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Protection of Boronic Acids Using a Tridentate Aminophenol ONO Ligand for Selective Suzuki-Miyaura Coupling

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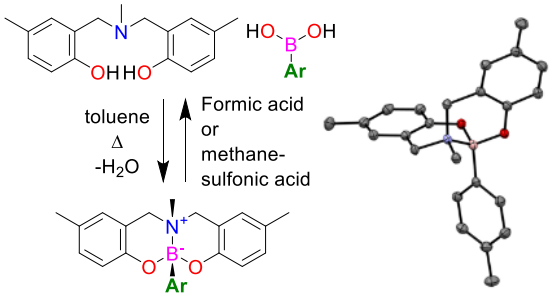
Supporting Information Placeholder



ABSTRACT: Boronic acid protecting group chemistry powerfully enhances the versatility of Suzuki-Miyaura cross-coupling. Prominent examples include trifluoroborate salts, *N*-methyliminodiacetic acid (MIDA) boronates, and 1,8-diaminonaphthalene (DAN) boronamides. In this work, we present a bis(2-hydroxybenzyl)methylamine (BOMA) ligand that forms tridentate complexes with boronic acids much like the MIDA ligand but the deprotection is facilitated by organic acids. The BOMA boronates showed considerable stability in both aqueous base and acid and a variety of chemoselective reactions were performed on these boronates including selective Suzuki-Miyaura coupling, palladium-catalyzed borylation, ester hydrolysis, alkylation, lithiation-borylation, and oxidative hydroxydeboronation.

Introduction

Organoboron reagents have become a staple of organic chemistry, largely due to the widespread use of Suzuki-Miyaura (SM) cross-coupling, a ubiquitous transition metal-catalysed C–C bond-forming reaction with wide scope and functional group tolerance. Since its discovery in 1979, the reaction has been studied and improved upon by a vast number of researchers.[1-3] A particularly noteworthy recent development is the discovery of protected boron functionalities, which could be rendered inert to SM coupling as well as other reaction conditions, then later unmasked to reveal an active boron species capable of coupling.[4] The first general functionalities demonstrating this behaviour were trifluoroborate salts in the late 90s.[5,6] In 2007, *N*-methyliminodiacetic acid (MIDA) boronates[7] and 1,8-diaminonaphthalene (DAN) boronamides[8] were published in quick succession. MIDA boronates have found much success in iterative coupling for the synthesis of complex natural products,[9,10] and have been central in a push for generalised synthetic methods inspired by solid phase peptide synthesis.[11-13]

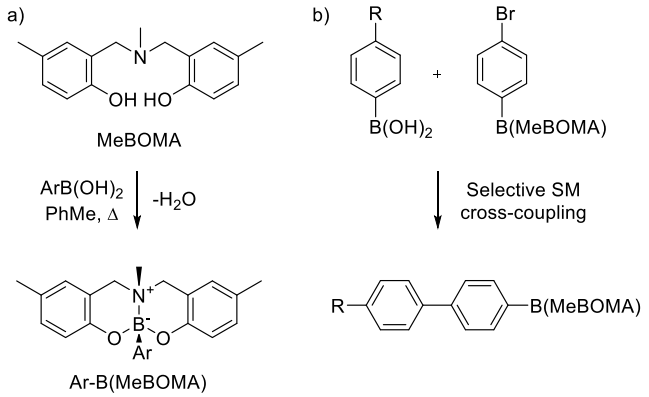
Our group is interested in developing a new methodology for iterative coupling using SM cross-coupling and boronic acid protecting groups, which demanded particularly efficient reactions and reliable protecting group chemistry. Building upon hydrolysis kinetic data of MIDA boronates, DAN boronamides and other boron ligands,[14,15] we then considered possible improvements to boron protecting groups.

We were interested in developing a tridentate ligand capable of forming stable tetrahedral boron complexes which were tolerant to typical SM coupling conditions employing aqueous base. From the beginning, strong B-N coordination was sought by use of a highly basic nitrogen functionality, which lead us to consider tertiary amines. To maximize the strength of the B-N bond and to favor tridentate coordination, the remaining functionalities were chosen to be phenols, which struck a balance of reduced σ-donation character while not being such weak donors that hydrolysis of the complex would become exceedingly favourable. Lastly, we aimed for a synthetically convenient symmetric ligand capable of forming a cage-like complex, for additional kinetic stabilization.

Taking all these considerations into account, we wish to bring to light our findings on the bis(2-hydroxybenzyl)methylamine (BOMA) framework, with specific focus on a dimethylated variant, MeBOMA (**Scheme 1a**). Related ligands have been investigated since the 1950s,[16,17] with an especially large

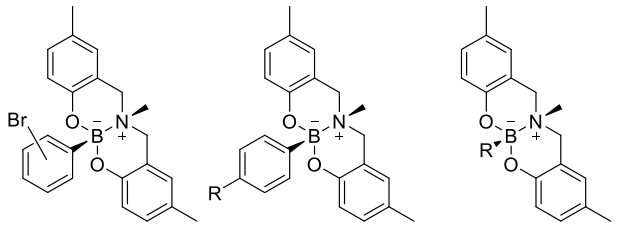
contribution by Woodgate et al.[18] In all cases, the authors noted the resilience towards hydrolysis of boronic acids upon coordination with the ligand. We therefore began investigation of the BOMA framework as a possible route towards quaternized boronic acid derivatives with superior stability towards hydrolysis in aqueous basic conditions typical of SM coupling allowing for selective SM cross-coupling **(Scheme 1b)**.

Scheme 1: A) Coordination of MeBOMA ligand to boronic acids to form a protected (cis)-MeBOMA boronate. B) General scheme for selective SM cross-coupling.



Results and discussion

After initially investigating reductive amination methods, we determined that Mannich reactions between primary amines and phenols provided a convenient one-step process to obtain the desired compounds. Indeed, MeBOMA was inexpensively synthesised from *p*-cresol, paraformaldehyde, and methylamine, and was obtained pure from a single recrystallization in decagram scale. *p*-Cresol was chosen instead of phenol to fully inhibit *para* aminomethylation without greatly modifying the electronics of the aryl rings. Clearly, other ligands in the BOMA series may be obtained by similar methods, allowing variation of properties such as solubility and binding strength. Refluxing the ligand and arylboronic acid with azeotropic removal of water provided crude MeBOMA boronates in near quantitative yield with acceptable purity (**Figure 1**).



1a: (para) 92%
1b: (meta) 98%
1c: (ortho) 92%

2: R = -OH, 69%
3: R = -OMe, 93%
4: R = -Me, 93%
5: R = -CN, 90%

6: R = 3-pyridyl, 96%
7: R = 4-pyridyl, 94%
8: R = -Me, 91%

Figure 1: MeBOMA coordinated to bromophenyl boronic acid isomers, and arylboronic acids with a variety of electron donating and withdrawing substituents in good yield.

Traces of unreacted reagents could be removed by washing with NaOH (1 M aq.) during workup and recrystallization from hot toluene to yield analytically pure material in >90% yield. All MeBOMA boronates in this study showed good solubility in organic solvents such as THF and chloroform allowing facile characterization and use in reactions. ^{1}H NMR spectra of the compounds were strongly indicative of rigid tridentate coordination, due to the appearance of the AB quartet signal with chemical shift around 4 ppm (**Figure 2a**). These were caused by geminal coupling of the now magnetically inequivalent bridging methylene protons, similarly to MIDA boronates. Tridentate coordination was corroborated by single crystal X-ray crystallography data for multiple compounds (**Figure 2b** and ESI), which show B–N distances consistent with covalent bonding, and by ^{11}B NMR spectroscopy for all compounds, due the appearance of signals with a chemical shift of around 5 ppm, consistent with similar tetrahedral boronates.[19] In all cases, binding of the MeBOMA ligand was consistent with the thermodynamically most stable *cis* configuration, as determined by Woodgate et al.,[20] and confirmed again by X-ray diffraction data (**Figure 2b** and ESI). No *trans* isomers were observed, presumably due to their formation in trace amounts and subsequent removal during purification. The MeBOMA boronates were typically stable to storage at ambient conditions in light, and heating under high vacuum at 150 °C for 48 h was tolerated with no change in mass or NMR spectrum.

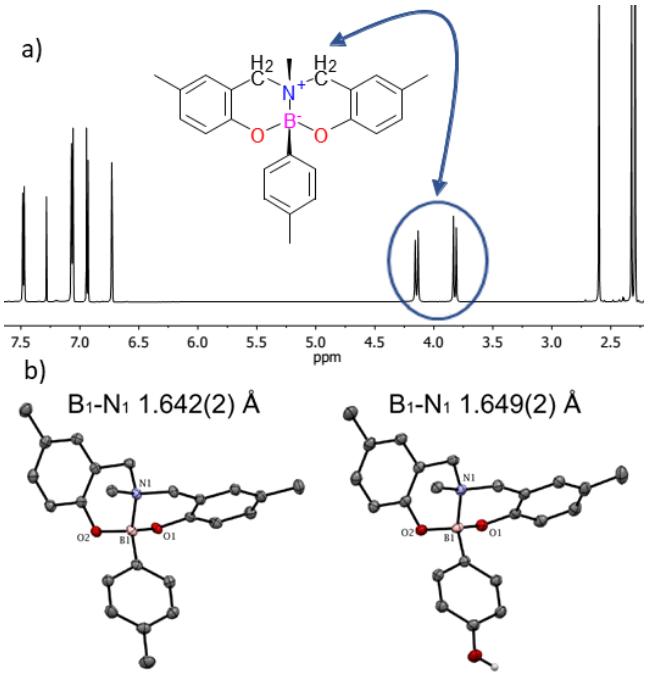
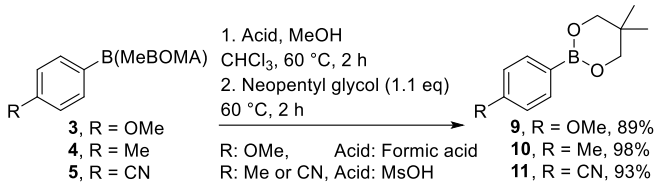


Figure 2: a) ^{1}H NMR spectrum of (*cis*)-4-tolyl-B(MeBOMA) **4** showing magnetically inequivalent methylene protons at 4 ppm, indicating tridentate coordination to boron. b) Thermal ellipsoid illustrations (50% probability) of structures obtained from single crystal X-ray diffraction data for (*cis*)-*p*-tolyl-B(MeBOMA) **4** and (*cis*)-4-hydroxyphenyl-B(MeBOMA) **2**. Hydrogen atoms were excluded for clarity.

