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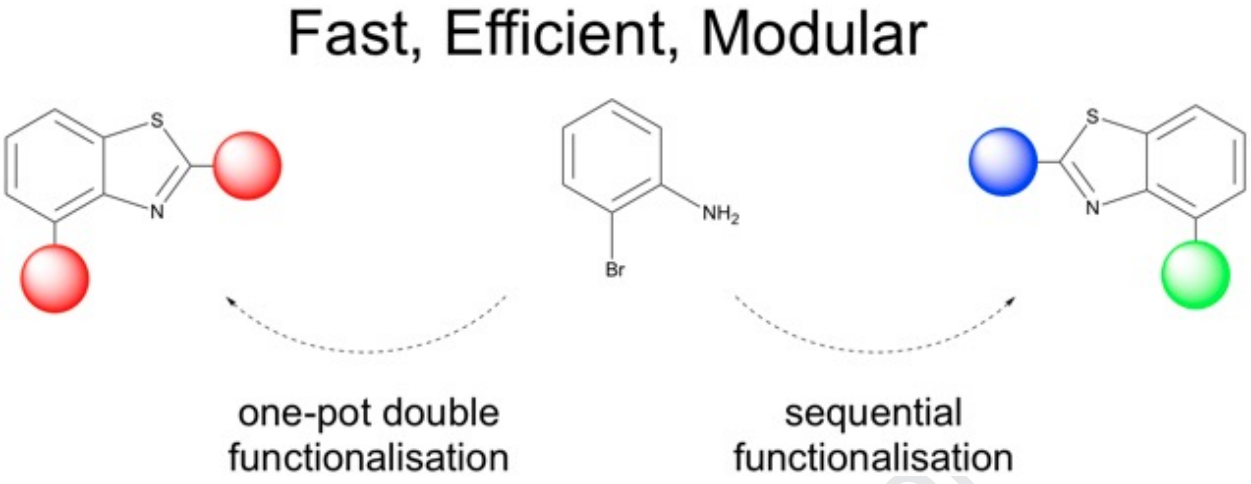

# Straightforward convergent access to 2-arylated polysubstituted benzothiazoles

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## Abstract:

A modular access to 2,4 disubstituted benzothiazoles has been achieved though the intermediacy of 4-bromo-2-iodobenzothiazole. The difference in reactivity of both halogens was advantageously exploited to achieve sequential Suzuki-Miyaura cross-coupling giving access to a range of polyaromatic derivatives featuring a central benzothiazole core.

## Keywords:

Orthogonal Reaction; Suzuki-Miyaura cross coupling; benzothiazole; boronic derivatives.

## Introduction

The benzothiazole core is considered a privileged fused bicyclic heterocycle in light of its applications in pharmaceutical, agrochemical, and materials chemistry.[1] This has driven the development of increasingly efficient methodologies towards the synthesis of functionalised 2-arylated benzothiazole scaffolds.[2] More recently, these scaffolds have found applications in organocatalyzed (de)hydrosilylation reactions where they function

as carbon-centred Lewis acids in the activation of Si–H σ bonds.[3] Substituted benzothiazoles are also involved in important applications in organic light-emitting devices (OLEDs).[4] Similar to other benzazoles,[5] they quite commonly exhibit interesting photochemical properties including processes such as Excited State Intramolecular Proton Transfer (ESIPT).[6] These molecules have also been intensively studied for their dual action potential as metal chelators and as intercalating compounds targeting pathological peptidic aggregates that of interest for imaging various dementias e.g. Alzheimer's Disease.[7]

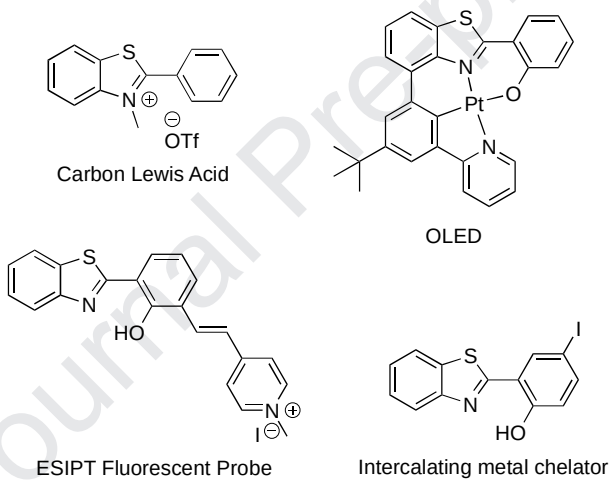



**Figure 1: Benzothiazole scaffolds integrated into various applications**

Considering that the nitrogen atom of the benzothiazole is key in all the applications mentioned and illustrated above, we focused our attention on modulating its environment by introducing substituents on position 2 and 4 of the benzothiazole core in a convergent fashion. Although numerous strategies have been designed to access substituted benzothiazoles, in nearly all cases, strategies have required non-versatile and non-modular syntheses.[1a] One major path relies on the cyclisation of functionalised arylthioamides or arylthioureas. Such starting materials require time-

consuming methods to generate thioamides (or thioureas) prior to cyclisation, most commonly from the corresponding amide with Lawesson's reagent. Alternatively, benzothiazoles can also be accessed by condensing aldehydes with 2-aminothiophenols in the presence of an oxidant (air being the mildest) or reaction with activated esters and/or acid halides. However, drawbacks with these approaches are readily appreciated by considering the poor shelf-life of many aldehydes, the high-reactivity of acid halides, as well as the poor availability of functionalized 2-aminothiophenols, which are themselves air-sensitive and easily decomposed.

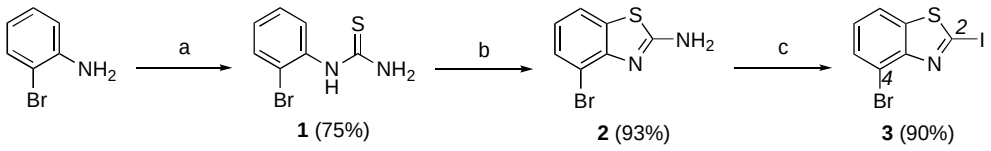
A more facile and highly convergent approach, based on readily available and stable building blocks, would be to leverage the extensive portfolio of boronic acids to access polysubstituted benzothiazole derivatives through Suzuki-Miyaura cross coupling starting with a suitable 2-iodobenzothioazole as a readily accessed coupling partner. Moreover, taking advantage of the C-2 activated position of the heterocycle might prove sufficiently selective for orthogonal coupling thus providing diversely polysubstituted benzothiazoles in a highly convergent and straightforward fashion. Herein, we present a preliminary report that establishes this strategy as a viable route to polysubsituted benzothiazoles. To test this hypothesis, we envisioned a practical and convergent strategy involving 4-bromo-2-iodobenzothiazole **3** (Scheme **1**) as a key intermediate that would enable regio/chemoselective coupling to deliver a series of C2/C4 arylated benzothiazoles. This strategy is attractive as it is highly modular as it allows for considerable synthetic versatility considering the expansive library of aryl boronic acids and derivatives available, both commercially and synthetically, as suitable coupling partners.[8] Herein, we describe the swift synthesis of versatile intermediate **3**,

substituted with two different halogens that, as part of our design, demonstrates efficient access to the said benzothiazoles via chemoselective and regioselective functionalisation with various aromatic substituents.

