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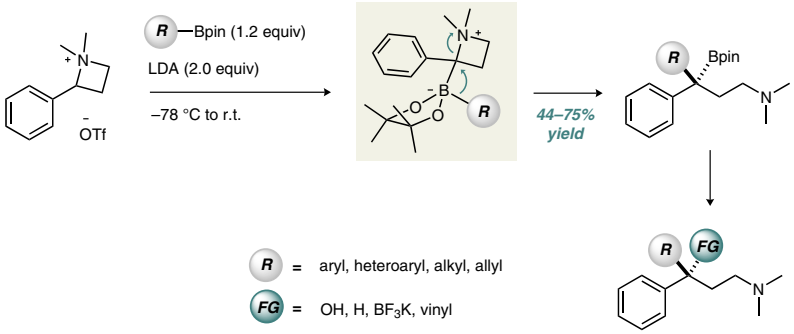
Synthesis of 3-Aryl-1-aminopropane Derivatives: Lithiation–Borylation–Ring-Opening of Azetidinium Ions

Giorgia Casoni
Eddie L. Myers
Varinder K. Aggarwal*

School of Chemistry, University of Bristol, Cantock's Close, Bristol, BS8 1TS, UK
v.aggarwal@bristol.ac.uk

Dedicated to the memory of Professor Jean Normant



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Abstract In situ generated 2-phenyl-azetidinium ylides react with boronic esters to form acyclic γ-dimethylamino tertiary boronic esters. The transformation is believed to involve the formation of a zwitterionic boronate, which subsequently undergoes ring-opening 1,2-migration, which is promoted by the relief of ring strain. Owing to the configurational instability of the initially formed ylides, which appear to be in equilibrium with the open-chain carbene form, the reaction is not stereospecific. The C–B bond of the γ-dimethylamino tertiary boronic esters can be transformed into a variety of functional groups (C–OH, C–vinyl, C–H, C–BF_3), thus giving a diverse selection of 3-aryl-1-aminopropanes, which represent a privileged motif among drug molecules.

Key words 3-aryl-1-aminopropanes, azetidinium ion, lithiation, borylation, ring-opening, boronic esters

Boronic esters are arguably the most versatile of organic functional groups. This group can be transformed to introduce C–O, C–N, C–C, or C–X bonds under mild conditions, a characteristic that makes boronic esters (and boronic acids) extremely valuable late-stage intermediates in medicinal chemistry programs.[1] Although this value has mostly been demonstrated in the context of sp^2-hybridised boron-bearing carbon centres (the transformation of aryl and vinyl boronic esters and acids through Suzuki–Miyaura cross-coupling),[2] the diversification of sp^3-hybridised boron-bearing carbon centres is much less common, despite the identified need to populate compound libraries with such 3D molecules.[3] However, the relatively recent development of robust and generally applicable methods for the enantioselective preparation of secondary and tertiary alkyl boronic esters,[4] together with stereospecific methods for the subsequent transformation of the C–B bonds,[5] is expected to lead to a step-change in the use of organoboron chemistry in the pharmaceutical industry.

One of the most privileged structural motifs among marketed drugs and drug candidates is the 3-aryl-1-aminopropane unit (Figure 1).[6] Bedaquiline, an antituberculosis agent, is one of the more high-profile and structurally complex members of this class of drug molecule (Figure 1).[7] This motif can be introduced through the addition of aryl metal reagents to β-aminoketones,[8] the hydroformylation/reductive amination of styrenes,[9] the Heck–Matsuda addition of aryl halides/pseudohalides to allyl amines[10] and the electrophilic addition of amine-containing electrophiles to diarylmethyl anions.[11]

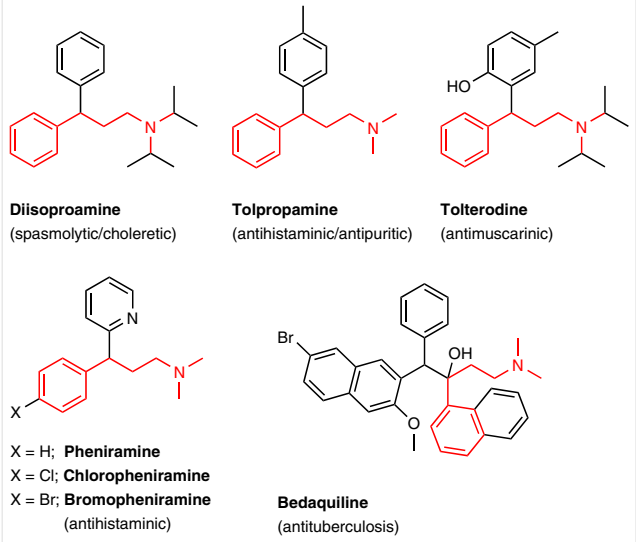
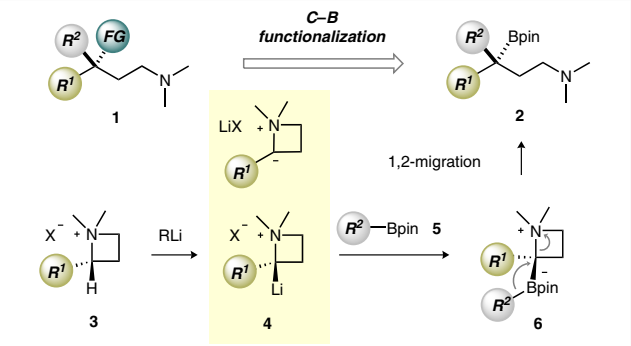


