_3$) $\delta$ 32. HRMS *m/z*: calcd for $C_{20}H_{26}BO_2S$ (MH+): 341.1747, found: 341.1748.

**6.1.2. 2-[2-*tert*-Butylsulfanylmethyl)phenyl]-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane 4a.** Yield 60 mg (39%) of a yellow oil. $^1H$ NMR ($CDCl_3$) $\delta$ 1.28 (s, 9H), 1.29 (s, 12H), 4.05 (s, 2H), 7.0–7.3 (m, 3H), 7.80 (1H, d, $J$=8 Hz). $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.3, 31.4, 32.9, 43.3, 83.9, 126.3, 130.2, 131.2, 136.4, 145.4.

**6.1.3. 2-[2-*sec*-Butylsulfanylmethyl)phenyl]-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane 4b.** Yield 70 mg (46%) of a pale yellow oil. $^1H$ NMR ($CDCl_3$) $\delta$ 0.89 (t, 3H, $J$=7 Hz), 1.16 (m, 3H), 1.28 (s, 12H), 1.29 (m, 3H), 3.98 (s, 2H), 7.0–7.4 (m, 3H), 7.68 (d, 1H, $J$=8 Hz). $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.3, 19.7, 23.8, 27.4, 33.2, 40.0, 82.5, 124.9, 127.3, 128.3, 129.5, 134.9, 144.7. MS (FAB) 307 (20 MH+).

**6.1.4. 2-[2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzylsulfanyl]-pyridine 4d.** Yield 37 mg (37%, made on a 0.25 mmol scale) of a yellow oil. $^1$H NMR ($CDCl_3$) $\delta$ 1.32 (s, 12H), 4.75 (s, 2H), 7.19 (t, 1H, $J$=7.5 Hz), 7.24–7.37 (m, 3H), 7.70 (d, 2H, $J$=7.5 Hz), 7.86 (d, 1H, $J$=7.5 Hz), 8.49 (m, 1H). $^{13}$C NMR ($CDCl_3$) $\delta$ 24.8, 33.9, 83.7, 119.2, 119.7, 121.1, 121.9, 126.3, 129.6, 130.8, 136.0, 144.7, 149.2, 159.7. MS (ESI) 350 (100 M+Na), 328 (65 MH+).

**6.1.5. 2-[2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzylsulfanylmethyl]-nicotinamide 4e.** Yield 30 mg (17%) of a white solid, synthesized as for **4c** but using 1.2 equiv. diisopropylethylamine as base and dichloromethane as solvent. Recrystallised from dichloromethane/hexane. $^1$H NMR ($CDCl_3$) $\delta$ 1.25 (s, 12H), 4.75 (s, 2H), 5.70, 6.40 (2brs, 2H), 7.19 (t, 1H, $J$=8 Hz), 7.2–7.6 (m, 3H), 7.85 (m, 1H), 7.95 (m, 1H), 8.40 (m, 1H). $^{13}$C NMR ($CDCl_3$) $\delta$ 25.2, 33.9, 84.0, 119.6, 126.9, 128.8, 130.3, 131.1, 136.5, 137.8, 144.7, 151.1, 157.5, 168.3. MS (ESI) 763 (50 2M+Na), 393 (100 M+Na).

**6.1.6. 4-Pyridin-3-yl-2-[2-(4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl)-benzylsulfanyl]-pyrimidine 4f.** Yield 70 mg (35%) of a yellow solid: mp 191–192°C. (Found: C, 58.23; H, 5.83; N, 8.40. $C_{22}H_{24}BN_3O_2S{\cdot}0.75\ CH_2Cl_2$ requires C, 58.26; H, 5.48; N, 8.96). $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (s, 12H), 4.75 (s, 2H), 7.16–7.50 (m, 5H), 7.75 (d, 1H, $J$=6.5 Hz), 8.36 (d, 1H, $J$=4 Hz), 8.55 (d, 1H, $J$=5 Hz), 8.70 (d, 1H, $J$=5 Hz), 9.22 (d, 1H, $J$=2 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 24.8, 34.9, 83.7, 111.9, 123.7, 126.4, 129.6, 130.8, 132.2, 134.6, 136.3, 144.6, 148.5, 151.7, 157.9, 161.6, 173.4. HRMS $m/z$: calcd for $C_{17}H_{28}BO_2S$ (MH+): 406.1761, found: 406.1764.

**6.1.7. 6-{4-Methyl-5-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzylsulfanyl]-4H-[1,2,4]triazol-3-yl}-quinoline 4g.** Yield 130 mg (57%) of a yellow solid. (Found: C, 65.37; H, 5.96; N, 12.09. $C_{25}H_{27}BN_4O_2S$ requires C, 65.51, H, 5.94, N, 12.22). $^1$H NMR ($CDCl_3$) $\delta$ 1.31 (s, 12H), 3.14 (s, 3H), 4.63 (s, 2H), 7.19 (t, 1H, $J$=4.5 Hz), 7.20 (m, 2H), 7.42 (t, 1H, $J$=4 Hz), 7.78 (m, 2H), 8.01 (s, 1H), 8.14 (m, 2H), 8.92 (d, 1H, $J$=4 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 23.5, 30.6, 38.1, 82.9, 121.0, 124.4, 126.0, 126.9, 127.4, 127.7, 128.7, 129.3, 129.9, 135.5, 135.6, 143.3, 147.4, 150.7, 150.8, 154.3. MS (ESI) 369 (M−PhCH$_3$, 100%), MS (FAB) 459 (MH+, 75%).