# Results and Discussion

## Synthesis of di-halogenated intermediate

We sought a simple, efficient, and high-yielding synthetic route with an eye to utilizing affordable and common laboratory reagents. Starting from commercially-available 2-bromoaniline, thiourea **1** was obtained following standard protocol.[9] Subsequent Hugershoff cyclization with $Br_2$ yielded the desired 2-amino-4-bromobenzothiazole (**2**) in excellent yield,[10] as usually observed for Hugershoff cyclization.[11] Although metal-free conditions have been recently reported,[12] we found out that one-pot iodination of **2**, under Sandmeyer conditions using catalytic amount of CuI, provided 4-bromo-2-iodo-benzothiazole (**3**) in excellent yield (Scheme **1**). Key intermediate **3** is obtained in three synthetic steps in 63% global yield without further optimization. This represents a significant improvement over the 5-step approach from the less available 2,3-dibromoaniline as reported in patent literature.[13]

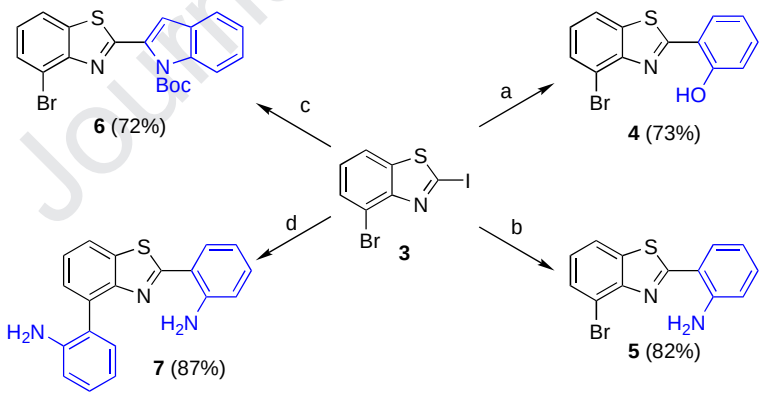



**1** (75%) **2** (93%) **3** (90%)

**Scheme 1** Synthesis of 4-bromo-2-iodobenzothiazole. **a**, BzCl, $NH_4SCN$, acetone, reflux, 1 hour. **b**, $Br_2$, $CHCl_3$, reflux 1.5 hours. **c**, (i) *p*-TsOH·$H_2O$, MeCN, room temperature, (ii) *t*-BuONO, -5 °C, 30 minutes, (iii) KI, cat. CuI, $H_2O$, 0 °C then room temperature, 18 hours.

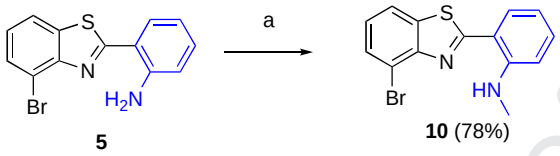
## Functionalisation of key benzothiazole intermediate

Given the well-established reactivity differences between C($sp^2$)-I and C($sp^2$)-Br bonds with respect to oxidative addition at a transition metal centre, **3** should submit to chemoselective and regioselective Suzuki-Miyaura cross-coupling with various aryl boron derivatives (Scheme **2**).[14] Indeed, products of selective mono-arylation of **3** were obtained by initial cross-coupling at C-2, at moderate reaction temperature (90 ℃), selective arylation could be achieved while safeguarding the C-Br bond intact for further functionalization (*vide infra*). Notably, 2-hydroxyphenyl-boronic acid, 2-aminophenyl-boronic acid, and *N*-Boc-indole-2-boronic acid could be coupled to **3**, furnishing 2-aryl-4-bromobenzthiazoles **4**, **5** and **6**, respectively in good yields. Notably, if desired, one-pot, double cross-coupling with 2-aminophenylboronic acid was found to be highly efficient, providing the corresponding 2,4-dianiline (**7**) in 87% yield.



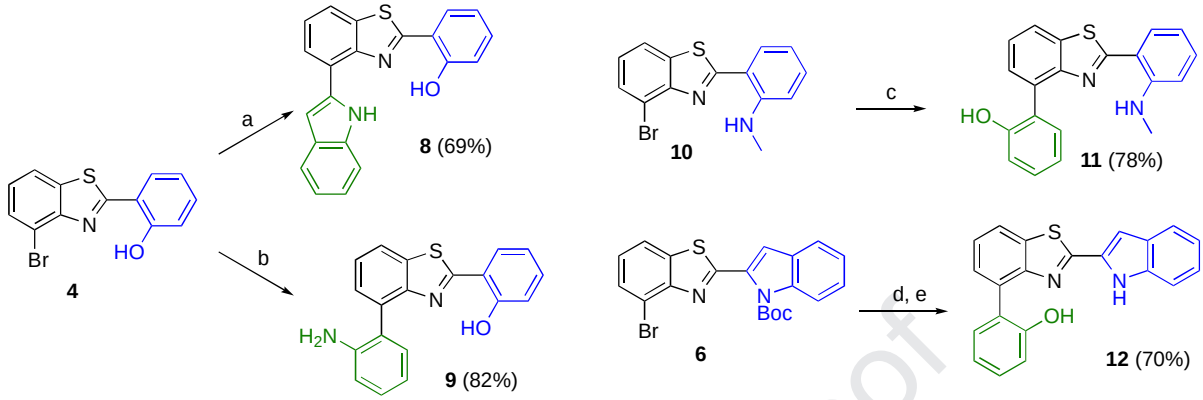

**Scheme 2.** Selective coupling at position 2 and double cross-coupling
**a**, 2-hydroxyphenylboronic acid, $Pd(PPh_3)_4$, $Na_2CO_3$, DMF/$H_2O$, microwave, 90 °C, 1 hour. **b**, 2-aminophenylboronic acid, $Pd(PPh_3)_4$, XantPhos, $Na_2CO_3$, 1,4-dioxane/$H_2O$, microwave, 90 °C, 1 hour. **c**, *N*-Boc-indole-2-boronic acid, $Pd(PPh_3)_4$, $Cs_2CO_3$, 1,4-dioxane/$H_2O$, microwave, 90 °C, 1 hour. d) 2-aminophenylboronic acid, $Pd(PPh_3)_4$, $Na_2CO_3$, DMF/$H_2O$, microwave, 120 °C, 5 hour.

The aniline in benzothiazole **5** was shown to efficiently undergo selective mono-*N*-methylation using Re-catalysed reaction in MeOH, while conserving the C-Br bond and avoiding tedious separation with polymethylated products, providing **10** in good yield. (Scheme 3).[16]




**Scheme 3.** Monomethylation of **5**
a) $Re(NH(CH_2CH_2PPh_2)_2)(CO)_3Br$, $Cs_2CO_3$, MeOH, 140 °C, 5 days.

To capitalize on the extant C-Br bond, compounds **4**,**6**, and **10** could be further functionalised in step-wise fashion, at C-4, via cross-coupling with various arylboronic acids or trifluoroborates. For example, reaction of **4** with potassium *N*-Boc-indole-2-trifluoroborate, under conditions reported by Molander *et al.*,[15] or with 2-aminophenylboronic acid furnished 2,4-diarylbenzthiazoles **8** and **9**, respectively, in good yields. Benzothiazole derivative **10** could be further cross-coupled with 2-hydroxyphenylboronic acid to furnish 2,4-diarylbenzothiazole **11** in good yield. Finally, 4-bromo-2-indolebenzothiazole **6**, after Boc-deprotection of **6** to **6a**, could be coupled with 2-hydroxyphenylboronic acid to provide **12** in high yield.




**Scheme 4.** Secondary coupling at position 4 yielding 2,4-disubstituted benzothiazoles. **a**, potassium *N*-Boc-indole-2-trifluoroborate, $Pd(OAc)_2$, SPhos, $Na_2CO_3$, EtOH, 85 °C, 5 hours. **b**, 2-aminophenylboronic acid, $Pd(PPh_3)_4$, $Na_2CO_3$, DMF/$H_2O$, microwave, 120 °C, 1 hour. **c**, 2-hydroxyphenylboronic acid, $Pd(PPh_3)_4$, $Na_2CO_3$, DMF/$H_2O$, 120 °C, 18 hours. **d**, TFA/DCM (1:1), room temperature, 2 hours. **e**, 2-hydroxyphenylboronic acid, $Pd(PPh_3)_4$, $Na_2CO_3$, DMF/$H_2O$, 120 °C, 1 hour.