Figure 1 Marketed drugs containing the 3-aryl-1-aminopropane motif

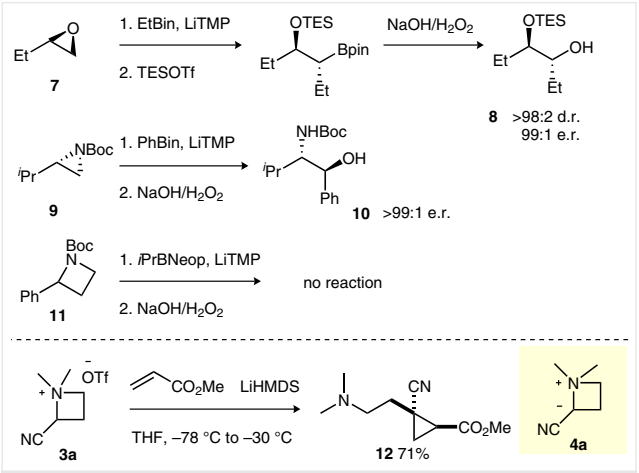
We were particularly interested in accessing a diverse selection of 3-aryl-1-aminopropanes **1** through C–B functionalisation of γ-dimethylamino tertiary boronic esters (Scheme 1). We envisioned that these boronic ester intermediates could be accessed through lithiation–borylation of

azetidinium ions **3**. Specifically, we hoped that azetidinium ions **3** could be deprotonated to give ylide/lithium-stabilised carbenoid **4**, which could then be trapped with boronic ester **5** to give zwitterionic boronate **6**, which in turn could undergo ring-opening 1,2-migration to give γ-amino tertiary boronic ester **2**. Ideally, the entire transformation would be stereospecific, a characteristic that would require conditions under which enantiomerically enriched azetidinium ion **3** could be deprotonated to give **4** that rests in the lithium-stabilised carbenoid form (rather than the ylidic form), is configurationally stable, and undergoes stereospecific trapping with a boronic ester **5**; the resulting boronate **6** would then undergo 1,2-migration, processes that are usually highly stereospecific and involve inversion at the leaving-group-bearing carbon atom, thus giving enantiomerically enriched tertiary boronic ester **2**.



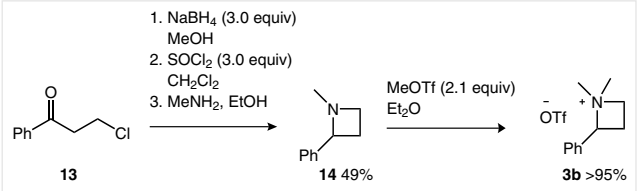
Scheme 1 Synthesis of 3-aryl-1-aminopropanes through C–B functionalisation of γ-dimethylamino tertiary boronic esters, which could be formed through lithiation–borylation

Previous experience within our laboratory gave us cause to be both optimistic and hesitant. For example, we have shown that such ring-opening lithiation–borylation reactions can be carried out with both epoxides **7** and *N*-Boc aziridines **9** to give the corresponding products **8** and **10** with high levels of enantiospecificity (Scheme 2).[12,13] However, this type of reaction failed with *N*-Boc azetidines **11**, presumably owing to the ring-opening 1,2-migration step being slow (Scheme 2).[14] However, the recent work of Couty and David suggested that ring-opening of the corresponding azetidinium ions might be more facile.[15] Specifically, they showed that cyano-substituted azetidinium ions **3a** can be deprotonated with LiHMDS to give ylides **4a** that can be trapped with electrophiles; when the electrophile is an aldehyde, ketone, or acrylate, the resulting alkoxide or enolate undergoes an intramolecular S_N2 reaction to open the azetidinium ion (Scheme 2). The ylides were chemically unstable, even at cryogenic temperatures, necessitating that the electrophile be present during their formation. These studies also showed that these stabilised azetidinium ylides are configurationally unstable, even within the short lifetime imposed by in situ trapping. However, the level of configurational stability of less stabilised ylides, such as those derived from phenyl-substituted azetidinium ions, was unclear.



Scheme 2 Previous studies from our laboratory and that of Couty and David

To test our reaction, we first prepared the triflate salt of phenyl-substituted azetidinium ion **3b** in four steps from commercially available 3-chloro-1-propiophenone (**13**) (Scheme 3). Ketone **13** was first reduced to the alcohol[16] and then converted into the corresponding dichloride.[14b] A ring-closing double displacement reaction with methylamine gave azetidine **14**, which was subsequently N-alkylated in good yield to give azetidinium ion **3b**.[14b,15b]

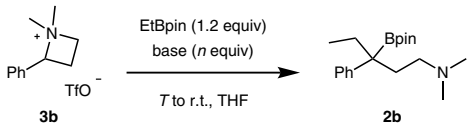


Scheme 3 Synthesis of phenyl-substituted azetidinium ion **3b**

With azetidinium ion **3b** in hand, we subjected it to the conditions similar to those established by Couty and David[15b]—LiHMDS (1.7 equiv), THF, –78 °C, 1 hour, then warming to room temperature—in the presence of EtBpin. Under these conditions, γ-dimethylamino tertiary boronic ester **2b** was isolated in 41% yield (Table 1, entry 1). When the putative ylide was generated in the absence of the boronic ester, which was subsequently added, the desired product was not observed, thus highlighting the instability of the ylide. Increasing the amount of base to 3.0 equivalents, adding the base at –20 °C, or subsequently warming the reaction mixture to reflux (to promote 1,2-migration) did not result in improved yields (Table 1, entries 2–4). The use of KHMDS and LiTMP in place of LiHMDS led to reduced yields; however, the use of LDA led to a higher yield (57%;