The ligand was coordinated to various bromophenylboronic acid isomers (**1a-c**) as well as arylboronic acids with a variety of electron donating and withdrawing substituents and heteroarylboronic acids (**2-7**), all in excellent

yields (**Figure 1**. See experimental section for details). Additionally, coordination of alkylboronic acids is possible (**8**). Deprotection of MeBOMA boronates was fast and quantitative in alcoholic solutions of acid (**Scheme 2**). The solution was washed with aqueous acid to protonate the MeBOMA ligand and remove it from the organic phase. The presumed intermediate alkyl esters could be hydrolysed to the free boronic acids or quantitatively transesterfied *in situ* to more hydrolytically stable boronic esters, such as neopentyl glycol esters, to facilitate subsequent isolation and purification. Interestingly, formic acid was a relatively weak acid capable of deprotecting the electron rich 4-methoxyphenyl MeBOMA boronate **3** without protodeboronation. Electron-neutral or electron-deficient MeBOMA boronates were deprotected by using methanesulfonic acid without protodeboronation. We have thus shown a general methodology for the deprotection of MeBOMA boronates to free boronic acid/esters in relatively mild conditions.

Scheme 2: General procedure for the deprotection of MeBOMA protected boronic acids.

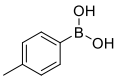
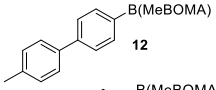
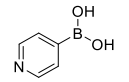
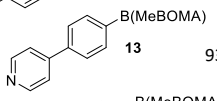
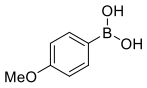
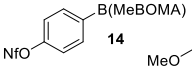
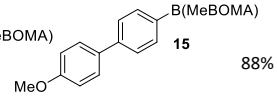
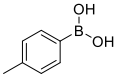
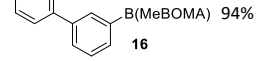
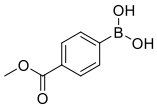
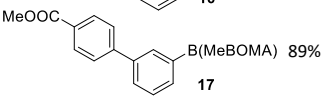


While further investigation will be required, we speculate the mechanism of acid-mediated deprotection would involve an initial protonation at one of the boronate oxygen atoms, as these are the most basic sites in the complex, followed by cleavage of the B–O bond (**Figure S27**). An alcohol molecule from the solvent can then insert into the vacant boron orbital. This process is repeated until both phenol rings are displaced. Ultimately, protonation of the amine occurs, and the ligand is detached as the ammonium salt, which provides the thermodynamic drive towards complete deprotection in the acidic environment.

The stability of the MeBOMA boronates was investigated in neutral or basic aqueous conditions. Tests indicated considerable stability even in relatively forcing conditions (e.g. 5 M aq. NaOH in toluene at 120 °C for 48 h), with >90% recovery of the MeBOMA boronate and no significant degradation by ^{1}H NMR spectroscopy (**Figure S26**. See experimental section for details). In dilute aqueous acid (e.g. 1 M aq. HCl), the MeBOMA boronates had prolonged stability around 20 °C (**Figure S25**. See experimental section for details). Protodeboronation is a competing side-reaction to deprotection of the boronates. The rates of protodeboronation are increased by using stronger acid, decreased amount of protic co-solvent, increased temperature, and more electron-rich arenes. In general, BOMA boronates may be primed for electrophilic attack at the borylated carbon atom due to the weak inductively donating character of quaternized boron atoms.[21] Indeed the ability of various boronate complexes to act as hydrocarbyl transfer agents has been discussed elsewhere.[22]

In an initial study of reaction scope, selective SM cross-coupling was performed with active boron species in the presence of MeBOMA boronates (**Table 1**. See experimental section for details). Usage of fluoride or oxide bases in aqueous conditions was well tolerated, with optimised reaction conditions making use of K_3PO_4 (2 M aq.) mixtures with THF at 65 °C for 2-6 h. In some cases when reactions were allowed to progress for long periods (typically over 24 h), side products began to accumulate, in particular protodeboronated compounds. However, high coupling yields could be obtained in short times using Fu's bulky trialkylphosphine ligands,[23,24] with TLC indicating clean conversion to a single product.

Table 1: Scope for selective Suzuki-Miyaura cross-couplings.

Entry	Ar_1-B(OR)$_2$	X-Ar_2B(MeBOMA)	Product	Yield
1		**1a**	 **12**	94%
2		**1a**	 **13**	93%
3		 **14**	 **15**	88%
4		**1b**	 **16**	94%
5		**1b**	 **17**	89%

Optimised reaction conditions: X-Ar-B(MeBOMA) (1.0 eq.), Ar-B(OR)$_2$ (1.1 eq.), 2 M aq. K_3PO_4 (4 eq.), Pd_2dba_3 (2 mol%), phosphine ligand ($PtBu_3$·HBF_4, or PCy_3·HBF_4, 5 mol%), THF at 65 °C or dioxane at 100 °C for 2-16 h. Isolated yields.

The MeBOMA protecting group was effective in masking the boronates during SM cross-coupling, even under aqueous basic conditions, allowing for selective cross-coupling (**Table 1**). The biaryl MeBOMA boronates were synthesized in high yield and purity from the corresponding isomer of the bromophenyl MeBOMA boronates (**Table 1**: Entries 1-2 and 4-5)**.** Coupling reactions at positions adjacent to a MeBOMA boronate functionality were slower and more prone to deboronation, likely due to the steric bulk of the boronate hindering the transmetalation step. Coupling was not limited to halides, as demonstrated by the successful coupling of a MeBOMA boronate containing an aryl nonaflate (**Table 1**: Entry 3). Synthesis of the nonaflate **14** was performed by treating 4-hydroxyphenyl B(MeBOMA) **2** with nonafluorobutanesulfonyl fluoride and Et_3N (**Table 2**: Entry 1).

To show the potential for iterative coupling, 4-cyanophenyl B(MeBOMA) **5** was activated by a trans-esterification to boronic acid neopentyl glycol ester **11**. This activated boronic acid was coupled to 3-bromophenyl B(MeBOMA) **1b**, obtaining the biaryl product **18** in 84%

yield over two steps (**Schemes 2** and **3a**). Furthermore, a differentially protected bisboronic acid **19** was synthesized via Miyaura borylation from 3-bromophenyl B(MeBOMA) **1b** (**Table 2**: Entry 2). The desymmetrized bisboronic acid was reacted with 2-bromopyridine, selectively coupling to the position with the pinacol ester to give compound **20** (**Scheme 3b**). This SM cross-coupling route to 2-pyridyl-substituted compounds avoids the widely known instability of 2-pyridyl boronic acids.[25]

Scheme 3: Selective SM cross-couplings of MeBOMA boronates with a) activated B(MeBOMA) substrate and b) differentially protected boronic acids.

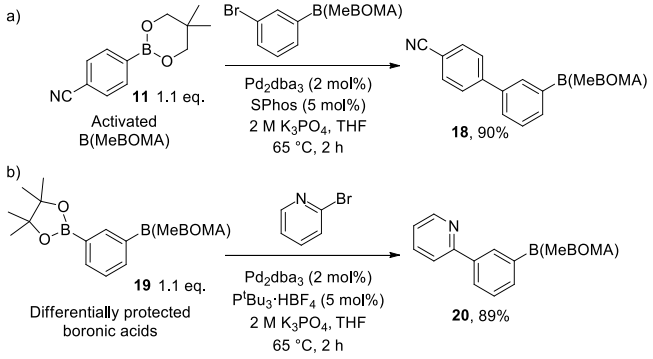


Table 2: Examples of chemistry tolerated by MeBOMA boronates.