## Photophysical Properties

Given the increasing interest and application of the absorptive and emissive properties of benzothiazoles, we briefly studied the photophysical properties of these novel benzothiazoles. As a general trend, these benzothiazoles exhibit similar absorption spectra, consisting of large bands in the UV region of the spectrum; they absorb strongly with absorption maxima ranging from 339 to 405 nm that are attributed to characteristic π-π* transitions. However, on closer inspection it becomes evident that the nature of the aromatic group at C-2 determines the absorption profile, while the substitution at C-4 delivers fine-tuning of the absorption maximum (Figures 2, 3 and 4). These compounds were also found to be fluorescent, with broad emission bands ranging from 403 to 519 nm, corresponding to Stokes shifts ($\Delta_{SS}$) varying from 39 to 180 nm (Figure 5). The large $\Delta_{SS}$ are only observed for compounds **4, 8** and **9** which feature

2-hydroxylphenyl at C-2, allowing for the possibility of ESIPT which induces significant structural reorganisation in the excited state, accounting for the large $\Delta_{SS}$. In contrast to the relationship observed in absorption, the substituent at C-4 has no effect on emission profiles or maxima.

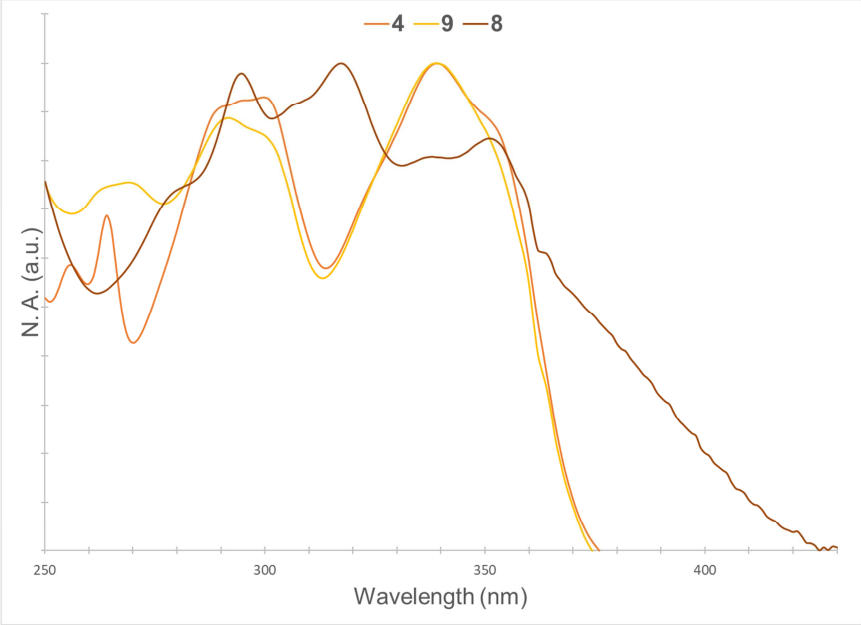



**Figure 2: UV Absorption spectra of 4,8 and 9.**

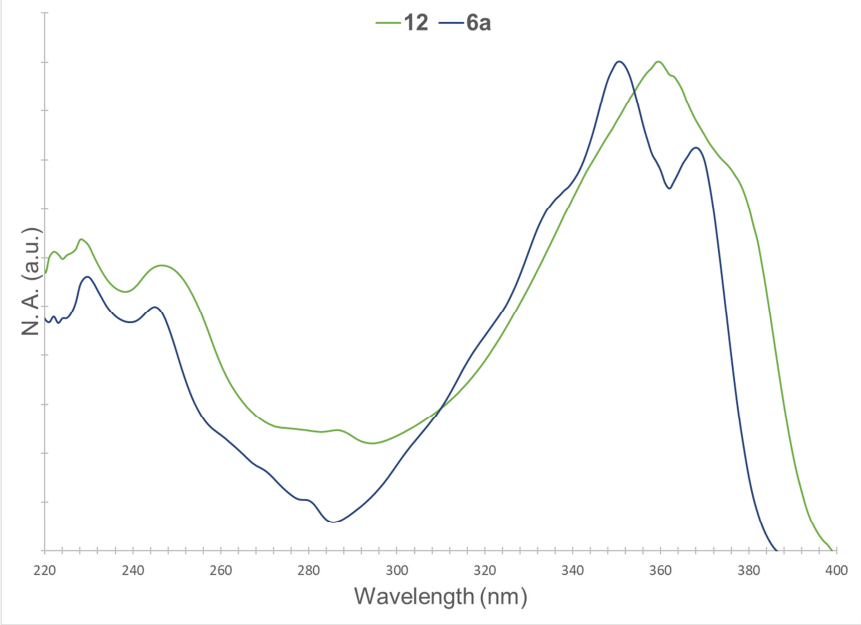


**Figure 3: UV Absorption spectra of 12 and 6a.**

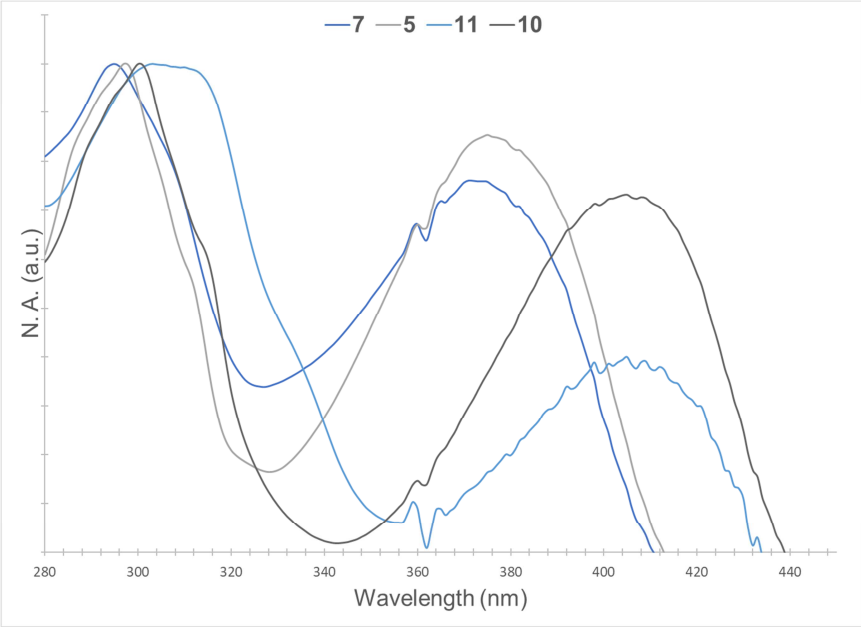



**Figure 4: UV Absorption spectra of 5, 7, 10 and 11.**

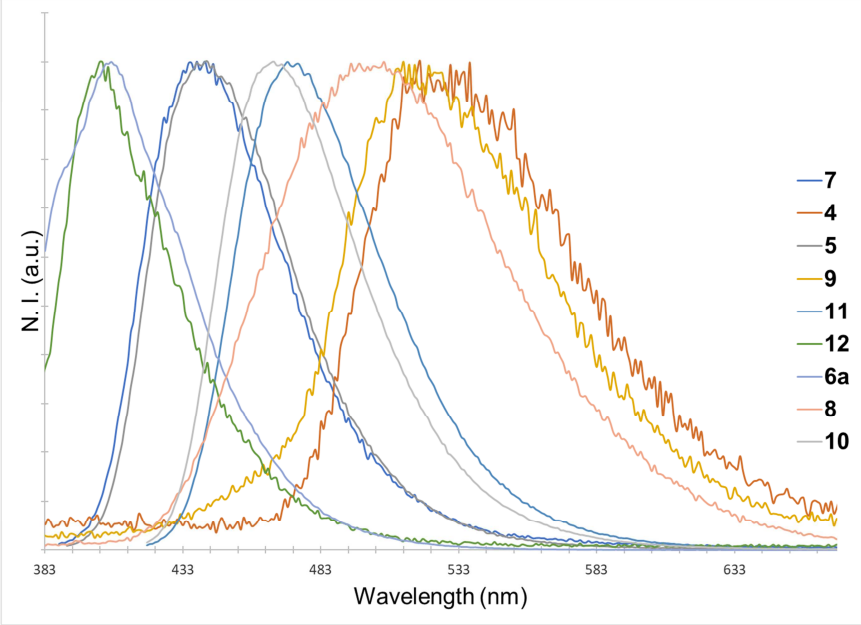



**Figure 5: Fluorescence spectra of 4, 5, 6a, 7, 8, 9, 10, 11 and 12.**

**Table 1 Photophysical properties of compounds 4-12**

| Compound | $\lambda_{abs}$ (nm) | log ε ($M^{-1}$ $cm^{-1}$) | $\lambda_{em}$ (nm) | $\Delta_{ss}$ (nm - $cm^{-1}$) |
|---|---|---|---|---|
| **4** | 339 | 4.1 | 519 | 180 - 10231 |
| **5** | 376 | 4.0 | 442 | 66 -3971 |
| **6a** | 368 | 4.4 | 407 | 39 - 2604 |
| **7** | 373 | 4.0 | 438 | 65 - 3979 |
| **8** | 351 | 4.1 | 506 | 155 - 8727 |
| **9** | 339 | 4.2 | 513 | 174- 10005 |
| **10** | 405 | 4.1 | 466 | 61- 3232 |
| **11** | 405 | 3.6 | 471 | 66 - 3460 |
| **12** | 360 | 4.5 | 403 | 43 - 2964 |

# Conclusion

In conclusion, here we have demonstrated the facile synthesis of a wide variety of 2-aryl-4-bromo and 2,4-diarylbenzothiazole derivatives via selective Suzuki-Miyaura cross-coupling with key benzothiazole intermediate **3**. This scaffold has proven versatile, allowing selective structural elaboration firstly at the C-2 position, in high yields, followed by functionalisation at the C-4 position; the scaffold can also be di-functionalised in one-pot at both the C-2 and C-4 positions. This strategy gives rapid access to a diverse family of benzothiazoles with tuneable photophysical properties. Although our synthesis is somewhat limited in scope, we suggest that this reaction manifold should be readily amenable to preparing a large number of tricyclic compounds starting with (hetero)arylboronic acids. Hence, in this preliminary report, we acknowledge this methodology serves as a proof of concept for its expansion towards

the functionalisation of other positions on the benzothiazole core in a similar fashion. It is readily anticipated more densely functionalized bromoanilines should readily submit to this reaction scheme. The novel benzothiazoles derivatives reported here accessible through **3**, or derivatives thereof, are further anticipated to be of interest for photophysical studies in both solution and the solid-state, as well as their investigation as Lewis acid catalysts and as chelators for various metal cations. Studies towards these goals are currently underway.

# Experimental section:

## General Information

*Solvents and Reagents*