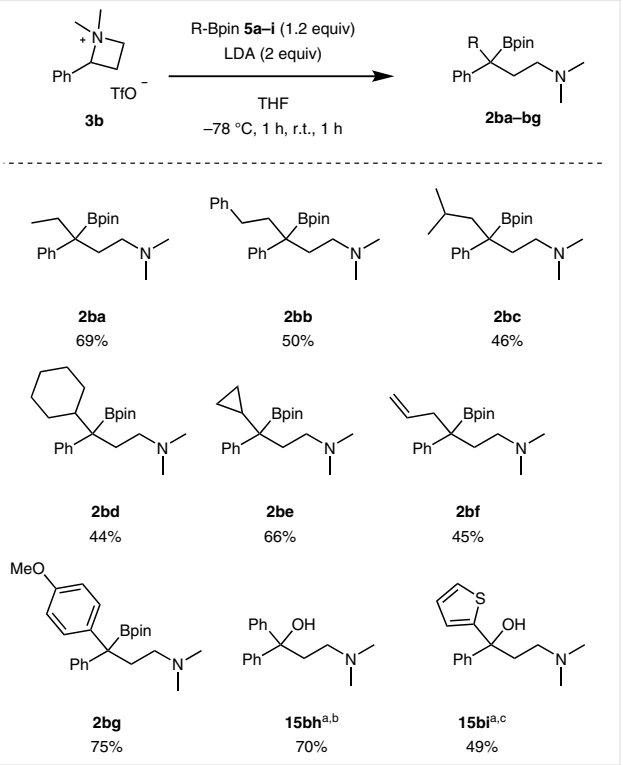
Table 1, entry 7). Further investigation informed us that the addition of 2.0 equivalents of this base was optimum (Table 1, entry 10).

Table 1 Optimisation of the Lithiation–Borylation Reaction of Azetidinium Ion **3b**[a]



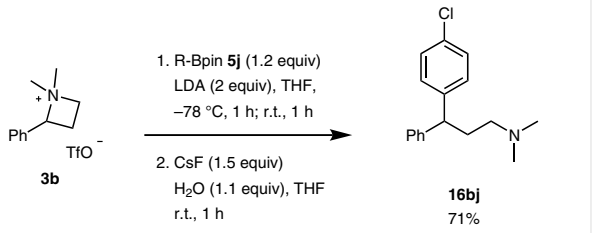
Entry	Base	Equiv of base	T (°C)	Yield of **2b** (%)
1	LiHMDS	1.7	–78	41[b]
2	LiHMDS	1.7	–20	<5[b]
3[c]	LiHMDS	1.7	–78	23[d]
4	LiHMDS	3.0	–78	33[d]
5	KHMDS	1.7	–78	26[d]
6	LiTMP	1.7	–78	26[d]
7	LDA	1.7	–78	57[b]
8	LDA	1.2	–78	16[d]
9	LDA	1.5	–78	43[d]
10	LDA	2.0	–78	69[b]
11	LDA	3.0	–78	58[d]

[a] Reactions were carried out using 0.2 mmol of **3b**.
[b] Yield of isolated material.
[c] After stirring the reaction mixture at –78 °C (1 h), the mixture was warmed to reflux.
[d] Yield determined by ^{1}H NMR analysis of the crude mixture in the presence of an internal standard.



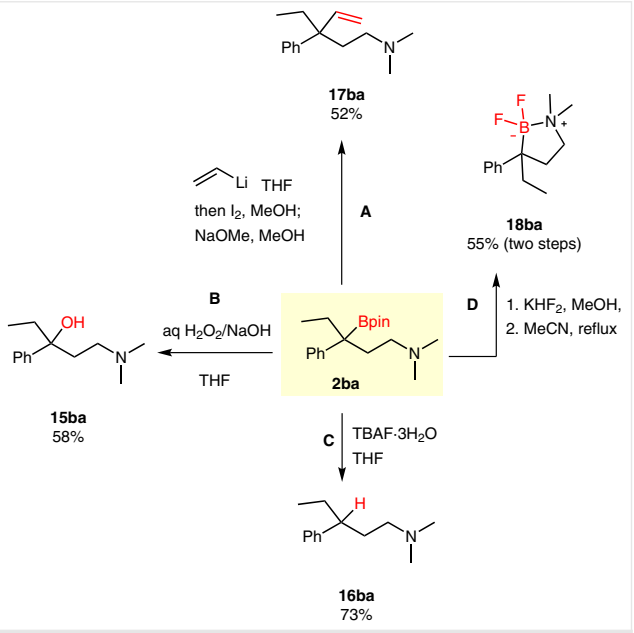
Scheme 4 Scope of the boronic ester for the lithiation–borylation of **3b**. [a] Isolation of the tertiary boronic ester was not possible owing to protodeboronation; in situ oxidation using aqueous H_2O_2/NaOH allowed the isolation of the corresponding tertiary alcohols. [b] The in situ oxidation was carried out at 0 °C. [c] The in situ oxidation was carried out at –40 °C.