**6.1.8. 4,4,5,5-Tetramethyl-2-[2-(methylsulfanylmethyl)-phenyl]-[1,3,2]dioxaborolane 4h.** The bromide **3** (290 mg, 0.99 mmol) and sodium thiomethoxide (90 mg, 1.28 mmol) were heated to 80°C overnight in DMF (15 ml). After cooling, the mixture was diluted with water and ether (20 ml each). The organic layer was separated and washed with water, brine then dried over $MgSO_4$. Filtration and concentration yielded orange oil in virtually quantitative yield. $^1$H NMR ($CDCl_3$) $\delta$ 1.29 (s, 12H), 3.34 (s, 3H), 4.63 (s, 2H), 7.18–7.26 (m, 2H), 7.34 (d, 1H, $J$=4 Hz), 7.71 (d, 1H, $J$=7 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 15.1, 25.3, 37.8, 84.0, 126.5, 129.8, 130.9, 136.5, 145.7. $^{11}$B NMR ($CDCl_3$) $\delta$ 32. MS (FAB) 265 (85 MH+), 250 (35−Me), 218 (100−SMe).

### 6.2. General method for the synthesis of 5

A suspension of the bromide **3** (0.15 g, 0.50 mmol), $K_2CO_3$ (230 mg, 1.67 mmol) and the appropriate piperazine (0.6 mmol) in acetonitrile (10 ml) was stirred overnight at 80°C. After cooling and filtration to remove solids, the filtrate was concentrated in vacuo to afford the product.

**6.2.1. 1-Methyl-4-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine 5a.** Orange oil made on a 2 mmol scale. 560 mg (89%). $^1$H NMR ($CDCl_3$) $\delta$ 1.27 (s, 12H), 2.20 (s, 3H), 2.20–2.30 (m, 8H), 3.63 (s, 2H), 7.20–7.30 (m, 3H), 7.70 (d, 1H, $J$=8 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 25.6, 46.5, 53.0, 55.0, 61.9, 83.1, 126.8, 129.3, 130.1, 134.9, 143.6. MS (ESI) 317 (100 MH+).

**6.2.2. 1-Pyridin-2-yl-4-[2-(4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl)-benzyl]-piperazine 5b.** Pale yellow oil. 91 mg (48%). $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (s, 12H), 2.52 (m, 4H), 3.44 (m, 4H), 3.67 (s, 2H), 6.52 (t, 2H, $J$=7 Hz), 7.18–7.30 (m, 4H), 7.63 (m, 1H), 8.10 (m, 1H). $^{13}$C NMR ($CDCl_3$) $\delta$ 23.0, 41.5, 51.0, 59.8, 81.7, 105.3, 111.4, 114.5, 124.8, 125.9, 128.3, 133.0, 146.0, 156.7. HRMS $m/z$: calcd for $C_{22}H_{31}BN_3O_2$ ($MH^+$): 380.2509, found: 380.2513.

**6.2.3. 2-{4-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazin-1-yl-}pyrimidine 5c.** Orange oil made in virtually quantitative yield and giving crystals on slow diffusion of hexane into a $CH_2Cl_2$ solution: mp 45–47°C. (Found 66.34; H, 7.69; N, 14.43. $C_{21}H_{29}BN_4O_2$ requires C, 66.32; H, 7.57; N, 14.73). $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (s, 12H), 2.43 (t, 4H, $J$=5 Hz), 3.41 (t, 4H), 3.65 (s, 2H), 6.38 (t, 1H, $J$=5 Hz), 7.20–7.27 (m, 3H), 7.64 (dd, 1H, $J$=5 Hz), 8.21 (t, 2H, $J$=5 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 23.8, 42.5, 51.9, 61.1, 82.3, 108.7, 125.5, 126.7, 128.3, 129.7, 134.8, 142.8, 156.6, 160.7. $^{11}$B NMR ($CDCl_3$) $\delta$ 20.5. HRMS $m/z$: calcd for $C_{22}H_{30}BN_4O_2$ ($MH^+$): 381.2462, found: 381.2464.

**6.2.4. 1-Phenyl-4-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine 5d.** Orange oil. Quantitative yield. (Found C, 72.91; H, 8.20. $C_{23}H_{31}BN_2O_2$ requires C, 73.02; H, 8.26). $^1$H NMR ($CDCl_3$) $\delta$ 1.25 (s, 12H), 2.51 (t, 4H, $J$=5 Hz), 3.05 (t, 4H, $J$=5 Hz), 3.65 (s, 2H), 6.75 (m, 3H), 7.12–7.27 (m, 5H), 7.64 (dd, 1H, $J$=5 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$ 22.8, 46.9, 51.0, 60.1, 82.3, 114.0, 122.9, 124.7, 127.3, 127.5, 128.1, 133.1, 142.0, 149.6. HRMS $m/z$: calcd for $C_{22}H_{32}BN_2O_2$ ($MH^+$): found: 379.2557.

### 6.3. X-Ray crystallographic studies of 4f and 5c

*Data collection*: single crystals of compounds **4f** and **5c** were mounted on a quartz fibre and X-ray intensity data were collected with graphite-monochromated radiation, on a Bruker P4 four-circle diffractometer.[18] The only crystals of **4f** and **5c** that could be obtained diffracted relatively weakly at high angle. Following data collection, Lorentz-polarisations were applied to the data of both compounds.

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18. Inquiries concerning the X-ray structures of **4f** and **5c** should be addressed to T. Adatia. Crystallographic data (excluding structural factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 160738 and 160739, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ (fax +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).