All chemicals were purchased from commercial sources and used as received unless otherwise noted. Solvents used were all commercial grade and used as received with no drying, all reactions were performed in oven-dried glassware under ambient atmosphere unless otherwise stated. Deuterated solvents for NMR spectroscopic analysis were purchased from Euriso-top.

*Analysis*

NMR experiments were performed in deuterated solvents. $^{1}$H NMR, $^{13}$C NMR, $^{11}$B NMR and $^{19}$F spectra were recorded on 300 Avance (300 MHz), 400 Avance (400 MHz) and 400 AvanceIII (400 MHz) Bruker spectrometers. All spectra were recorded at ambient temperature (298 K). Chemical shifts (δ) are reported in parts per million (ppm) relative to the residual protium in the solvents ($^{1}$H) or the solvent carbon ($^{13}$C) as internal standards. Multiplicity of signals is indicated using the following abbreviations: s (singlet), b (broad), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplet), td (triplet of doublet), hept (heptet) and m (multiplet). Reactions were monitored using Merck Silica gel 60 $F_{254}$ glass backed plates. TLC plates were

visualized by UV fluorescence (λ= 254, 365 nm) and $KMNO_4$ stain. Flash column chromatography was performed using VWR Chemicals Silica gel 60 – 200 µm or on an automated Interchim puriFlash system using pre-packed Interchim 30 µm Silica gel cartridges. IR spectra were recorded on a PerkinElmer Spectrum One or Frontier FT-IR spectrometer with frequencies expressed in $cm^{-1}$. UV/Vis spectra were recorded on an Agilent 8453 Spectroscopy System using a 10 mm Quartz cuvette. Fluorescence spectra were recorded on a HORIBA Jobin Yvon FluoroMax-4 Spectrofluorometer. High-resolution mass spectra (HRMS) were recorded using either electrospray ionization (ESI) or desorption chemical ionization (DCI) using a Waters GCT Premier or Sciex QTRAP 4500 AB or Thermo Fisher Scientific DSQ II spectrometers.

## Synthetic procedures and characterisation data for 1 – 12

### 2-bromophenylthiourea (1)

A two-necked 250 mL round-bottom flask was charged with a stir bar, condenser, $NH_4SCN$ (10.9250 g, 0.13 mol) and acetone (50 mL). Benzoyl chloride (13.93 mL, 0.12 mol) was added dropwise via syringe to the rapidly stirring reaction mixture. The mixture was heated at reflux for 15 minutes, and then cooled back down to room temperature. In an addition funnel, 2-bromoaniline (22.63 mL, 0.1 mol) was dissolved in acetone (25 mL), this solution was added dropwise to the vigorously stirring reaction mixture over 15 minutes; the reaction mixture was then heated at reflux for 1 hour. The crude mixture was then dropped onto excess water and vigorously stirred. A yellow precipitate formed and was collected by filtration and washed with water until washes were colourless. The precipitate was then washed with cold MeOH/$H_2O$ solution (1:1). In a 1L Erlenmeyer flask, 10% aq. NaOH solution (400 mL) was prepared and heated to 80 ℃. The washed precipitate was then added to this base solution for hydrolysis. The precipitate dissolved into the base solution producing a clear yellow solution, this was stirred at 80 ℃ for 15 minutes. The solution was then acidified to pH 2 using concentrated HCl (37%, 12 M), producing a white precipitate. The solution was then basified to pH 9 using a 25% aq. $NH_4OH$ solution producing a white precipitate which was collected by filtration and washed with water until washes were neutral. The product, a white powder, was then

dried under high vacuum (17.3748 g, 75%). IR $v_{max}/cm^{-1}$ (neat film): 3425, 3253, 3245, 3124, 3002, 1619, 1500, 1466, 1427, 1290, 1063, 1039, 1025, 818, 758, 706. $^{1}H$ NMR (400 MHz, Acetone-$d_6$) δ 8.66 (bs, 1H), 7.72 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.40 (td, *J* = 7.9, 1.4 Hz, 1H), 7.20 (td, *J* = 7.8, 1.6 Hz, 1H), 7.09 (bs, 2H). $^{13}C$ NMR (101 MHz, Acetone-$d_6$) δ 184.2 ($C_q$), 138.2 ($C_q$), 133.8 (CH), 130.1 (CH), 128.9 (CH), 128.9 (CH), 121.1 ($C_q$). HRMS-ESI (*m/z*): found $[M^{79}Br+H]^+$ 230.9595, calc'd $C_7H_8N_2S^{79}Br$ requires 230.9592, found $[M^{81}Br+H]^+$ 232.9574, calc'd $C_7H_8N_2S^{81}Br$ requires 232.9572.