Having established optimum conditions for this transformation, we explored the scope of the methodology by testing a range of boronic esters (**5a–i**) (Scheme 4). The use of primary (**5a–c**) and secondary boronic esters (**5d** and **5e**) gave moderate to good yields of the corresponding γ-dimethylamino tertiary boronic esters **2ba–be**. Additionally, the use of allylic boronic ester **5f** gave the corresponding product in 45% yield. Aryl boronic esters proved to be more challenging. When electron-rich boronic esters, such as **5g**, was employed the expected product **2bg** could be isolated in good yield. However, when more electron-poor aryl boronic esters were used, such as phenyl- and 2-thienyl-boronic ester, the corresponding boronic ester products could not be isolated owing to facile protodeboronation. Pleasingly, the unstable boronic ester products could be functionalised in situ, prior to work-up, to give more stable derivatives; the addition of aqueous H_2O_2/NaOH to the reaction mixture led to the corresponding tertiary alcohols **15bh** and **15bi** being isolated in good yields. Interestingly, in our experience, similar tertiary boronic esters, not containing a dimethylamino group, do not undergo protodeboronation so readily,[4n,17] suggesting that complexation of the boronic ester with the proximal amino group promotes fragmentation. Because protodeboronation can be desirable—γ-amino diarylmethines are prominent members of this family of therapeutics (Figure 1)—we sought conditions to effect this transformation more efficiently. Considering our previously reported conditions for the protodeboronation of diarylalkyl boronic esters,[5c] upon lithiation–borylation of **3b** and **5j**, the reaction mixture was warmed to room temperature and CsF (1.5 equiv) and H_2O (1.1 equiv) were added sequentially; within 1 hour of stirring the resulting mixture at room temperature, the tertiary boronic ester was completely consumed and, subsequently, diarylmethine **16bj** could be isolated in 71% yield (Scheme 5).



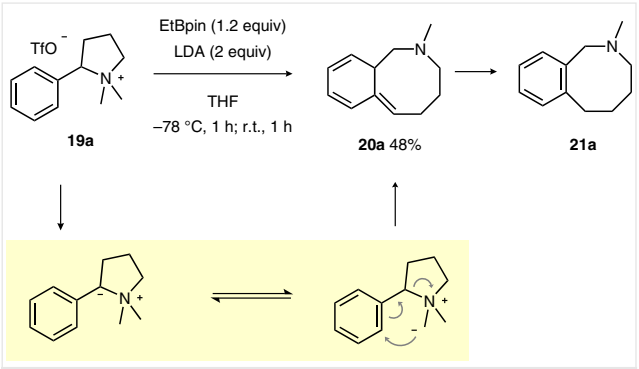
Scheme 5 Lithiation–borylation with in situ protodeboronation

To further demonstrate the versatility of these tertiary boronic esters, we subjected **2ba** to a variety of conditions to effect functionalisation of the C–B bond (Scheme 6). In situ oxidation of **2ba** using H_2O_2/NaOH gave the corresponding tertiary alcohol **15ba** in 58% yield. Other oxidizing conditions ($NaBO_3{\cdot}4H_2O$, $NaBO_3{\cdot}4H_2O$/CH_3COOH,[18] Oxone/acetone,[19] TMANO·$2H_2O$[20]) were less effective and led to partial oxidation of the tertiary amine group. Olefination of isolated **2ba** under modified Zweifel conditions[21] with vinyl lithium gave alkene **17ba** in 52% yield. Protodeboronation of isolated **2ba** using TBAF·$3H_2O$ gave the desired γ-dimethylamino aryl-dialkyl methine **16ba** in 73% yield.[5c] We also attempted to transform **2ba** into the corresponding trifluoroborate salt using standard conditions (KHF_2, MeOH).[22] However, the trifluoroborate moiety underwent partial ligand exchange with the pendant amine to give a mixture of the desired trifluoroborate salt and intramolecularly complexed difluoroborane **18ba** (2:1, 82% overall yield), as determined by ^1H and ^{19}F NMR analysis.[23] Pleasingly, when the crude mixture was heated at reflux in MeCN, complete conversion into **18ba** was effected (67% yield).



Scheme 6 C–B Functionalisation of γ-tertiary boronic ester **2ba**. *Reaction conditions*: (A) (i) vinyl lithium (5 equiv), THF, –78 °C, 30 min, –40 °C, 20 min; (ii) I_2 (5 equiv), MeOH, –78 °C, 15 min; (iii) NaOMe (10 equiv), MeOH, r.t., 1 h. (B) Lithiation–borylation; then aq H_2O_2/NaOH, THF, 1 h. (C) TBAF·$3H_2O$ (1.5 equiv), THF, reflux, 90 min. (D) (i) KHF_2 (4.5 equiv), MeOH, 30 min, r.t.; (ii) MeCN, 5 h, reflux.

We then set out to understand the mechanism of the transformation. First, we prepared pyrrolidinium ion **19a** and subjected it to the lithiation–borylation conditions to investigate the contribution of relief of ring strain in the putative 1,2-migration step. The substrate, **19a**, was prepared through reductive alkylation/alkylation of commercially available 2-phenylpyrrolidine. Upon treatment of a THF solution of **19a** and EtBpin at –78 °C with LDA (2 equiv) with subsequent warming to room temperature, 1,2,3,4,7,8-hexahydroazocine **20a** (48%) was initially isolated, a species that in solution isomerised over a short period of time into the corresponding benzo-fused 1,2,3,4,5,8-hexahydroazocine **21a**; the desired tertiary boronic ester was not observed (Scheme 7). Hexahydroazocine **20a** presumably arises from a Sommelet–Hauser rearrangement: proton transfer of the initially formed benzylic ylide to the methylenic ylide followed by a 2,3-sigmatropic rearrangement.[24] The transformation suggests that either the Sommelet–Hauser rearrangement is faster than the trapping of the benzylic ylide with EtBpin, or that trapping is indeed efficient but that the subsequent 1,2-migration of the boronate is slow, thus allowing fragmentation back to the ylide. Operation of the latter scenario would suggest that the relief of ring-strain in the 1,2-migration of the azetidinium boronates is an important contributor to the success of the transformation.