Entry	R-MeBOMA	Reaction conditions	Product
1	HO, B(MeBOMA) **2**	Et_3N, $C_4F_9SO_2F$, DMF, 80 °C, 16 h	NfO, B(MeBOMA) **14**, Nf = $C_4F_9SO_2$, 92% yield
2	Br, B(MeBOMA) **1b**	B_2pin_2, KOAc, $Pd(dppf)Cl_2$, Dioxane, 100 °C, 16 h	B(MeBOMA) **19**, 86% yield
3	MeOOC, B(MeBOMA) **17**	5 M NaOH, THF, 60 °C, 2 h	HOOC, B(MeBOMA) **21**, 83% yield
4	N, B(MeBOMA) **7**	Methyl iodide, Acetone, 70 °C, 16 h	I⁻ N⁺, B(MeBOMA) **22**, 88% yield
5	Br, B(MeBOMA), C_8H_{17} C_8H_{17} **23**	1. n-BuLi, -78 °C, 30 min; $B(OMe)_3$; 2. UHP, MeOH, 22 °C, 90 min	HO, B(MeBOMA), C_8H_{17} C_8H_{17} **24**, 89% yield

Entry 1) Nonaflation of a phenol. Entry 2) Hydrolysis of a methyl ester. Entry 3) Miyaura borylation. Entry 4) Pyridine methylation with methyl iodide. Entry 5) Lithiation-borylation, followed by oxidative hydroxydeboronation.

As other examples of chemistry tolerated by MeBOMA boronates, cleavage of a methyl ester to form carboxylic acid **21** was possible by refluxing methoxycarbonyl MeBOMA boronate **17** in a mixture of 5 M NaOH/THF for 2 h (**Table 2**: Entry 3). Characterisation of the product showed no degradation of the MeBOMA moiety. Treatment of 4-pyridyl B(MeBOMA) **7** with iodomethane gave the *N*-methylated pyridinium salt **22** (**Table 2**: Entry 4).

MeBOMA boronates were found to tolerate strong nucleophilic organometallic bases such as n-BuLi, allowing lithium-halogen exchange reactions to take place at -78 °C in high yield (**Table 2**: Entry 5). Examples of protected boronic acids that can tolerate organometallic bases are rare. Trifluoroborate salts have been shown to tolerate organolithium chemistry,[26] though it appears the chemistry is relatively sensitive. The tetramethyl variation of MIDA also tolerates t-BuLi,[11] though more nucleophilic organometallic bases are likely to attack the carbonyl functionalities.

MeBOMA boronates were also found to be stable to hydroxydeboronation with peroxides in conditions which would convert most other boron species into their corresponding phenol.[27]

Conclusions

In summary, we have presented MeBOMA, a tridentate ONO ligand, as an alternative boron protecting group suitable for a variety of reactions, including selective SM cross-coupling in the presence of aqueous base. The robust ligand renders the boronic acid inert and chemically stable. Removal of the protecting group is quantitative using non-aqueous acid solutions, and the activated boronic acid could be used for subsequent SM cross-coupling. MeBOMA can be utilised as a protecting group for boronic acids, and potentially for iterative coupling chemistry due to its selectivity, stability, quantitative protection and deprotection of boronic acids. We expect the work described here to be complementary to existing boron protecting group chemistry.

Experimental section

General Information

Unless otherwise indicated, all reagents and solvents were purchased from commercial sources and used without further purifications. Petroleum spirits refer to the fraction of boiling point range 40-60 °C. Silica gel 60 (0.015 – 0.040 mm) was used to carry out dry column vacuum chromatography (DCVC).

The crystals of suitable quality were obtained from EtOAC solution (**MeBOMA**), MeCN/Et_2O solution (**2**), toluene solution (**3, 4** and **7**) by slow evaporation under air conditions. X-ray diffraction data for compounds **MeBOMA**, **2**, **3**, **4,** and **7** were collected with a Rigaku Synergy Diffractometer using either Cu-Kα or Mo-Kα radiation with the temperature during data collection maintained at 100.0(1) or 150.0(1) K using an Oxford Cryosystems cooling device. X-ray diffraction data for compound 5 was collected on the MX1 beamline at the Australian Synchrotron with the temperature during data collection maintained at 100.0(1) K.[28] The structures were solved by direct methods and difference Fourier synthesis.[29] Thermal ellipsoid plots were generated using the program Mercury integrated within the WINGX suite of programs.[30,31] The single-crystal X-ray data for all structures were deposited with the Cambridge Crystallographic Data Centre (CCDC) as CCDC: 2164697 (**MeBOMA**), 2164695 (**2**), 2164700 (**3**), 2164696 (**4**), 2164698 (**5**), and 2164694 (**7**). Single crystal X-ray diffraction data summary can be found in the Supporting Information file.

^{1}H NMR (400 MHz, 500 MHz or 600 MHz) and ^{13}C NMR (100 MHz or 125 MHz) spectra were acquired in a 400 MHz JEOL spectrometer, 500 MHz Agilent DD2 spectrometer or 600 MHz Bruker Avance III spectrometer and chemical shifts were referenced to the residual solvent peaks. ^{11}B NMR (128 MHz) spectra were acquired on a 400 MHz JEOL spectrometer or 400

MHz Bruker Ascend spectrometer, using a borosilicate NMR tube or quartz NMR tube and the shifts were referenced to an external $BF_3.Et_2O$ standard in $CDCl_3$. ^{19}F NMR (376 MHz) spectrum were acquired on a 400 MHz JEOL spectrometer and shifts were referenced to an external C_6F_6 standard in $CDCl_3$. High-resolution mass spectra were acquired using a Thermo Scientific Q Exactive Plus Orbitrap LC-MS/MS instrument. FT-IR measurements were acquired using a Perkin Elmer Spectrum One FTIR instrument.

Synthesis of **MeBOMA:**

2,2'-((methylazanediyl)bis(methylene))bis(4-methylphenol) (**MeBOMA**): Previously reported compound.[32] 20.0 mL (191 mmol, 2.0 equiv) of *p*-cresol, 12.0 mL (96 mmol, 1.0 equiv) of 33% $MeNH_2$ in EtOH, 5.72 g (191 mmol, 2.0 equiv) of paraformaldehyde and 200 mL MeOH were transferred to a round-bottom flask, and the flask was stoppered. The reaction mixture was stirred at r.t. for 110 h, and then dried by rotary evaporation to a viscous oil. The oil was dissolved in 100 mL hot EtOAc and cooled to -20 °C o/n. The precipitated solid was filtered and rinsed with cold EtOAc, providing 10.0 g (38% yield) of product as white crystals. ^1H NMR (500 MHz, $CDCl_3$) δ 10.11 (s, 2H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.92 (s, 2H), 6.77 (d, *J* = 8.0 Hz, 2H), 3.75 (s, 4H), 2.28 (m, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 154.2, 130.7, 129.4, 128.4, 122.6, 115.8, 59.4, 40.9, 20.6. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}NO_2^+$ = 262.1645. Found 262.1645 (+0.1 ppm error). FT-IR (film, cm^{-1}): 3264.9, 2963.3, 2827.8, 1615.8, 1513.7, 1497.2, 1455.2, 1422.1, 1380.7, 1310.3, 1271.0, 1248.2, 1235.4, 1206.7, 1142.7, 1114.7, 1013.5, 959.5, 936.5, 890.2, 849.3, 812.8, 785.0, 775.6, 756.4, 687.0, 647.4.

General procedure for protecting boronic acids with MeBOMA

In a round-bottom flask charged with a stir bar, boronic acid (1.0 equiv.), MeBOMA (1.05-1.20 equiv.) and toluene (150 mL) were added. To the flask was attached a Soxhlet apparatus filled with activated 4 Å molecular sieves and a condenser, and the reaction mixture was refluxed in an oil bath for 16 h. After cooling to room temperature, the reaction mixture was transferred to a separatory funnel and washed with 1 M NaOH(aq). The organic layer was collected and concentrated using a rotary evaporator. The crude product was recrystallized in toluene (90 °C to -20 °C) and dried under high vacuum at 80 °C.

6-(4-bromophenyl)-2,10,13-trimethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine (**1a**)

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 4-bromophenyl boronic acid (1.3 g, 6.5 mmol), **MeBOMA** (1.85 g, 6.82 mmol), and toluene (150 mL). Obtained 1.20 g white crystals, in 92% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.32 (m, 2H), 7.05 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 2.2 Hz, 2H), 4.13 (d, *J* = 14.8 Hz, 2H), 3.77 (d, *J* = 14.8 Hz, 2H), 2.55 (s, 3H), 2.27 (s, 6H). $^{13}C\{^1H\}$.NMR (126 MHz, $CDCl_3$) δ 151.2, 135.1, 130.6, 130.5, 128.7, 127.4, 122.5, 119.2, 116.0, 58.6, 44.9, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.30. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}BBrNO_2^+$ = 436.1078, 438.1058. Found 436.1079, 438.1058 (+0.1 ppm, +0.1 ppm error). FT-IR (powder, cm^{-1}): 3012.0, 2919.7, 2199.4, 2163.3, 2137.9, 1945.8, 1616.6, 1580.1, 1504.3, 1470.9, 1422.6, 1378.1, 1360.8, 1298.8, 1284.9, 1267.3, 1232.8, 1192.9, 1130.3, 1107.1, 1087.1, 1053.3, 1011.0, 999.4, 930.8, 879.9, 818.5, 784.8, 738.1, 675.5.