**2-amino-4-bromobenzothiazole (2)**

A 50 mL, two-necked, round-bottom flask was charged with a stir bar, 2-bromophenylthiourea (2.3204 g, 10 mmol) and $CHCl_3$ (10 mL). Bromine (0.51 mL, 10 mmol) was dissolved in $CHCl_3$ (5 mL) in an addition funnel and affixed to the main neck of the round-bottom flask, the second neck was connected to a base trap to neutralize HBr fumes developed during the reaction. The flask was cooled to 0 ℃ in an ice-bath and the bromine solution was added dropwise to the vigorously stirring reaction mixture (note: often the sides needed to be scraped down as the bromine solution would coagulate on the bottom and sides of the flask). The addition funnel was then replaced with a condenser and the reaction mixture heated at reflux for 1.5 hours until complete conversion of starting material was determined by TLC; with external heat HBr gas evolution became rapid. During the reaction, a fine yellow precipitate evolved in a clear red/brown solution. After cooling to room temperature, all solvent was removed under reduced pressure. The remaining residue was dissolved in EtOAc (100 mL) and washed with sat'd aq. $NaHCO_3$ (2 x 100 mL), 5% aq. $Na_2S_2O_3$ (2 x 50 mL) and brine (2 x 50 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure and further dried under high vacuum overnight to furnish the product as a yellow powder (2.1296 g, 93%). IR $v_{max}/cm^{-1}$ (neat film): 3446, 3277, 3073, 2926, 1635, 1531, 1415, 1269, 882, 750, 725. $^{1}H$ NMR (400 MHz, Acetone-$d_6$) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.51 (bs, 2H), 7.45 (d, *J* = 7.8 Hz, 1H), 6.96 (t, *J* = 7.8 Hz, 1H). $^{13}C$ NMR (101 MHz, Acetone-$d_6$) δ 168.2 ($C_q$), 151.8 ($C_q$), 132.9 ($C_q$), 129.7 (CH), 123.1

(CH), 121.0 (CH), 111.9 (CH). HRMS-ESI (*m/z*): found $[M^{79}Br+H]^+$ 228.9440, calc'd $C_7H_6N_2S^{79}Br$ requires 228.9435, $[M^{81}Br+H]^+$ 230.9418, calc'd $C_7H_6N_2S^{81}Br$ requires 230.9419.

**4-bromo-2-iodobenzothiazole (3)**

A 500 mL round-bottom flask was charged with a stir bar, 2-amino-4-bromobenzothiazole (9.85 g, 42 mmol), *p*-TsOH·$H_2O$ (24.9 g, 129 mmol) and MeCN (172 mL). The heterogenous reaction mixture was stirred and cooled in an ice-brine bath to -5 ℃, at which point *t*-BuONO (15.3 mL, 129 mmol) was added dropwise, over 10 minutes, via an addition funnel; after the addition was complete the reaction mixture was stirred at -5 ℃ for 30 minutes. An additional funnel was then charged with a water (43 mL) solution of KI (21.4 g, 129 mmol) and CuI (819 mg, 4.3 mmol). The KI solution was added dropwise to the vigorously stirred reaction mixture at 0 ℃ over 20 minutes; the reaction mixture was then allowed to warm to room temperature overnight. The crude reaction mixture was concentrated under reduced pressure to ~70 mL and then dropped on sat'd aq. $NaHCO_3$ (150 mL), the phases separated, and the aqueous phase extracted with EtOAc (4 x 150 mL). The combined organic phases were then washed with a 5% aqueous $Na_2S_2O_3$ solution (4 x 150 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to furnish the product as a brown powder (13.1607 g, 90%). IR $\nu_{max}/cm^{-1}$ (neat film): 3089, 3064, 2931, 2851, 1442, 1391, 1203, 952, 842, 764, 732. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.12 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 152.0 ($C_q$), 139.8 ($C_q$), 129.7 (CH), 126.9 (CH), 121.1 (CH), 114.6 ($C_q$), 112.8 ($C_q$). HRMS-ESI (*m/z*): found $[M^{79}Br+H]^+$ 339.8298, calc'd $C_7H_4NS^{79}BrI$ requires 339.8293, $[M^{81}Br+H]^+$ 341.8279, calc'd $C_7H_4NS^{81}BrI$ requires 341.8272.

**2-(2-hydroxyphenyl)-4-bromobenzothiazole (4)**

A 10 mL μwave vial was charged with a stir bar, 4-bromo-2-iodobenzothiazole (35 mg, 0.1 mmol), 2-hydroxyphenylboronic acid (20.5 mg, 0.15 mmol), $Pd(PPh_3)_4$ (12 mg, 10 mol%), $Na_2CO_3$ (74 mg, 0.7 mmol), DMF (0.8 mL) and water (0.2 mL). The reaction mixture was stirred at room temperature for 5 minutes, while bubbling the reaction mixture with Ar. The vial was then loaded into a microwave reactor and heated at 90 ℃ for 1 hour, after which TLC (cyclohexane/$CH_2Cl_2$, 3:2) showed complete conversion of starting material. The crude was dropped onto brine (10 mL) and the phases separated, the aqueous phase was extracted with EtOAc (3 x 15 mL) and the combined organic phases washed with brine (2 x 10 mL). The organic phase was dried over anhydrous $MgSO_4$, then filtered and concentrated on Celite. The crude was purified on Silica gel flash column chromatography using 100% cyclohexane to 4:1 cyclohexane/$CH_2Cl_2$ as the eluent. Fractions were collected and concentrated to furnish the product as an off-white powder which was further dried under high vacuum (23 mg, 73%). IR $\nu_{max}/cm^{-1}$ (neat film): 3045, 2922, 2851, 1586, 1482, 1266, 1218, 1091, 977, 743. $^1$H NMR (400 MHz, Chloroform-*d*) δ 7.79 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.66 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.63 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.39 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.11 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.94 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 169.8 ($C_q$), 158.2 ($C_q$), 150.3 ($C_q$), 133.4 ($CH_{Arom}$, $C_q$), 130.1 ($CH_{Arom}$), 128.5 ($CH_{Arom}$), 126.5 ($CH_{Arom}$), 120.7 ($CH_{Arom}$), 119.7 ($CH_{Arom}$), 118.2 ($CH_{Arom}$), 116.5 ($C_q$), 115.8 ($C_q$). HRMS-DCI-$CH_4$ (*m/z*): found $[M]^+$ 305.9602, calc'd $C_{13}H_9NOS^{79}Br^+$ requires 305.9588.

**2-(2-aminophenyl)-4-bromobenzothiazole (5)**

A 10 mL microwave vial was charged with a stir bar, 4-bromo-2-iodobenzothiazole (34.1 mg, 0.1 mmol), 2-aminophenylboronic acid (21.8 mg, 0.15 mmol), $Na_2CO_3$ (48 mg, 0.45 mmol), $Pd(PPh_3)_4$ (12 mg, 10 mol%), 1,4-dioxane (0.8 mL) and water (0.2 mL). The vial was purged with Ar and loaded into a microwave reactor and heated at 90 ℃ for 1 hour. The reaction mixture was cooled to room temperature before being transferred to a

separatory funnel with sat'd aq. $NaHCO_3$ (10 mL), the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined aqueous phases were washed with brine (3 x 20 mL), then dried over anhydrous $MgSO_4$, filtered and the filtrate concentrated onto Celite under reduced pressure. The crude material was purified by Silica gel flash column chromatography using an eluent of 100% cyclohexane to cyclohexane/EtOAc (4:1). Desired fractions were collected and concentrated under reduced pressure, and further under high vacuum overnight to furnish the desired compound as a yellow powder (25 mg, 82%). IR $\nu_{max}/cm^{-1}$ (neat film): 3460, 3295, 3063, 2924, 1615, 1594, 1494, 1449, 1227, 964, 735. $^1$H NMR (300 MHz, Chloroform-*d*) δ 7.79 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.64 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.24 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 6.82 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.74 (ddd, *J* = 8.2, 7.2, 1.1 Hz, 1H). $^{13}$C NMR (75 MHz, Chloroform-*d*) δ 169.7 ($C_q$), 152.0 ($C_q$), 147.0 ($C_q$), 134.1 ($C_q$), 132.2 ($CH_{Arom}$), 130.3 ($CH_{Arom}$), 129.5 ($CH_{Arom}$), 125.8 ($CH_{Arom}$), 120.4 ($CH_{Arom}$), 117.3 ($CH_{Arom}$), 117.1 ($CH_{Arom}$), 116.1 ($C_q$), 114.9 ($C_q$). HRMS-ESI (*m/z*): found $[M^{79}Br+H]^+$ 304.9752, calc'd $C_{13}H_{10}N_2SBr^+$ requires 304.9748.