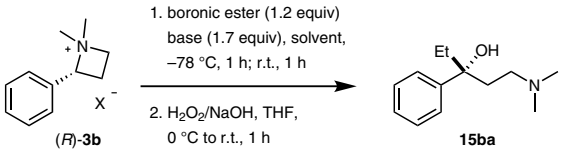


Scheme 7 Competing Sommelet–Hauser rearrangement of pyrrolidinium ylides

The configurational stability of azetidinium ylide **4b** was then investigated. Enantiomerically enriched azetidinium ion (*R*)-**3b** was prepared from (*S*)-3-chloro-1-phenylpropan-1-ol, which was obtained through asymmetric reduction of ketone **13**.[25] When a solution of (*R*)-**3b** and EtBpin in THF at –78 °C was treated with LiHMDS followed by an oxidative work-up (aq H_2O_2/NaOH), the resulting tertiary alcohol **15ba** was found to be racemic, thus revealing that **4b** (like **4a**) is configurationally unstable (Table 2, entry 1).

Presumably, lithium-stabilised ylide **4b**-Li, should it be an intermediate, would undergo solvent-mediated dissociation into the ylide **4b** (deprotonation might lead to **4b** directly), which if pyramidalised, undergoes rapid inversion, a process that could occur via the ring-open carbene form of **4b** (Scheme 8).[14c,26] We surmised that in a less-coordinating solvent, such as TBME, **4b**-Li might be more stable. However, when the lithiation–borylation–oxidation reac-

Table 2 Investigation of the Enantiospecificity of the Lithiation–Borylation–Oxidation Reaction of (*R*)-**3b**[a]

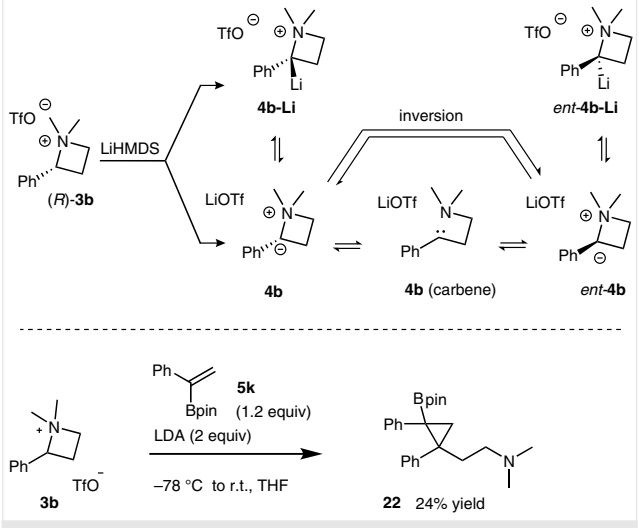


(*R*)-**3b** **15ba**

Entry	Boronic ester	X^-	Base	Solvent	Yield (%)	ee (%)
1	EtBpin	$F_3CSO_3^-$	LiHMDS	THF	27	0
2	EtBpin	$F_9C_4SO_3^-$	LiHMDS	TBME	37	0
3	EtBNeo	$F_9C_4SO_3^-$	LiHMDS	TBME	26	0
4	EtBpin	$F_9C_4SO_3^-$	LDA	TBME	n.d.	0

[a] Reactions conducted using 0.3 mmol of (*R*)-**3b**. n.d. = not determined.

tion was performed in TBME [the nonaflate salt of (*R*)-**3b** was used owing to the poor solubility of the corresponding triflate salt in TBME], the tertiary alcohol was again isolated as the racemate. The insolubility of the azetidinium substrate frustrated attempts to use even less-coordinating solvents (e.g., hexanes). The use of LDA in place of LiHMDS or the use of the less-sterically hindered neopentylglycol boronic ester, EtBNeo, did not lead to enantiomerically enriched product. The intermediacy of a carbene was supported by the isolation of cyclopropane **22** when using vinyl boronic ester **5k** (Scheme 8). Presumably, the desired boronate does not form or undergo 1,2-migration owing to steric hindrance and instead the carbene reacts with the alkene moiety.[27]



Scheme 8 Possible mechanism of racemisation of **4b**

In conclusion, when 2-phenyl-azetidinium ions are converted into azetidinium ylides, through deprotonation with LDA in the presence of boronic esters, they undergo ring-opening carboboration to give γ-dimethylamino tertiary boronic esters. The transformation presumably involves the complexation of the boronic ester with the carbanion of the ylide to form a boronate, which then undergoes ring-opening 1,2-migration, a process that is promoted by the relief of ring-strain of the azetidinium ion. This strain also contributes to the configurational instability of the in situ formed ylides, which appear to be in equilibrium with the ring-opened carbene form. The C–B bond of the products can be transformed into a range of functional groups to give a selection of highly functionalised 3-aryl-aminopropanes, which are attractive targets for the pharmaceutical industry.