6-(3-bromophenyl)-2,10,13-trimethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(1b)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 3-bromophenyl boronic acid (1.84 g, 9.17 mmol), **MeBOMA** (2.6 g, 9.63 mmol) and toluene (150 mL). Obtained 3.91 g white crystals, in 98% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (t, *J* = 1.7 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.12 – 7.00 (m, 3H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 2.3 Hz, 2H), 4.14 (d, *J* = 14.8 Hz, 2H), 3.79 (d, *J* = 14.8 Hz, 2H), 2.56 (s, 3H), 2.27 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 151.1, 136.3, 131.5, 131.0, 130.6, 129.3, 128.8, 127.4, 122.5, 119.2, 115.9, 58.7, 45.0, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.54 ppm. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}BBrNO_2^+$ = 436.1078, 438.1058. Found 436.1082, 438.1059 (+1.0 ppm, +0.4 ppm error). FT-IR (powder, cm^{-1}): 3017.1, 2921.6, 2859.5, 2202.1, 2027.7, 1977.4, 1881.7, 1618.0, 1584.8, 1553.4, 1500.0, 1465.4, 1444.3, 1422.0, 1392.9, 1360.2, 1299.3, 1283.9, 1267.9, 1256.0, 1230.9, 1184.7, 1169.7, 1150.8, 1000.8, 983.2, 933.6, 908.4, 890.8, 867.1, 849.8, 814.9, 804.2, 770.6, 734.0, 717.4, 702.8, 696.3.

6-(2-bromophenyl)-2,10,13-trimethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(1c)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 2-bromophenyl boronic acid (1.84 g, 9.17 mmol), **MeBOMA** (2.6 g, 9.63 mmol), and toluene (150 mL). Obtained 3.70 g white crystals, in 92% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 1H), 7.48 – 7.43 (m, 1H), 7.08 (dt, *J* = 8.1, 2.7 Hz, 4H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.74 (d, *J* = 2.3 Hz, 2H), 4.10 (d, *J* = 14.6 Hz, 2H), 3.80 (d, *J* = 14.6 Hz, 2H), 2.70 (s, 3H), 2.28 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 150.9, 136.1, 134.5, 130.8, 129.7, 129.3, 128.3, 127.5, 126.5, 118.9, 115.9, 58.8, 46.3, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.08. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}BBrNO_2^+$ = 436.1078, 438.1058. Found 436.1081, 438.1059 (+0.8 ppm, +0.3 ppm error). FT-IR (powder, cm^{-1}): 3083.6, 3056.2, 3015.0, 2917.8, 2860.0, 2735.9, 2590.2, 2313.2, 2199.7, 2163.1, 2104.6, 2056.2, 2036.3, 2020.3, 1977.3, 1884.9, 1616.7, 1583.5, 1555.9, 1499.8, 1465.5, 1416.6, 1358.1, 1303.7, 1290.6, 1268.9, 1244.6, 1230.8, 1194.7, 1170.5, 1127.9, 1116.4, 1069.7, 1039.8, 1012.9, 980.0, 941.3, 816.0, 807.0, 778.1, 756.6, 719.9, 686.8.

2-(2,10,13-trimethyl-13,14-dihydro-12H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinin-6-yl)phenol **(2)**

4-Hydroxyphenyl boronic acid (1.9 g, 13.75 mmol) and **MeBOMA** (3.9 g, 14.4 mmol) were refluxed in 50 mL MeCN for 16 h. After cooling to room temperature, the reaction mixture was filtered and washed with a small amount of MeCN and Et_2O. Obtained 1.38 g white powder, in 69% yield. ^1H NMR (500 MHz, DMSO-d_6) δ 9.11 (s, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.81 (s, 2H), 6.70 (d, *J* = 8.2 Hz, 2H),

6.59 (d, *J* = 8.0 Hz, 2H), 4.06 (d, *J* = 15.2 Hz, 2H), 3.86 (d, *J* = 15.3 Hz, 2H), 2.46 (s, 3H), 2.20 (s, 6H). $^{13}C\{^{1}H\}$NMR (126 MHz, DMSO-d_6) δ 156.8, 151.3, 134.0, 129.7, 127.7, 127.3, 117.8, 117.1, 114.0, 56.8, 43.8, 20.1. ^{11}B NMR (128 MHz, DMSO-d_6) δ 4.11. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{23}H_{25}BNO_3^+$ = 374.1922. Found 374.1922 (+0.1 ppm error). FT-IR (powder, cm^{-1}): 3351.5, 3006.8, 2920.9, 2862.5, 2359.6, 2348.3, 2026.0, 1997.3, 1907.9, 1740.8, 1605.3, 1582.4, 1497.1, 1467.7, 1459.7, 1418.1, 1360.0, 1340.1, 1300.0, 1281.3, 1257.0, 1230.6, 1200.2, 1186.9, 1175.7, 1151.5, 1127.0, 1107.5, 1088.7, 1052.5, 934.0, 891.2, 873.2, 866.0, 845.6, 838.1, 815.7, 791.7, 774.4, 724.3, 714.7, 657.0.

6-(4-methoxyphenyl)-2,10,13-trimethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(3)**

Prepared following the general procedure. In a round-bottom flask charged with stir bar was added p-anisyl boronic acid (3.87 g, 25.47 mmol), **MeBOMA** (6.91 g, 25.47 mmol) and toluene (150 mL). Obtained 3.60 g white crystals, in 93% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 2H), 7.04 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 6.81 – 6.75 (m, 2H), 6.71 (d, *J* = 2.2 Hz, 2H), 4.12 (d, *J* = 14.7 Hz, 2H), 3.78 (d, *J* = 16.7 Hz, 5H), 2.57 (s, 3H), 2.27 (s, 6H). $^{13}C\{^{1}H\}$NMR (126 MHz, $CDCl_3$) δ 159.6, 151.6, 134.6, 130.4, 128.4, 127.3, 119.2, 116.3, 112.9, 58.6, 55.1, 44.8, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.21. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{24}H_{27}BNO_3^+$ = 388.2079. Found 388.2079 (+0.1 ppm error). FT-IR (powder, cm^{-1}): 3600.0, 3018.8, 2925.9+, 2027.7, 1976.3, 1738.7, 1602.5, 1583.9, 1568.1, 1499.3, 1469.5, 1445.9, 1425.0, 1360.3, 1299.6, 1282.6, 1264.0, 1231.5, 1198.1, 1182.4, 1150.6, 1127.6, 1112.0, 1090.2, 1071.8, 1046.8, 1009.8, 981.0, 942.3, 931.3, 899.2, 884.1, 866.9, 844.6, 832.0, 816.8, 786.1, 771.1, 724.6, 658.7.

2,10,13-trimethyl-6-(p-tolyl)-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(4)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 4-tolylboronic acid (3.57 g, 29.4 mmol), **MeBOMA** (8.0 g, 29.4 mmol) and toluene (150 mL). Obtained 3.72 g white crystals, in 93% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.7 Hz, 1H), 7.04 (m, *J* = 8.2, 2.5 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.71 (d, *J* = 2.2 Hz, 1H), 4.12 (d, *J* = 14.7 Hz, 1H), 3.80 (d, *J* = 14.7 Hz, 1H), 2.58 (s, 1H), 2.30 (s, 2H), 2.27 (s, 3H). $^{13}C\{^{1}H\}$NMR (126 MHz, $CDCl_3$) δ 151.6, 137.4, 133.4, 130.4, 128.4, 128.2, 127.3, 119.2, 116.3, 58.6, 44.9, 21.5, 20.6. ^{11}B (128 MHz, $CDCl_3$) δ 4.11. HRMS (ESI-MS [positive mode]) m/z: [M+H]+ Calcd for $C_{24}H_{27}BNO_2^+$ = 372.2129. Found 372.2129 (+0.1 ppm error). FT-IR (powder, cm^{-1}): 3014.3, 2921.2, 1616.9, 1584.8, 1498.8, 1468.7, 1445.5, 1420.9, 1359.0, 1299.0, 1286.9, 1271.9, 1259.4, 1233.5, 1182.5, 1148.8, 1131.5, 1113.6, 1088.0, 1071.1, 1046.9, 1025.8, 979.4, 932.5, 883.9, 867.8, 845.6, 821.0, 783.8, 770.6, 721.6, 657.1.

4-(2,10,13-trimethyl-13,14-dihydro-12H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinin-6-yl)benzonitrile **(5)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 4-cyanophenyl boronic acid (1.75 g, 11.95 mmol), **MeBOMA** (3.4 g, 12.55 mmol) and toluene (200 mL). Obtained 3.70 g white powder, in 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.07 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.73 (d, 2H), 4.19 (d, *J* = 14.8 Hz, 2H), 3.79 (d, *J* = 14.8 Hz, 2H), 2.57 (s, 3H), 2.28 (s, 6H). $^{13}C\{^{1}H\}$NMR (126 MHz, $CDCl_3$) δ 151.0, 133.8, 130.9, 130.8, 129.1, 127.4, 119.7, 119.2, 115.8, 111.5, 58.8, 45.0, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.85. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{24}H_{24}BN_2O_2^+$ = 383.1925. Found 383.1926 (+0.2 ppm error). FT-IR (powder, cm^{-1}): 3013.4, 2916.4, 2359.5, 2226.8, 2097.9,97.3, 1997.4, 1739.6, 1617.8, 1584.3, 1501.0, 1470.7, 1452.5, 1421.9, 1393.0, 1365.0, 1299.3, 1286.2, 1268.5, 1260.0, 1231.9, 1209.2, 1190.4, 1173.8, 1151.2, 1128.4, 1115.6, 1090.6, 1078.6, 1052.5, 1028.3, 1005.1, 989.0, 931.3, 893.5, 878.7, 849.5, 834.9, 822.8, 812.8, 793.3, 767.3, , 728.8, 712.4, 658.4.