**_tert_-butyl 2-(4-bromobenzothiazol-2-yl)-1*H*-indole-1-carboxylate (6)**

A 35 mL microwave vial was charged with a stir bar, 4-bromo-2-iodobenzothiazole (34.3 mg, 0.1 mmol), *N*-Boc-indole-2-boronic acid (32 mg, 0.12 mmol), $Pd(PPh_3)_4$ (65 mg, 50 mol%), $Cs_2CO_3$ (84.7 mg, 0.26 mmol), 1,4-dioxane (7.7 mL) and water (0.3 mL). The reaction mixture was degassed (3 x freeze-pump-thaw) and then purged with Ar. The vial was loaded into a microwave reactor and programmed to be heated at 90 ℃ for 1 hour, after which the crude was dropped onto water (10 mL) and the phases separated. The aqueous phase was extracted with EtOAc (3 x 10 mL), the combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated onto Celite. The crude residue was purified by Silica gel flash column chromatography using 100% cyclohexane to cyclohexane/EtOAc (9.5:0.5). Desired fractions were collected and concentrated to furnish the desired product as a yellow oil which was further dried under vacuum overnight (31 mg, 72%). IR $\nu_{max}/cm^{-1}$ (neat film): 3066, 2978, 2930, 1735, 1442, 1368, 1321, 1221, 1157, 1132, 1006, 739. $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.22 (dd,

*J* = 8.3, 0.9 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.59 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.40 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.03 (s, 1H), 1.34 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 161.0 ($C_q$), 151.8 ($C_q$), 149.5 ($C_q$), 138.3 ($C_q$), 136.3 ($C_q$), 131.4 ($C_q$), 130.1 ($CH_{Arom}$), 128.3 ($C_q$), 126.5 ($CH_{Arom}$), 126.3 ($CH_{Arom}$), 123.5 ($CH_{Arom}$), 121.6 ($CH_{Arom}$), 120.8 ($CH_{Arom}$), 117.1 ($C_q$), 115.5 ($CH_{Arom}$), 115.1 ($CH_{Arom}$), 84.5 ($C_q$), 27.8 ($CH_{3t\text{-}Bu}$). HRMS-DCI($CH_4$) (*m/z*): found $[M]^+$ 428.0194, calc'd $C_{20}H_{17}{}^{79}BrN_2O_2S$ requires 428.0194.

**4-bromo-2-(1*H*-indol-2-yl)benzothiazole (6a)**

A 10 mL round-bottom flask was charged with a stir bar, *tert*-butyl 2-(4-bromobenzo[d]thiazol-2-yl)-1H-indole-1-carboxylate (150 mg, 0.35 mmol) and $CH_2Cl_2$ (1 mL). Trifluoroacetic acid (TFA) (1 mL) was added via syringe dropwise and the reaction mixture stirred at room temperature for 2 hours. All solvent was removed under reduced pressure and the residue dissolved in $CH_2Cl_2$ (10 mL) and dropped onto sat'd aq. $NaHCO_3$. The phases were separated, and the aqueous phase extracted with $CH_2Cl_2$ (3 x 10 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated onto Celite. The crude residue was purified by Silica gel flash column chromatography using 100% cyclohexane to cyclohexane/EtOAc (9:1). Desired fractions were collected and concentrated to furnish the desired product as a yellow powder which was further dried under vacuum overnight (111.3 mg, 97%). IR $\nu_{max}/cm^{-1}$ (neat film): 3398, 3380, 3058, 2960, 2921, 2852, 1588, 1557, 1459, 1439, 1397, 1339, 1302, 1142, 1035, 917, 788, 766, 747, 733, 668. $^1$H NMR (400 MHz, Chloroform-*d*) δ 9.54 (bs, 1H, N-H), 7.81 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.68 (ddd, *J* = 8.0, 2.2, 1.0, 2H), 7.45 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.31 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.19 – 7.13 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 160.5 ($C_q$), 151.9 ($C_q$), 137.2 ($C_q$), 135.6 ($C_q$), 131.0 ($C_q$), 130.1 ($CH_{Arom}$), 128.5 ($C_q$), 126.2 ($CH_{Arom}$), 125.1 ($CH_{Arom}$), 121.9 ($CH_{Arom}$), 121.01 ($CH_{Arom}$), 120.95 ($CH_{Arom}$), 116.5 ($C_q$), 111.8 ($CH_{Arom}$), 106.2 ($CH_{Arom}$). HRMS-DCI($CH_4$) (*m/z*): found $[M+H]^+$ 328.9749, calc'd $C_{15}H_9{}^{79}BrN_2S$ requires 328.9748.

**2,2'-(benzothiazole-2,4-diyl)dianiline (7)**

A 10 mL microwave vial was charged with a stir bar, 4-bromo-2-iodobenzothiazole (34 mg, 0.1 mmol), 2-aminophenylboronic acid (41.1 mg, 0.3 mmol), $Na_2CO_3$ (106 mg, 1 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), DMF (0.6 mL) and water (0.2 mL). The crude mixture was then degassed (3 x freeze-pump-thaw) and purged with Ar. The vial was loaded into a microwave reactor and heated at 120 °C for 5 hours. The reaction mixture was cooled to room temperature before being transferred to a separatory funnel with sat'd aq. $NaHCO_3$ (10 mL), the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine (3 x 20 mL), then dried over anhydrous $MgSO_4$, filtered and the filtrate concentrated onto Celite under reduced pressure. The crude material was purified using Silica gel flash chromatography using an eluent of 100% cyclohexane to 70:30 cyclohexane/EtOAc. Desired fractions were collected and concentrated under reduced pressure, and further under high vacuum overnight to furnish the desired compound as a red powder (27.6 mg, 87%). IR $\nu_{max}/cm^{-1}$ (neat film): 3457, 3372, 3305, 3055, 3024, 2924, 2853, 1698, 1614, 1593, 1494, 1223, 963, 748. $^1$H NMR (300 MHz, Acetone-$d_6$) δ 8.03 (dq, *J* = 5.8, 3.6 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.50 (dd, *J* = 4.6, 0.8 Hz, 2H), 7.28 – 7.10 (m, 3H), 6.95 (bs, 2H), 6.91 – 6.83 (m, 2H), 6.74 (td, *J* = 7.4, 1.2 Hz, 1H), 6.66 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 4.46 (bs, 2H). $^{13}$C NMR (75 MHz, Acetone-$d_6$) δ 156.5 ($C_q$), 152.6 ($C_q$), 148.8 ($C_q$), 146.4 ($C_q$), 134.9 ($C_q$), 134.6 ($C_q$), 132.5 ($CH_{Arom}$), 131.9 ($CH_{Arom}$), 130.7 ($CH_{Arom}$), 129.5 ($CH_{Arom}$), 128.4 ($CH_{Arom}$), 126.2 ($CH_{Arom}$), 125.4 ($C_q$), 121.6 ($CH_{Arom}$), 117.8 ($CH_{Arom}$), 117.5 ($CH_{Arom}$), 116.9 ($CH_{Arom}$), 116.4 ($CH_{Arom}$), 114.9 ($C_q$). HRMS-ESI (*m/z*): found $[M+H]^+$ 318.1062, calc'd $C_{19}H_{16}N_3S^+$ requires 318.1065.