Reaction mixtures were stirred magnetically. Air- and moisture-sensitive reactions were carried out in flame-dried glassware under a nitrogen atmosphere using standard Schlenk manifold techniques. Fine chemicals were purchased from Acros Organics, Alfa Aesar, Inochem-Frontier Scientific, Sigma-Aldrich, TCI Europe or Santa Cruz Biotechnology and used as received unless otherwise stated. The following pinacol boronic esters were purchased from commercial suppliers: **5e** (Frontier Scientific), **5f** (Sigma-Aldrich), **5h** (Sigma-Aldrich). *n*-BuLi was received from Acros Organics as a 1.6 M solution in hexane. Lithium diisopropylamide (LDA) was freshly prepared from *n*-BuLi and distilled diisopropylamine immediately before use. Et_3N and diisopropylamine were distilled over CaH_2 before use. Anhydrous MeCN, CH_2Cl_2, Et_2O, THF and toluene were obtained from a purification column composed of activated alumina and stored subsequently over 3 Å molecular sieves. Analytical TLC was carried out on aluminium-backed silica plates (Merck, Silica Gel 60 F254, 0.25). Flash column chromatography was carried out on silica gel (Aldrich, Silica Gel 60, 40–63 µm). Microwave reactions were performed using a Biotage Initiator EXP EU microwave synthesiser. Infrared (IR) spectra were recorded on neat compounds using a PerkinElmer Spectrum One FT-IR spectrophotometer, irradiating between 4000 cm^{-1} and 600 cm^{-1}. Only strong and selected absorbance values (ν_{max}) are reported. ^1H NMR spectra were acquired using a Joel ECS 300, Joel ECS 400 or Varian 400-MR Fourier transform spectrometer for samples in $CDCl_3$ or CD_3OD at 301 or 400 MHz as indicated. Chemical shifts (δ_H) are expressed in parts per million (ppm) and are referred to the residual protio solvent signals of $CHCl_3$ (7.26 ppm) or MeOH (3.31 ppm). ^1H NMR coupling constants are expressed in hertz (Hz) and are quoted as apparent multiplicities (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sept = septet, m = multiplet, dd = doublet of doublets, ps = pseudo). ^{13}C NMR spectra were recorded at 101 MHz; chemical shifts (δ_C) and are expressed in ppm. Carbon atoms attached to boron or to bromine are usually not observed due to quadrupolar relaxation. See the Supporting Information for proton and carbon assignments and molecule numbering. ^{11}B NMR spectra were measured using Norell S-200-QTZ quartz tubes at 128 MHz with complete proton decoupling. Some γ-dimethylamino tertiary boronic esters show two or even three signals, the upfield signals indicative of amine-assisted complexation of CD_3OD (the solvent) and/or H_2O. ^{19}F NMR spectra were recorded at 376 MHz. HRMS ESI was performed on either a Bruker Daltonics Apex IV, 7-Tesla FT-ICR or micrOTOF II. MS samples were submitted in EtOAc or CH_2Cl_2. Optical rotations were

observed using a Bellingham + Stanley Ltd. ADP220 polarimeter at 589 nm (Na D-line) in a cell with path length of 1 dm. GC–MS experiments were carried out using an Agilent 6890 apparatus (column: Supelco SLBTM-5ms capillary column 15 m × 0.25 mm × 0.25 μm).

Synthesis of Pinacol Boronic Esters from Boronic Acids; General Procedure (GP1)

A mixture of boronic acid (1.0 equiv), pinacol (1.0 equiv) and anhydrous $MgSO_4$ (4.0 equiv) in Et_2O (0.5 M) was stirred at r.t. for 16 h. The reaction mixture was filtered and the solvent removed in vacuo. The crude material was purified by distillation or flash column chromatography to give the pure boronic ester.

Lithiation–Borylation of 1,1-Dimethyl-2-phenylazetidin-1-ium Trifluoromethanesulfonate (3b) To Give the Tertiary 3-Dimethylamino-Boronic Ester; General Procedure (GP2)

To a solution of diisopropylamine (2.0 equiv) in anhydrous THF (2.0 M) was added *n*-BuLi (2.0 equiv) at –78 °C. After stirring for 30 min, the solution was added dropwise to a mixture of azetidinium salt **3b** (1.0 equiv) and the boronic ester (1.2 equiv) in dry THF (0.03 M) at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm to r.t. The solvent was removed in vacuo and the crude residue was taken up with H_2O and extracted with CH_2Cl_2 (3 times). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford the crude tertiary boronic ester, which was purified by chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford the γ-dimethylamino tertiary boronic ester.

Lithiation–Borylation of 1,1-Dimethyl-2-phenylazetidin-1-ium Trifluoromethanesulfonate (3b) with in situ Oxidation; General Procedure (GP3a)

To a solution of diisopropylamine (2.0 equiv) in anhydrous THF (2.0 M) was added *n*-BuLi (2.0 equiv) at –78 °C. After stirring for 30 min, the solution was added dropwise to a mixture of azetidinium salt **3b** (1.0 equiv) and the boronic ester (1.2 equiv) in dry THF (0.03 M) at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm to r.t. The reaction mixture was cooled to 0 °C and a 2:1 mixture of aq NaOH (2.0 M) and 30% H_2O_2 was added under vigorous stirring. The cooling bath was removed and the reaction mixture was stirred at r.t. for 1 h. The solvent was removed in vacuo and the residue was partitioned between H_2O and CH_2Cl_2. The phases were separated and the aq layer was re-extracted with CH_2Cl_2 (2 times). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford the pure tertiary alcohol.