2,10,13-trimethyl-6-(pyridin-3-yl)-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(6)**

Prepared following the general procedure. In a 250 mL round-bottom flask charged with a stir bar was added 3-pyridyl boronic acid (245 mg, 2.0 mmol), **MeBOMA** (570 mg, 2.1 mmol) and toluene (150 mL). Obtained 566 mg white powder, in 96% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.49 (d, *J* = 4.6 Hz, 1H), 7.81 (dt, *J* = 7.6, 1.9 Hz, 1H), 7.12 (dd, J = 7.6, 4.8 Hz, 1H), 7.05 (dd, J = 8.3, 2.2 Hz, 2H), 6.90 (d, *J* = 8.3 Hz, 2H), 6.73 – 6.69 (m, 2H), 4.18 (d, *J* = 14.8 Hz, 2H), 3.78 (d, *J* = 14.8 Hz, 2H), 2.58 (s, 3H), 2.26 (s, 6H). $^{13}C\{^{1}H\}$NMR (126 MHz, $CDCl_3$) δ 154.5, 151.0, 149.3, 140.9, 130.6, 129.0, 127.4, 122.9, 119.2, 115.8, 58.6, 44.8, 20.6. ^{11}B (128 MHz, $CDCl_3$) δ 3.64. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{22}H_{24}BN_2O_2^+$ = 359.1925. Found 359.1928 (+0.8 ppm error). FT-IR (powder, cm^{-1}): 3019.6, 2927.2, 2201.2, 2027.8, 1977.7, 1740.0, 1617.0, 1582.9, 1561.5, 1498.9, 1469.7, 1447.5, 1420.4, 1398.6, 1358.5, 1331.2, 1300.2, 1285.3, 1263.0, 1233.6, 1215.9, 1201.9, 1181.6, 1149.8, 1131.3, 1107.5, 1085.7, 1074.4, 1053.5, 1039.2, 1026.7, 1011.0, 979.4, 932.1, 891.9, 881.5, 866.2, 844.3, 819.6, 776.0, 747.4, 722.8, 686.8, 671.7, 657.8.

2,10,13-trimethyl-6-(pyridin-4-yl)-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(7)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added 4-pyridyl boronic acid (1.78 g, 14.5 mmol), **MeBOMA** (4.13 g, 15.25 mmol) and toluene (150 mL). Obtained 1.68 g white powder, in 94% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 5.3 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.05 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 2.2 Hz, 2H), 4.17 (d, *J* = 14.8 Hz, 2H), 3.78 (d, *J* = 14.8 Hz, 2H), 2.56 (s, 3H), 2.27 (s, 6H). $^{13}C\{^{1}H\}$NMR (126 MHz, $CDCl_3$) δ 150.9, 148.8, 130.7, 129.0, 128.2, 127.4, 119.2, 115.8, 58.7, 44.9, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.35. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{22}H_{24}BN_2O_2^+$ = 359.1925. Found 359.1928 (+1.0 ppm error). FT-IR (powder, cm^{-1}): 3010.4, 2970.8, 2349.2, 2026.6, 1976.9, 1738.3, 1618.0, 1585.2, 1500.6, 1470.9, 1425.0, 1404.1, 1364.9, 1299.2, 1285.1, 1266.1, 1233.1, 1216.9, 1197.2,

1150.6, 1129.4, 1096.0, 1071.8, 1052.3, 1013.5, 998.4, 932.8, 878.1, 848.9, 820.1, 814.1, 784.5, 743.5, 714.4, 660.3.

2,6,10,13-tetramethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(8)**

Prepared following the general procedure. In a round-bottom flask charged with a stir bar was added methyl boronic acid (120 mg, 2.0 mmol), **MeBOMA** (570 mg, 2.1 mmol), and toluene (150 mL). Obtained 536 mg white powder, in 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.70 (s, 2H), 4.13 (d, *J* = 14.8 Hz, 2H), 3.85 (d, *J* = 14.8 Hz, 2H), 2.68 (s, 3H), 2.24 (s, 6H), 0.04 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.1, 130.1, 128.4, 127.2, 119.4, 116.2, 58.5, 44.6, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 5.66. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}BNO_2^+$ = 296.1816. Found 296.1818 (+0.5 ppm error). FT-IR (powder, cm^{-1}): 3017.7, 2958.1, 1739.5, 1618.0, 1581.8, 1500.7, 1472.2, 1458.0, 1424.0, 1360.3, 1315.1, 1298.2, 1265.7, 1234.7, 1194.8 , 1150.9, 1129.7, 1094.4, 1084.0, 1039.9, 1011.9, 967.0, 947.7, 889.5, 880.1, 865.8, 818.5, 734.7, 717.0, 697.0.

General procedure for the deprotection of MeBOMA boronates

In a vial charged with a stir bar and aryl MeBOMA boronate was added $CHCl_3$ (2 mL), MeOH (0.1 mL), and neat acid (1 mL). The solution was stirred at 60 °C in a heating mantle for 2 h while monitoring via TLC. Once the deprotection was complete, the solution was cooled to room temperature was washed three times with 1 M HCl (aq.). The organic layer was washed with water and brine, and then concentrated to obtain the free boronic acid as a crude product. To the crude boronic acid was added $CHCl_3$ (1 mL), neopentyl glycol (1.05 equiv.), and $MgSO_4$ **(**excess). The mixture was stirred at 60 °C for 2 h while monitoring via TLC. Once the conversion was complete, the solution was passed through a short silica plug. The product was then dried to obtain the neopentyl glycol ester.

2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane **(9)**

The general procedure was followed using 4-methoxyphenyl B(MeBOMA) (251 mg, 0.650 mmol) and neat formic acid. Collected 127 mg white solid, in 89% yield. This product was synthesized previously, and the NMR spectra was compared to literature.[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 3.83 (s, 3H), 3.76 (s, 4H), 1.02 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 161.9, 135.6, 113.3, 72.4, 55.2, 32.0, 22.1.

5,5-dimethyl-2-(p-tolyl)-1,3,2-dioxaborinane **(10)**

The general procedure was followed using 4-tolyl B(MeBOMA) (241 mg, 0.650 mmol) and neat methanesulfonic acid. Collected 130 mg white solid, in 98% yield. This product was synthesized previously, and the NMR spectra was compared to literature.[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.3 Hz, 2H), 3.77 (s, 4H), 2.37 (s, 3H), 1.03 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 140.8, 134.0, 128.5, 72.4, 32.0, 22.0, 21.8.

4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzonitrile **(11)**

The general procedure was followed using 4-cyanophenyl B(MeBOMA) (248 mg, 0.650 mmol) and neat methanesulfonic acid. Collected 130 mg white solid, in 93% yield. This product was synthesized previously, and the NMR spectra was compared to literature.[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 3.78 (s, 4H), 1.02 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 134.4, 131.2, 119.3, 114.3, 72.5, 32.3, 22.0, 21.9.

General procedure for selective SM cross-coupling

In a microwave vial a stir bar was added Ar-X (1.0 eq), Ar-$B(OR)_2$ (1.1 equiv. – 1.2. equiv.), Pd_2dba_3 (2 mol%) and $PCy_3{\cdot}HBF_4$, $P^tBu_3{\cdot}HBF_4$ or SPhos (5 mol%). The vial was sealed, and N_2/vacuum cycles were performed three times. THF or dioxane and 2 M aqueous K_3PO_4 (4 equiv) were sparged with N_2 and added. The reaction mixture was stirred at 65 °C (THF) or 100 °C (dioxane) in an oil bath for between 2 h and 16 h, while monitoring via TLC. Once the reaction was complete, it was cooled to room temperature and the cap was removed. The product was extracted into EtOAc and washed with water. The organic layer was washed with brine and dried over $MgSO_4$. The mixture was filtered and solvent was evaporated from the filtrate to provide crude product. The biaryl MeBOMA boronate was purified via DCVC or recrystallization.

2,10,13-trimethyl-6-(4'-methyl-[1,1'-biphenyl]-4-yl)-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(12)**

The general procedure was followed using 4-tolyl boronic acid (74 mg, 550 μmol), 4-bromophenyl B(MeBOMA) **1a** (218 mg, 500 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $P^tBu_3{\cdot}HBF_4$ (7.25 mg, 25 μmol), THF (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 65 °C for 2 h. Purified by DCVC (20% toluene/petroleum spirits). Obtained 209 mg white solid, in 94% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.43 (m, 4H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.06 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 2.2 Hz, 2H), 4.16 (d, *J* = 14.7 Hz, 2H), 3.85 (d, *J* = 14.7 Hz, 2H), 2.63 (s, 3H), 2.38 (s, 3H), 2.28 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 151.6, 140.41, 138.8, 136.8, 133.8, 130.5, 129.5, 128.5, 127.3, 127.0, 125.9, 119.3, 116.2, 58.7, 45.0, 21.2, 20.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.13. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{30}H_{31}BNO_2^+$ = 448.2412. Found 448.2424 (+2.7 ppm error) FT-IR (powder, cm^{-1}): 3019.2, 2923.8, 1739.5, 1617.0, 1499.8, 1444.3, 1420.0, 1360.6, 1298.7, 1284.6, 1265.3, 1232.6, 1189.1, 1150.1, 1129.2, 1113.5, 1089.4, 1071.3, 1047.4, 1004.5, 979.1, 932.1, 878.7, 850.2, 837.9, 811.0, 790.6, 739.3, 708.7, 660.6.