**Potassium *N*-Boc-indole-2-trifluoroborate**

A 25 mL round-bottom flask was charged with a stir bar, *N*-(tert-butoxycarbonyl)indole-2-boronic acid (1.1653 g, 4.5 mmol) and MeOH (1.3 mL). The reaction mixture was stirred until all boronic acid had dissolved then aq. $KHF_2$ (4.5 M, 3.3 mL, 14.9 mmol) was added dropwise; the reaction became a pink slurry, additional MeOH was added to

ensure efficient stirring. The reaction mixture was stirred at room temperature for 2 hours after which complete conversion was determined by $^{11}$B NMR. All solvent was removed under reduced pressure and the white residue left to dry under high vacuum for 6 hours. The crude was triturated with acetone (3 x 20 mL) and filtered to remove insoluble solids. The acetone filtrate was concentrated to saturation then dropped onto pentane to precipitate the desired salt as a white powder which was collected by filtration, washed with pentane then dried under high vacuum overnight (1.4246 g, >99%). $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.07 – 7.95 (m, 1H), 7.42 – 7.35 (m, 1H), 7.05 (pd, *J* = 7.1, 1.5 Hz, 2H), 6.40 (d, *J* = 0.8 Hz, 1H), 1.57 (s, 9H). $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ -135.84 – -136.78 (m). $^{11}$B NMR (128 MHz, DMSO-$d_6$) δ 1.46 (bs). LRMS-ESI (*m/z*): $[M-K]^-$ 284. Characterisation data matches previous literature reports.[15]

**2-(4-(1*H*-indol-2-yl)benzothiazol-2-yl)phenol (8)**

A 10 mL microwave vial was charged with a stir bar, 2-(4-bromobenzo[d]thiazol-2-yl)phenol (31.4 mg, 0.1 mmol), potassium *N*-(*tert*-butoxycarbonyl)indole-2-trifluoroborate (41.3 mg, 0.12 mmol), $Pd(OAc)_2$ (2.6 mg, 10 mol%) and SPhos (10.3 mg, 25 mol%). The vial was placed under vacuum and purged with Ar (x 3) before EtOH (1 mL) was added. The vial was loaded into a microwave reactor and heated at 85 ℃ for 5 hours. The crude was dropped onto brine (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and all solvent removed under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (1 mL) and TFA (1 mL) and stirred at room temperature for 2 hours. Solvent was removed under reduced pressure and the residue dissolved in $CH_2Cl_2$ (10 mL) and washed with sat'd aq. $NaHCO_3$ (2 x 10 mL) until pH was basic (~8) then brine (10 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated onto Celite. The crude residue was purified on Si gel flash column chromatography using an eluent of 100% cyclohexane to 8.5:1.5 cyclohexane/EtOAc. Desired fractions were collected and concentrated to furnish the desired product as an orange powder which was further dried under high vacuum overnight (23.6 mg, 69%). IR $\nu_{max}$/cm$^{-1}$ (neat film): 3441, 3357, 3054, 2956, 2919, 2846, 1621, 1583, 1481, 1450, 1418, 1301, 1222, 747. $^{1}$H NMR (400

MHz, Chloroform-*d*) δ 11.91 (s, 1H, O-H), 9.32 (s, 1H, N-H), 7.83 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.80 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.70 (td, *J* = 7.8, 7.4, 1.3 Hz, 2H), 7.51 (dq, *J* = 8.1, 0.9 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.40 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.12 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.09 (dd, *J* = 2.2, 0.9 Hz, 1H), 6.98 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 169.6 ($C_q$), 157.5 ($C_q$), 148.1 ($C_q$), 137.0 ($C_q$), 135.4 ($C_q$), 134.2 ($C_q$), 133.3 ($CH_{Arom}$), 128.76 ($CH_{Arom}$), 128.7 ($C_q$), 126.3 ($C_q$), 126.0 ($CH_{Arom}$), 125.1 ($CH_{Arom}$), 123.0 ($CH_{Arom}$), 121.0 ($CH_{Arom}$), 120.47 ($CH_{Arom}$), 120.43 ($CH_{Arom}$), 120.1 ($CH_{Arom}$), 118.0 ($CH_{Arom}$), 117.0 ($C_q$), 111.5 ($CH_{Arom}$), 102.4 ($CH_{Arom}$). HRMS-ESI (*m/z*): found $[M+H]^+$ 343.0902, calc'd $C_{21}H_{15}N_2OS$ requires 343.0905.

**2-(2-hydroxyphenyl)-4-(2-aminophenyl)benzothiazole (9)**

A 10 mL microwave vial was charged with a stir bar, 2-(2-hydroxyphenyl)-4-bromobenzothiazole (33.6 mg, 0.1 mmol), 2-aminophenylboronic acid (28.7 mg, 0.21 mmol), $Pd(PPh_3)_4$ (12 mg, 10 mol%), $Na_2CO_3$ (78 mg, 0.7 mmol), DMF (0.8 mL) and water (0.2 mL). The reaction mixture was degassed (3 x freeze-pump-thaw) then purged with Ar. The vial was loaded into a microwave reactor and programmed to be heated at 120 ℃ for 1 hour, after which the crude was dropped onto water (10 mL) and the phases separated. The aqueous phase was extracted with EtOAc (3 x 10 mL), the combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated onto Celite. The crude residue was purified by Silica gel flash column chromatography using cyclohexane/EtOAc (4:2 to 1:1). Desired fractions were collected and concentrated to furnish the desired product as a yellow powder which was further dried under vacuum overnight (28.7 mg, 82%). IR $\nu_{max}$/cm$^{-1}$ (neat film): 3466, 3371, 3211, 3057, 3021, 2920, 2250, 1936, 1612, 1577, 1482, 1467, 1219, 1151, 977, 726. $^1$H NMR (400 MHz, Chloroform-*d*) δ 12.27 (bs, 1H, O-H), 7.91 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.68 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.56 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.36 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H), 7.31 – 7.20 (m, 2H), 7.04 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.98 – 6.84 (m, 3H), 3.76 (bs, 2H, N-$H_2$). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 169.2 ($C_q$), 158.0 ($C_q$), 150.0 ($C_q$), 144.0 ($C_q$), 133.6 ($C_q$), 133.4 ($C_q$), 133.0 ($CH_{Arom}$), 131.3 ($CH_{Arom}$),

129.5 ($CH_{Arom}$), 128.4 ($CH_{Arom}$), 128.2 ($CH_{Arom}$), 126.1 ($CH_{Arom}$), 124.4 ($C_q$), 120.9 ($CH_{Arom}$), 119.6 ($CH_{Arom}$), 118.7 ($CH_{Arom}$), 118.0 ($CH_{Arom}$), 116.9 ($C_q$), 116.2 ($CH_{Arom}$). HRMS-ESI (*m/z*): found $[M+H]^+$ 319.0905, calc'd $C_{19}H_{15}N_2OS$ requires 319.0905.