Lithiation–Borylation of 1,1-Dimethyl-2-phenylazetidin-1-ium Trifluoromethanesulfonate (3b) with in situ Oxidation at Low Temperature; General Procedure (GP3b)

To a solution of diisopropylamine (2.0 equiv) in anhydrous THF (2.0 M) was added *n*-BuLi (2.0 equiv) at –78 °C. After stirring for 30 min, the solution was added dropwise to a mixture of azetidinium salt **3b** (1.0 equiv) and the boronic ester (1.2 equiv) in dry THF (0.03 M) at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm to r.t. The reaction mixture was cooled to –40 °C and a 2:1 mixture of aq NaOH (2.0 M) and 30% H_2O_2 was added under vigorous stirring. The cooling bath was removed and the reaction mixture was stirred at r.t. for 1 h. The solvent was removed in vacuo and the residue was partitioned between H_2O and CH_2Cl_2. The phases were separated and the aq layer was re-extracted with CH_2Cl_2 (2 times). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford the pure tertiary alcohol.

Lithiation–Borylation of 1,1-Dimethyl-2-phenylazetidin-1-ium Trifluoromethanesulfonate (3b) with in situ Protodeboronation; General Procedure (GP4)

To a solution of diisopropylamine (2.0 equiv) in anhydrous THF (2.0 M) was added *n*-BuLi (2.0 equiv) at –78 °C. After stirring for 30 min, the solution was added dropwise to a mixture of azetidinium salt **3b** (1.0 equiv) and the boronic ester (1.2 equiv) in dry THF (0.03 M) at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm to r.t. CsF (1.5 equiv) was added at r.t., followed by H_2O (1.1 equiv) and the reaction mixture was stirred at r.t. for 1 h. The solvent was removed in vacuo and the residue was partitioned between H_2O and CH_2Cl_2. The phases were separated and the aq layer was re-extracted with CH_2Cl_2 (2 times). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford the pure protodeboronated product.

2-Ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5a)

Following general procedure GP1, ethylboronic acid (5.0 g, 67.4 mmol) and pinacol (8.0 g, 64.7 mmol) afforded, after distillation (40–50 °C, ambient pressure), boronic ester **5a** (10.1 g, 96%) as a colourless liquid. All analytical data matched that previously reported.[28]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 12 H, 4 × C-CH_3), 0.95 (t, *J* = 7.7 Hz, 3 H, CH_2-CH_3), 0.76 (q, *J* = 7.8 Hz, 2 H, CH_2).

4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (5b)

Following general procedure GP1, 2-phenethylboronic acid (10.0 g, 66.7 mmol) and pinacol (7.9 g, 66.7 mmol) afforded pure **5b** as a white crystalline solid (15.4 g, >99%), which was used in the next step without further purification. All analytical data matched that previously reported.[29]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.19 (m, 4 H, Ar-H), 7.14 (m, 1 H, Ar-H), 2.74 (t, *J* = 8.3 Hz, 2 H, CH_2-Ph), 1.21 (s, 12 H, 4 × C-CH_3), 1.13 (t, *J* = 8.2 Hz, 2 H, CH_2-B).

2-Isobutyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5c)

Following general procedure GP1, isobutylboronic acid (3.5 g, 34.5 mmol) and pinacol (4.1 g, 34.5 mmol) afforded, after chromatographic purification (SiO_2, PE/Et_2O = 20:1), boronic ester **5c** as a colourless liquid (5.4 g, 85%). All analytical data matched that previously reported.[30]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (sept, *J* = 6.7 Hz, 1 H, CH), 1.25 (s, 12 H, 4 × C-CH_3), 0.92 (d, *J* = 6.7 Hz, 6 H, 2 × CH_3), 0.73 (d, *J* = 7.2 Hz, 2 H, CH_2).

2-Cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5d)

Following general procedure GP1, cyclohexylboronic acid (1.5 g, 11.7 mmol) and pinacol (1.4 g, 11.7 mmol) afforded, after chromatographic purification (SiO_2, 3% Et_2O/pentane), boronic ester **5d** as a colourless liquid (2.2 g, 90%). All analytical data matched that previously reported.[29]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68–1.54 (m, 5 H, *c*Hex-H), 1.38–1.26 (m, 5 H, *c*Hex-H), 1.23 (s, 12 H, 4 × C-CH_3), 0.97 (m, 1 H, CH).

2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5g)

Following general procedure GP1, (4-methoxyphenyl)boronic acid (3.0 g, 20 mmol) and pinacol (2.4 g, 20 mmol) afforded boronic ester **5g** as a white solid (3.0 g, 85%), which was used in the next step without further purification. All analytical data matched that previously reported.[17b]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.6 Hz, 2 H, Ar-H), 6.90 (d, *J* = 8.6 Hz, 2 H, Ar-H), 3.83 (s, 3 H, O-CH_3), 1.33 (s, 12 H, 4 × C-CH_3).

4,4,5,5-Tetramethyl-2-(thiophen-2-yl)-1,3,2-dioxaborolane (5i)

Following a modified literature procedure,[30] *n*-BuLi (13.5 mL, 21.6 mmol) was added dropwise to a solution of thiophene (2.0 g, 1.90 mL, 23.8 mmol) in dry THF (50 mL) at –78 °C. The solution was stirred at r.t. for 1 h, then it was cooled again to –78 °C and 2-isopropoxy-4,4,5,5-tetramethydioxoborolane (5.2 g, 5.7 mL, 28.1 mmol) was added. The reaction mixture was stirred at r.t. for 16 h, then the solvent was removed under reduced pressure. The residue was taken up with H_2O (30 mL) and the aq phase was extracted with Et_2O (3 × 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by chromatography on silica gel (PE/EtOAc = 95:5) to give boronic ester **5i** as a white solid (3.99 g, 88%). All analytical data matched that previously reported.[31]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (m, 2 H, thio-H), 7.20 (t, *J* = 4.4 Hz, 1 H, thio-H), 1.35 (s, 12 H, 4 × C-CH_3).