2,10,13-trimethyl-6-(4-(pyridin-4-yl)phenyl)-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(13)**

The general procedure was followed using 4-pyridyl boronic acid (67 mg, 550 μmol), 4-bromophenyl B(MeBOMA) **1a** (218 mg, 500 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $PCy_3{\cdot}HBF_4$ (9.21 mg, 25 μmol), THF (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 65 °C for 2 h. Purified by DCVC (10%EtOAc/petroleum spirits). Obtained 200 mg white solid, in 93% yield. ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.1 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.49 – 7.46 (m, 2H), 7.07 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 2.3 Hz, 2H), 4.18 (d, *J* = 14.7 Hz, 2H), 3.84 (d, *J* = 14.7 Hz, 2H), 2.63 (s, 3H), 2.28 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 151.4, 150.3, 148.8, 137.4, 134.1, 130.6, 128.7, 127.3, 125.9, 121.6, 119.3, 116.1, 58.8, 45.0, 20.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.12. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{28}H_{28}BN_2O_2^+$ = 435.2238. Found 435.2238 (0.0 ppm error). FT-IR (powder, cm^{-1}): 3018.3, 2922.5, 2854.1, 1739.4, 1616.9, 1593.5, 1532.5, 1497.6, 1463.2, 1445.2, 1419.2, 1391.9, 1376.9, 1358.9, 1298.9, 1268.5, 1257.5, 1231.2, 1185.7, 1127.8, 1091.1, 1048.3, 991.1, 870.6, 851.9, 839.9, 813.7, 788.6, 740.9, 712.9, 657.4.

6-(4'-methoxy-[1,1'-biphenyl]-4-yl)-2,10,13-trimethyl-6,13-dihydro-12H,14H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinine **(15)**

The general procedure was followed using 4-nonaflatophenyl B(MeBOMA) **14** (328 mg, 500 μmol), 4-methoxyphenyl boronic acid (91 mg, 600 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $PCy_3{\cdot}HBF_4$ (9.21 mg, 25 μmol), dioxane (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 100 °C for 16 h. Purified by DCVC (30% EtOAc/petroleum spirits). Obtained 203 mg white solid, in 88% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.7 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.06 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.97 – 6.92 (m, 4H), 6.73 (d, *J* = 2.2 Hz, 2H), 4.16 (d, *J* = 15.0 Hz, 2H), 3.85 (d, *J* = 12.4 Hz, 5H), 2.63 (s, 3H), 2.28 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 159.0, 151.6, 140.1, 134.6, 134.2, 133.8, 130.5, 128.5, 128.1, 127.3, 125.7, 119.3, 116.2, 114.2, 112.9, 58.7, 55.5, 45.0, 20.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.68. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{30}H_{31}BNO_3^+$ = 464.2392. Found 464.2390 (-0.3 ppm error). FT-IR (film, cm^{-1}): 3010.4, 2925.1, 1607.8, 1498.3, 1464.1, 1441.9, 1358.0, 1284.3, 1232.6, 1195.7, 1175.7, 1150.7, 1131.2, 1112.1, 1040.3, 1013.7, 1000.5, 988.9, 931.4, 869.3, 821.4, 789.2, 753.6, 705.1, 666.3.

2,10,13-trimethyl-6-(4'-methyl-[1,1'-biphenyl]-3-yl)-6,7,13,14-tetrahydro-12H-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinine **(16)**

The general procedure was followed using 4-tolyl boronic acid (74 mg, 550 μmol), 3-bromophenyl B(MeBOMA) **1b** (218 mg, 500 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $P^tBu_3{\cdot}HBF_4$ (7.25 mg, 25 μmol), THF (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 65 °C for 2 h. Purified by DCVC (40% $CHCl_3$/petroleum spirits). This coupling was repeated twice to obtain 186 mg (83 % yield) and 210 mg (94% yield) of product as a white solid, in an average yield of 89%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (t, *J* = 1.6 Hz, 1H), 7.47 (s, 1H), 7.46 – 7.38 (m, 2H), 7.26 (s, 6H), 7.23 – 7.16 (m, 2H), 7.09 – 7.01 (m, 2H), 6.95 (d, *J* = 8.2 Hz, 2H), 6.71 (t, *J* = 2.8 Hz, 2H), 4.21 – 3.98 (m, 2H), 3.84 (d, *J* = 14.7 Hz, 2H), 2.63 (s, 3H), 2.37 (s, 3H), 2.27 (s, 7H). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 151.6, 139.7, 139.4, 136.6, 132.2, 132.1, 130.5, 129.5, 128.5, 127.8, 127.3, 127.1, 126.7, 119.3, 116.2, 58.8, 45.1, 21.2, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.03. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{30}H_{31}BNO_2^+$ = 448.2412. Found 448.2442 (+6.5 ppm error). FT-IR (powder, cm^{-1}): 3014.0, 2919.8, 1616.1, 1584.4, 1498.2, 1465.5, 1417.7, 1388.2, 1358.8, 1285.5, 1266.2, 1231.3, 1181.0, 1150.6, 1127.3, 1100.1, 1038.6, 992.9, 907.0, 871.5, 856.9, 816.6, 779.9, 725.1, 712.9.

methyl 3'-(2,10,13-trimethyl-7,12,13,14-tetrahydro-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinin-6-yl)-[1,1'-biphenyl]-4-carboxylate **(17)**

The general procedure was followed using 4-methoxycarbonylphenyl boronic acid (99 mg, 550 μmol), 3-bromophenyl B(MeBOMA) **1b** (218 mg, 500 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $P^tBu_3{\cdot}HBF_4$ (7.25 mg, 25 μmol), THF (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 65 °C for 2 h. Purified by recrystallization from toluene. Obtained 219 mg white solid, in 89% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.89 (t, *J* = 1.7 Hz, 1H), 7.59 – 7.50 (m, 4H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.06 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.75 – 6.70 (m, 2H), 4.19 (d, *J* = 14.8 Hz, 2H), 3.92 (s, 3H), 3.84 (d, *J* = 14.7 Hz, 2H), 2.64 (s, 3H), 2.27 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 167.1, 151.3, 146.6, 138.5, 133.1, 132.3, 130.5, 130.0, 128.6, 128.3, 128.0, 127.2, 127.0, 126.8, 119.2, 116.0, 58.7, 52.1, 44.9, 20.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.04. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{31}H_{31}BNO_4^+$ = 492.2341. Found 492.2339 (-0.3 ppm error). FT-IR (powder, cm^{-1}): 3016.7, 2950.0, 1719.6, 1608.5, 1584.6 , 1501.1, 1466.3, 1434.6, 1420.0, 1388.5, 1361.4, 1269.8, 1231.3, 1184.7, 1170.5, 1150.9, 1127.9, 1103.8, 1066.0, 1040.4, 1017.3, 993.5, 967.2, 932.7, 872.1, 856.4, 815.6, 789.5, 767.2, 747.9, 713.6, 705.0, 683.4, 667.5, 658.8.

3'-(2,10,13-trimethyl-7,12,13,14-tetrahydro-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinin-6-yl)-[1,1'-biphenyl]-4-carbonitrile **(18)**

The general procedure was followed using 4-cyanophenyl boronic acid neopentyl glycol ester **11** (106 mg, 495 μmol), 3-bromophenyl B(MeBOMA) **1b** (196 mg, 450 μmol), Pd_2dba_3 (8.24 mg, 9 μmol), SPhos (9.24 mg, 23 μmol), THF (4 mL) and 2 M K_3PO_4 (0.9 mL, 1.8 mmol) at 65 °C for 2 h. Purified by DCVC (40% $CHCl_3$/petroleum spirits) . Obtained 187 mg white solid, in 90% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (t, *J* = 1.7 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.58 (dd, *J* = 7.9, 3.4 Hz, 3H), 7.49 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.07 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 2.2 Hz, 2H), 4.20 (d, *J* = 14.8 Hz, 2H), 3.84 (d, *J* = 14.8 Hz, 2H), 2.64 (s, 3H), 2.28 (s, 6H). $^{13}C\{^1H\}$NMR (126 MHz, $CDCl_3$) δ 151.4, 146.8, 137.8, 133.7, 132.6, 132.3, 130.6, 128.8, 128.3, 127.8, 127.3, 126.9, 119.3, 116.1, 110.4, 58.8, 45.0, 20.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 4.55. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{30}H_{28}BN_2O_2^+$ = 459.2238. Found 459.2242 (+0.8 ppm error). FT-IR (powder, cm^{-1}): 2922.4, 2359.5, 2227.6, 2134.9, 2025.3, 1977.0, 1739.5, 1606.4, 1583.8, 1499.4, 1468.1, 1421.7, 1361.0, 1283.7, 1261.5, 1231.3, 1183.6, 1150.7, 1129.2, 1097.0, 1068.2, 1039.9, 980.7, 933.1, 869.1, 840.0, 813.2, 783.6, 732.8, 713.3, 698.8.