**2-(2-methylaminophenyl)-4-bromobenzothiazole (10)[16]**

An oven dried 10 mL Pyrex Wheaton vial was charged with a stir bar, [Re] (23 mg, 0.025 mmol, 5 mol%), $Cs_2CO_3$ (188.9 mg, 0.6 mmol, 100 mol%), 2-(2-aminophenyl)-4-bromobenzothiazole (174.5 mg, 0.6 mmol) and dry MeOH (2 mL). The vial was purged with Ar, then the reaction mixture degassed (3 x freeze-pump-thaw) and left under an atmosphere of Ar before being sealed with a Teflon lined cap. The vial was then placed in an oil bath at 140 ℃ and reaction progress monitored by TLC (9:1 cyclohexane/EtOAc). After 5 days, the reaction mixture was cooled to rt, diluted with EtOAc and passed through a Silica plug in a Pasteur pipette and eluted with EtOAc. The residue was concentrated onto Celite and purified using Silica gel flash column chromatography using 100% cyclohexane to cyclohexane/$CH_2Cl_2$ (7:3). Desired fractions were collected and concentrated under reduced pressure to furnish the desired product as a yellow powder, which was further dried under high vacuum overnight (142.3 mg, 78%). IR $\nu_{max}/cm^{-1}$ (neat film): 3275, 3098, 3056, 2924, 2890, 2859, 2820, 1612, 1575, 1525, 1499, 1454, 1305, 1218, 1173, 954, 732. $^1$H NMR (400 MHz, Chloroform-*d*) δ 9.05 (bs, 1H, N-H), 7.78 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.69 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.63 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.36 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.80 (dd, *J* = 8.5, 1.1 Hz, 1H), 6.69 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 3.08 (d, *J* = 3.9 Hz, 3H, $CH_3$). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 170.0 ($C_q$), 151.8 ($C_q$), 148.9 ($C_q$), 134.0 ($C_q$), 132.8 ($CH_{Arom}$), 130.6 ($CH_{Arom}$), 129.4 ($CH_{Arom}$), 125.7 ($CH_{Arom}$), 120.4 ($CH_{Arom}$), 115.8 ($C_q$), 115.1 ($CH_{Arom}$), 114.2 ($C_q$), 111.2 ($CH_{Arom}$), 30.0 ($CH_3$). HRMS-ESI (*m/z*): found $[M^{79}Br+H]^+$ 318.9892, calc'd $C_{14}H_{12}N_2S^{79}Br$ requires 318.9905.

**2-(2-methylaminophenyl)-4-(2-hydroxyphenyl)benzothiazole (11)**

A 10 mL round-bottom flask with condenser was charged with a stir bar, 2-(4-bromobenzo[d]thiazol-2-yl)-*N*-methylaniline (101.9 mg, 0.32 mmol), 2-hydroxyphenylboronic acid (71 mg, 0.5 mmol), $Pd(PPh_3)_4$ (36 mg, 10 mol%), $Na_2CO_3$ (212 mg, 2 mmol), DMF (2.4 mL) and water (0.6 mL). The reaction mixture was degassed (3 x freeze-pump-thaw) and then purged with Ar. The flask was placed in an oil bath at 120 ℃ for 18 hours. The crude was dropped onto water (10 mL) and the phases separated. The aqueous phase was extracted with EtOAc (3 x 10 mL), the combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated onto Celite. The crude residue was purified by Silica gel flash column chromatography using 100% cyclohexane to cyclohexane/EtOAc (4:1). Desired fractions were collected and concentrated to furnish the desired product as a yellow foam which was further dried under vacuum overnight (82.7 mg, 78%). IR $\nu_{max}/cm^{-1}$ (neat film): 3343, 3060, 2922, 2817, 1608, 1575, 1492, 1448, 1312, 1216, 1172, 961, 748. $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.27 (bs, 1H, N-H), 7.91 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.74 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.56 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.43 – 7.32 (m, 2H), 7.18 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.11 (td, *J* = 7.5, 1.3 Hz, 1H), 6.92 (bs, 1H, O-H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.70 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 2.92 (s, 3H, $CH_3$). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 171.1 ($C_q$), 153.8 ($C_q$), 150.5 ($C_q$), 148.5 ($C_q$), 133.4 ($C_q$), 133.0 ($CH_{Arom}$), 131.8 ($C_q$), 131.6 ($CH_{Arom}$), 130.8 ($CH_{Arom}$), 129.9 ($CH_{Arom}$), 128.2 ($CH_{Arom}$), 126.7 ($C_q$), 125.8 ($CH_{Arom}$), 121.2 ($CH_{Arom}$), 120.7 ($CH_{Arom}$), 118.0 ($CH_{Arom}$), 115.4 ($CH_{Arom}$), 114.1 ($C_q$), 111.4 ($CH_{Arom}$), 29.8 ($CH_3$). HRMS-DCI($CH_4$) (*m/z*): found $[M+H]^+$ 333.1048, calc'd $C_{20}H_{17}N_2OS$ requires 333.1062.

**2-(2-(1*H*-indol-2-yl)benzo[*d*]thiazol-4-yl)phenol (12)**

A 10 mL microwave vial was charged with a stir bar, *tert*-butyl 2-(4-bromobenzo[*d*]thiazol-2-yl)-1*H*-indole-1-carboxylate (33.1 mg, 0.077 mmol), 2-hydroxyphenylboronic acid (23.3 mg, 0.15 mmol), $Pd(PPh_3)_4$ (12 mg, 10 mol%), $Na_2CO_3$ (64 mg, 0.6 mmol), DMF (0.8 mL) and water (0.2 mL). The reaction mixture was degassed (3 x freeze-pump-thaw) and then purged with Ar. The vial was loaded into a microwave reactor and heated at 120 ℃ for 1 h. The crude was dropped onto water (10

mL) and the phases separated. The aqueous phase was extracted with EtOAc (3 x 10 mL), the combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated. The crude was dissolved in $CH_2Cl_2$ (1 mL) and TFA (1 mL) and stirred at room temperature for 2 hours. Solvent was removed under reduced pressure and the crude dissolved in $CH_2Cl_2$ (10 mL). The organic phase was washed with sat'd aq. $NaHCO_3$ (2 x 10 mL) until pH was basic (~8) and finally with brine (10 mL). The organic phase was dried over anhydrous $MgSO_4$, then filtered and concentrated onto Celite. The crude residue was purified by Silica gel flash column chromatography using 100% cyclohexane to cyclohexane/EtOAc (4:1). Desired fractions were collected and concentrated to furnish the desired product as a yellow powder which was further dried under vacuum overnight (18.4 mg, 70%). IR $\nu_{max}/cm^{-1}$ (neat film): 3348, 3061, 2927, 2846, 2248, 1584, 1549, 1458, 1340, 1230, 1141, 1024, 905, 728. $^1$H NMR (400 MHz, Chloroform-*d*) δ 9.27 (s, 1H, N-H), 7.90 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.67 (dq, *J* = 8.1, 1.0 Hz, 1H), 7.61 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.45 – 7.36 (m, 2H), 7.31 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.19 – 7.08 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 161.3 ($C_q$), 154.3 ($C_q$), 149.8 ($C_q$), 137.5 ($C_q$), 134.4 ($C_q$), 133.4 ($C_q$), 131.6 ($CH_{Arom}$), 130.2 ($C_q$), 130.1 ($CH_{Arom}$), 129.2 ($CH_{Arom}$), 128.4 ($C_q$), 127.1 ($C_q$), 126.4 ($CH_{Arom}$), 125.5 ($CH_{Arom}$), 121.9 ($CH_{Arom}$), 121.6 ($CH_{Arom}$), 121.2 ($CH_{Arom}$), 121.0 ($CH_{Arom}$), 119.7 ($CH_{Arom}$), 112.0 ($CH_{Arom}$), 107.2 ($CH_{Arom}$). HRMS-ESI (*m/z*): found $[M+H]^+$ 343.0904, calc'd $C_{21}H_{15}N_2OS$ requires 343.0905.

# Declaration of competing interest

We have no competing interest to declare

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boron-fluorine bonds for fluorination and synthesis of potential bi-modal imaging agents." Coordination chemistry. Université Paul Sabatier - Toulouse III; University of British Columbia. Library, 2018. English.

# Supporting Information

Supporting information including $^{1}H$ and $^{13}C$ NMR spectra are provided.

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Highlights :

Straightforward access to orthogonally dihalogenated benzothiazole core.

Orthogonal Suzuki-Miyaura cross coupling allowing a convergent approach to a benzothiazole based chemical space.

Synthesis driven taming of photophysical properties.

**Declaration of interests**

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☑ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

~~☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:~~