2,10,13-trimethyl-6-(3-(pyridin-2-yl)phenyl)-6,7,13,14-tetrahydro-12H-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinine **(20)**

The general procedure was followed using 3-(pinacolboryl)phenyl B(MeBOMA) **19** (265 mg, 550 μmol), 2-bromopyridine (79 mg, 500 μmol), Pd_2dba_3 (9.16 mg, 10 μmol), $P^tBu_3{\cdot}HBF_4$ (7.25 mg, 25 μmol), THF (5 mL) and 2 M K_3PO_4 (1 mL, 2 mmol) at 65 °C for 2 h. Purified by recrystallization from toluene. Obtained 213 mg white solid, in 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (dd, 1H), 8.15 (t, *J* = 1.6 Hz, 1H), 7.93 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.68 (td, *J* = 7.7, 1.8 Hz, 1H), 7.57 (ddt, *J* = 13.3, 7.5, 1.2 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.17 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 1H), 7.06 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.72 (d, *J* = 2.2 Hz, 2H), 4.16 (d, *J* = 14.7 Hz, 2H), 3.82 (d, *J* = 14.7 Hz, 2H), 2.63 (s, 3H), 2.27 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 158.8, 151.5, 149.5, 138.2, 136.8, 133.9, 132.1, 130.5, 128.6, 128.0, 127.4, 127.0, 121.8, 121.0, 119.2, 116.2, 58.7, 45.1, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.86. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{28}H_{28}BN_2O_2^+$ = 435.2238. Found 435.2244 (+1.3 ppm error). FT-IR (film, cm^{-1}): 2923.8, 1618.0, 1585.3, 1499.1, 1461.7, 1429.4, 1395.4, 1358.6, 1285.7, 1266.5, 1232.8, 1186.0, 1150.6, 1129.8, 1092.0, 1049.7, 997.5, 909.0, 867.7, 819.3, 792.5, 765.1, 731.3.

Procedure for reactions with MeBOMA boronates

4-(2,10,13-trimethyl-7,12,13,14-tetrahydro-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinin-6-yl)phenyl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate **(14)**

In a 20 mL microwave vial with a stir bar was added 4-hydroxyphenyl B(MeBOMA) **2** (500 mg, 1.34 mmol) and the vial was sealed. DMF (3 mL) and Et_3N (0.37 mL, 2.68 mmol) were added, and the mixture was heated to 80 °C in an oil bath. Nonafluorobutanesulfonyl fluoride (0.29 mL, 1.61 mmol) was then added, and heating continued for 16 h. The reaction mixture was cooled, then transferred to round-bottom flask with toluene and fully dried using a rotary evaporator. The crude product was loaded onto silica and passed through a short silica plug (50% $CHCl_3$/petroleum spirits). Recrystallized in 25% toluene in heptane. Collected 839 mg, 92% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.06 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.92 (d, *J* = 8.3 Hz, 2H), 6.76 – 6.71 (m, 2H), 4.18 (d, *J* = 14.8 Hz, 2H), 3.80 (d, *J* = 14.8 Hz, 2H), 2.59 (s, 3H), 2.27 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 151.1, 150.2, 135.2, 130.7, 129.0, 127.4, 120.1, 119.3, 115.9, 58.8, 45.0, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.72. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.52, -81.55, -81.59, -109.99, -110.02, -110.06, -121.80, -21.83, -126.69, -126.73, -126.77. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{27}H_{24}BF_9NO_5S^+$ = 656.1319. Found 656.1318 (-0.1 ppm error). FT-IR (powder, cm^{-1}): 3018.9, 2925.9, 2359.2, 1739.8, 1617.5, 1584.2, 1500.1, 1468.7, 1447.5, 1423.3, 1405.2, 1355.8, 1285.5, 1261.1, 1231.6, 1201.8, 1180.0, 1142.8, 1131.3, 1108.4, 1088.8, 1074.0, 1052.2, 1010.2, 988.6, 980.4, 932.7, 871.3, 850.3, 819.7, 794.7, 779.9, 736.0, 718.9, 697.1.

2,10,13-trimethyl-6-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-6,7,13,14-tetrahydro-12H-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinine **(19)**

In a 100 mL Schlenk tube charged with a stir bar were added 3-bromophenyl B(MeBOMA) **1b** (1.00 g, 2.30 mmol), B_2pin_2 (640 mg, 2.52 mmol, 1.1 equiv.), KOAc (315 mg, 3.21 mmol, 1.4 equiv.) and Pd(dppf)Cl_2 (67 mg, 92 μmol, 4 mol% relative to bromide). After vacuum/N_2 cycles, N_2-sparged dioxane (40 mL) was added, and the mixture was refluxed in an oil bath for 16 h. Once cooled to room temperature, the mixture was transferred to a round-bottom flask using ethyl acetate, and the solvents were removed by rotary evaporator. The crude material was loaded onto silica gel and purified via DCVC (50% petroleum spirits/$CHCl_3$). The product was then recrystallized in heptane. Obtained 948 mg white solid, in 86% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.05 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 2.1 Hz, 2H), 4.13 (d, *J* = 14.7 Hz, 2H), 3.77 (d, *J* = 14.7 Hz, 2H), 2.62 (s, 3H), 2.26 (s, 6H), 1.32 (s, 12H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 151.6, 140.3, 136.0, 134.6, 130.4, 128.4, 127.3, 126.8, 119.4, 116.2, 83.6, 58.8, 45.2, 25.0, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.69, 4.19. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{29}H_{36}B_2NO_4^+$ = 484.28249. Found 484.28246 (-0.1 ppm error). FT-IR (powder, cm^{-1}): 3017.3, 2976.2, 2119.0, 1997.7, 1976.7, 1738.7, 1616.8, 1594.3, 1499.7, 1463.7, 1446.0, 1417.7, 1400.1, 1372.2, 1354.0, 1312.4, 1298.3, 1283.6, 1266.3, 1253.8, 1229.7, 1188.3, 1166.5, 1142.3, 1124.5, 1105.1, 1085.3, 1061.4, 1037.2, 1005.5, 964.8, 940.2, 932.0, 878.2, 865.1, 852.7, 814.0, 784.9, 776.5, 745.5, 717.2, 690.2.

3'-(2,10,13-trimethyl-7,12,13,14-tetrahydro-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinin-6-yl)-[1,1'-biphenyl]-4-carboxylic acid **(21)**

In a 20 mL microwave vial with a stir bar was added **17** (163 mg, 0.33 mmol, 1.0 eq), 1 mL of 5 M NaOH (5 mmol, 15 equiv.) and 3 mL of THF. The mixture was heated to 65 °C in an oil bath for 2 h. After cooling to r.t., 1 mL of water was added, and the mixture neutralized with pH 7 phosphate buffer. The mixture was extracted into EtOAc, washed with brine, and dried over $MgSO_4$. The mixture was filtered, the solvent was evaporated from the filtrate, and the solids resuspended in $CHCl_3$. The solid was filtered and washed with $CHCl_3$ to obtain the product as 135 mg of white solid, in 83% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.92 (br. s, 1H) 8.02 – 7.94 (m, 2H), 7.78 (t, *J* = 1.6 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.57 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.01 (dd, *J* = 8.3, 2.2 Hz, 2H), 6.84 (d, *J* = 2.2 Hz, 2H), 6.76 (d, *J* = 8.2 Hz, 2H), 4.14 (d, *J* = 15.4 Hz, 2H), 3.93 (d, *J* = 15.4 Hz, 2H), 3.37 (s, 4H), 2.57 (s, 3H), 2.21 (s, 6H). ^{13}C{^{1}H}NMR (126 MHz, DMSO-d_6) δ 167.2, 151.1, 145.5, 137.6, 132.7, 131.7, 129.9, 129.8, 129.2, 127.8, 127.7, 127.7, 126.7, 126.3, 118.0, 117.1, 57.0, 44.1, 20.1. ^{11}B NMR (128 MHz, DMSO-d6) δ 1.86. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{30}H_{29}BNO_4^+$ = 478.2184. Found 478.2179 (-0.1 ppm error). FT-IR (powder, cm^{-1}): 3023.6, 2916.7, 2862.2, 2768.6, 2505.6, 2155.1, 2056.7, 1875.4, 1687.7, 1608.6, 1586.8, 1499.8, 1471.7, 1447.9, 1419.0, 1388.5, 1361.3, 1304.8, 1281.6, 1264.2, 1231.5, 1196.3, 1180.7, 1152.6, 1128.4, 1102.5, 1081.1, 1059.7, 1037.4, 1021.0, 982.0, 933.4, 914.2, 871.4, 853.0, 812.5, 790.3, 768.2, 729.1, 708.1.

1-methyl-4-(2,10,13-trimethyl-13,14-dihydro-12H-6λ^4,13λ^4-benzo[e]benzo[5,6][1,3,2]oxazaborinino[2,3-b][1,3,2]oxazaborinin-6-yl)pyridin-1-ium **(22)**

In a 20 mL microwave vial with a stir bar was added 4-pyridyl B(MeBOMA) **7** (358 mg, 1.0 mmol, 1.0 equiv.) and 5 mL of acetone. The microwave vial was sealed, and MeI (0.20 mL, 3.2 mmol, 3.2 equiv.) was added. The reaction mixture was heated to 70 °C in an oil bath for 16 h. After cooling to room temperature, the mixture was transferred to a round-bottom flask and evaporated to dryness. The solid was resuspended in cold acetone and filtered. Obtained 440 mg white solid, in 88% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.76 (d, *J* = 6.4 Hz, 2H), 7.94 – 7.88 (m, 2H), 7.06 (dd, *J* = 8.5, 2.2 Hz, 2H), 6.90 (d, *J* = 2.2 Hz, 2H), 6.80 (d, *J* = 8.2 Hz, 2H), 4.29 (s, 3H), 4.24 (d, *J* = 15.6 Hz, 2H), 4.04 (d, *J* = 15.7 Hz, 2H), 2.59 (s, 3H), 2.24 (s, 6H). ^{13}C{^{1}H}NMR (101 MHz, DMSO-d_6) δ 149.7, 149.7, 143.7, 142.8, 142.2, 131.2, 131.0, 130.6, 130.6, 129.3, 129.3, 128.5, 128.5, 128.4, 127.2, 127.0, 118.5, 118.2, 117.1, 116.4, 57.0, 20.0, 19.9. ^{11}B NMR (128 MHz, DMSO-d_6) δ 2.77. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{23}H_{26}BN_2O_2^+$ = 373.2082. Found 373.2086 (+1.1 ppm error). FT-IR (powder, cm^{-1}): 3428.0, 2917.5, 1706.0, 1638.0, 1618.0, 1585.7, 1497.1, 1456.5, 1360.7, 1326.7, 1283.5, 1260.8, 1229.9, 1207.9, 1151.6, 1130.0, 1082.3, 1058.7, 998.5, 932.3, 875.0, 819.7, 793.5, 775.5, 721.3, 656.8.

6-(7-bromo-9,9-dioctyl-9H-fluoren-2-yl)-2,10,13-trimethyl-6,7,13,14-tetrahydro-12H-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinine **(23)**

15.0 g (27.4 mmol, 1.0 equiv.) of 2,7-dibromo-9,9-dioctylfluorene was transferred to a 500 mL two-neck round-bottom flask and vacuum/N_2 cycles were performed. 350 mL dry THF was added, and the solution cooled to -78 °C. 11.0 mL (27.5 mmol, 1.0 equiv) of n-BuLi 2.5 M in hexanes was added dropwise over 10 min, and the mixture stirred at -78 °C for an additional 30 min. 3.4 mL (30.5 mmol, 1.1 equiv) of trimethyl borate was then added dropwise at -78 °C over 5 min, and the mixture was stirred at -78 °C for an additional 15 min. The mixture was then allowed to warm to r.t. o/n with stirring. The reaction mixture was concentrated to *ca*. 50 mL by rotary evaporation, then transferred to a separatory funnel and washed with sat. NH_4Cl(aq), water and brine. The organic layer was collected, dried with $MgSO_4$ and filtered. The solvent was removed by rotary evaporation to yield 15.0 g of crude 7-bromo-9,9-dioctyl-2-fluorenyl boronic acid as a pale yellow viscous oil, which was used directly in the next step. The crude boronic acid was transferred to a 250 mL round-bottom flask along with 7.43 g (27.4 mmol, 1.0 equiv) of MeBOMA and 100 mL of toluene. A Dean-Stark apparatus was attached to the flask, and the mixture was heated to a vigorous reflux for 4 h. The compound was loaded onto silica, dried, and transferred to a fresh silica plug. After washing with petroleum spirits, the product was collected by elution with neat toluene. The toluene filtrate was dried to 18.4 g (90% yield) of product as a colourless glassy resin which slowly crystallizes over time. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.09 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.71 (d, *J* = 2.1 Hz, 2H), 4.17 (d, *J* = 14.7 Hz, 2H), 3.78 (d, *J* = 14.7 Hz, 2H), 2.59 (s, 3H), 2.31 (s, 6H), 1.85 (t, *J* = 8.4 Hz, 4H), 1.33 – 1.24 (m, 4H), 1.24 – 1.18 (m, 4H), 1.18 – 1.11 (m, 4H), 1.10 – 0.98 (m, 8H), 0.90 (t, *J* = 7.3 Hz, 6H), 0.70 – 0.54 (m, 4H). ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$) δ 153.5, 151.5, 148.9, 141.1 (br, C-B), 140.5, 139.6, 131.8, 130.4, 129.7, 128.4, 127.9, 127.3, 126.1, 120.9, 120.6, 119.1, 118.6, 116.2, 58.5, 55.0, 44.7, 40.1, 31.9, 30.1, 29.4, 29.3, 23.9, 22.7, 20.6, 14.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 5.06. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd $C_{46}H_{60}BBrNO_2^+$ for = 748.3895, 750.3875. Found 748.3895, 750.3870 (+0.1 ppm, -0.5 ppm error). FT-IR (powder, cm^{-1}): 2923.8, 2852.9, 1619.0, 1500.3, 1455.1, 1285.3, 1262.4, 1232.5, 1150.2, 1129.9, 1051.8, 1004.6, 874.8, 815.9, 788.0.

9,9-dioctyl-7-(2,10,13-trimethyl-7,12,13,14-tetrahydro-6λ^4,13λ^4-benzo[e]benzo[4,5][1,2]azaborinino[2,1-b][1,3,2]oxazaborinin-6-yl)-9H-fluoren-2-ol **(24)**

18.4 g (24.6 mmol, 1.0 equiv.) of **23** was transferred to a 1 L two-neck round-bottom flask and vacuum/N_2 cycles were performed. 500 mL dry THF was added, and the solution cooled to -78 °C. 10.0 mL (25.0 mmol, 1.02 equiv.) of n-BuLi 2.5 M in hexanes was added dropwise over 6 min, and the mixture stirred at -78 °C for an additional 30 min. 3.0 mL (27.0 mmol, 1.1 equiv.) of trimethyl borate was then added dropwise at -78 °C over 3 min, and the mixture was stirred at -78 °C for an additional 15 min. The mixture was then allowed to warm to r.t. o/n with stirring. The reaction mixture was concentrated to *ca*. 300 mL by rotary evaporation, then 100 mL MeOH was added. To this solution was added 3.47 g (36.9 mmol, 1.5 equiv.) of hydrogen peroxide-urea adduct dissolved in 50 mL MeOH, and the reaction mixture was stirred at r.t. for 90 min, at which point full consumption of the intermediate bisborylated compound was observed by TLC. Excess hydrogen peroxide was destroyed by addition of 5 g of sodium metabisulfite dissolved in 25 mL of water. The reaction mixture was then once again concentrated by rotary evaporation, transferred to separatory funnel and extracted with $CHCl_3$. The organic layer was dried with $MgSO_4$ and filtered. The compound was loaded onto silica, dried, and transferred to a fresh silica plug. After washing with petroleum spirits:DCM 3:1 and 2:1, product was collected using neat DCM. The DCM filtrate was dried to 15.0 g (89% yield) of product as a light brown glassy resin. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.08 (dd, *J* = 8.2, 2.1 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 2.3 Hz, 1H), 6.74 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.72 (s, 2H), 4.87 (br s, 1H), 4.16 (d, *J* = 14.6 Hz, 2H), 3.79 (d, *J* = 14.7 Hz, 2H), 2.60 (s, 3H), 2.29 (s, 6H), 1.86 – 1.67 (m, 4H), 1.26 – 1.20 (m, 4H), 1.18 – 1.07 (m, 8H), 1.04 – 0.95 (m, 8H), 0.85 (t, *J* = 7.2 Hz, 6H), 0.64 – 0.51 (m, 4H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ 155.1, 153.6, 151.7, 148.7, 140.7, 134.7, 131.6, 130.5, 128.5, 127.8, 127.2, 120.5, 119.3, 117.7, 116.3, 113.8, 110.2, 58.8, 54.7, 44.9, 40.5, 32.1, 30.3, 29.5, 29.5, 24.0, 22.8, 20.7, 14.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 5.27. HRMS (ESI-MS [positive mode]) m/z: $[M+H]^+$ Calcd for $C_{46}H_{61}BNO_3^+$ = 686.4739. Found 686.4746 (+1.0 ppm error). FT-IR (powder, cm^{-1}): 3351.4, 2924.1, 2852.5, 2366.8, 1616.8, 1586.7, 1500.5, 1464.5, 1357.3, 1284.6, 1260.1, 1231.7, 1206.5, 1151.0, 1130.6, 1049.7, 998.3, 932.8, 869.3, 817.2, 788.2, 766.7, 748.6, 708.8.

Aqueous acid stability

111 mg (0.3 mmol, 1.0 eq.) of **4**, 29 mg (0.15 mmol, 0.5 eq.) of the internal standard, 1,4-di-*tert*-butylbenzene, and 6.0 mL of

$CDCl_3$ were added in a microwave vial with a stir bar. The vial was sealed, and the mixture was stirred at room temperature until homogenous. An aliquot was taken as the initial time point (0 h). In the vial was added 3.0 mL of 1 M HCl, and the mixture was stirred vigorously. Additional NMR aliquots were taken at times 1 h, 6 h, 24 h, and 96 h after the 1 M HCl was added. The stability of the boronate at room temperature in 1 M HCl was determined by the integration of signals of **4** relative to the internal standard. Data is shown in Figure S25.

Aqueous base stability

672 mg of **4** (1.8 mmol), 1.0 mL of 5 M NaOH (5.0 mmol) and 4 mL of toluene were added in a microwave vial with a stir bar. The microwave vial was sealed, and the mixture was stirred at 120 °C in an oil bath for 48 h. The vial was cooled to room temperature, and the seal was removed. The mixture was extracted with Et_2O and washed with pH 7 phosphate buffer. The organic layer was separated, dried with $MgSO_4$ and filtered. The solvents were removed by evaporation, and the solid resuspended in 1:1 petroleum spirits/toluene. The suspension was filtered off, and the solids were collected (616 mg, 92% recovery). A ^1H NMR spectrum of the recovered material was acquired in $CDCl_3$. Data is shown in Figure S26.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information Statement

Supporting Information file contains single crystal X-ray diffraction data summary and NMR spectra. FAIR Data is available as Supporting Information for Publication and includes the primary NMR FID files for all compounds reported. This is available free of charge on the ACS Publications website.

Accession Codes

CCDC 2164697 (**MeBOMA**), 2164695 (**2**), 2164700 (**3**), 2164696 (**4**), 2164698 (**5**), and 2164694 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif,o rbyemailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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