2-(4-Chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5j)

Following general procedure GP1, (4-chlorophenyl)boronic acid (3.9 g, 16.4 mmol) and pinacol (1.9 g, 16.4 mmol) afforded, after Kugelrohr distillation (80→110 °C/0.1 mbar), pure boronic ester **5j** as a white solid (5.5 g, 92%). All analytical data matched that previously reported.[17b]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 2 H, Ar-H), 1.34 (s, 12 H, 4 × C-CH_3).

3-Chloro-1-phenylpropan-1-ol (23)

Following a literature reported procedure,[16] $NaBH_4$ (5.7 g, 150 mmol) was added in small portions at 0 °C to a stirred solution of 3-chloro-1-propiophenone (**13**) (8.4 g, 50 mmol) in MeOH (104 mL). The mixture was stirred at r.t. for 18 h and was then quenched with H_2O (90 mL). The solvent was removed in vacuo and the residue was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give the title compound as a colourless oil (8.4 g, 98% yield). The product was used in the next step without further purification. All analytical data matched that previously reported.[16]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 5 H, Ar-H), 4.93 (dd, J_1 = 11.3 Hz, J_2 = 6.4 Hz, 1 H, C*H*-OH), 3.73 (ddd, J_1 = 14.5 Hz, J_2 = 10.8 Hz, J_3 = 7.6 Hz, 1 H, CH_2-Cl), 3.55 (m, 1 H, CH_2-Cl), 2.23 (m, 1 H, CH_2-CH), 2.10 (m, 1 H, CH_2-CH), 2.03 (br s, 1 H, OH).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.83 (Ar-C), 128.81 (2 C, Ar-C), 128.06 (Ar-C), 125.91 (2 C, Ar-C), 71.49 (CH), 41.84 (CH_2), 41.59 (CH_2).

(*S*)-3-Chloro-1-phenylpropan-1-ol [(*S*)-23]

Following a procedure recently reported by Wu and Li,[25] $Cu(OAc)_2{\cdot}H_2O$ (119.8 mg, 0.6 mmol) and (*S*)-P-Phos (151.4 mg, 0.2 mmol) were weighed under air and dissolved in toluene (66 mL). The reaction mixture was stirred at r.t. for 20 min, then a solution of phenylsilane (3 mL, 24 mmol) in toluene (32 mL) was added. The mixture was cooled to –20 °C and a solution of 3-chloro-1-propiophenone (**13**) (3.4 g, 20 mmol) in toluene (32 mL) was added under vigorous stirring. The flask was stoppered and the reaction mixture was stirred for 24 h at the above temperature. Upon completion, the mixture was treated with 10% HCl (130 mL) and the organic product was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by column chromatography on silica gel (hexane/EtOAc, 10:1) afforded alcohol (*S*)-**23** (2.5 g, 73%) as a white solid.

The ee value was determined by chiral HPLC analysis with a Chiralcel IB column (eluent: hexane/2-propanol = 98:2; flow rate: 1 mL/min; detection: 254 nm), t_R (*R*) = 16.2 min (area% 97), t_R (*S*) = 18.1 min (area% 3). Spectral data matched those previously reported for **23**. The optical rotation matched literature data.[32]

$[\alpha]_D^{27.4}$ –23 (*c* 1.0, $CHCl_3$).

1-Methyl-2-phenylazetidine (14)

Following a procedure by Luisi,[14b] to a solution of 3-chloro-1-phenylpropan-1-ol (**23**) (3.1 g, 18.2 mmol) in dry CH_2Cl_2 (18 mL), a solution of $SOCl_2$ (4.0 mL, 54.6 mmol) in dry CH_2Cl_2 (5.5 mL) was added dropwise at r.t. After stirring for 1 h, the reaction mixture was poured into H_2O (20 mL) and aq NaOH (15% w/v) was added slowly to neutralise the excess of HCl until the pH of the solution was 7. The aq phase was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum to afford 1-phenyl-1,3-dichloropropane that was employed in the next step without further purification.

To a solution of 1-phenyl-1,3-dichloropropane in EtOH (23 mL) and Et_3N (5.1 mL, 36.4 mmol) in a sealed flask, a solution of $MeNH_2$ (33% w/v in EtOH, 23 mL) was added at r.t. The reaction mixture was heated at 70 °C for 16 h and then allowed to cool to ambient temperature. The solvent was removed in vacuo and HCl (30 mL, 2.0 M) was added. The aq phase was extracted with CH_2Cl_2 (3 × 40 mL) and subsequently basified by addition of aq NaOH (15% w/v) until the pH of the solution was >12. The basic aq phase was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash silica gel column chromatography (EtOAc/Et_3N = 100:0.5) to afford azetidine **14** (1.34 g, 50%, over two steps) as a colourless oil. The analytical data matched that previously reported.[14b]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.30 (m, 4 H, Ar-H), 7.26–7.22 (m, 1 H, Ar-H), 3.87 (t, *J* = 8.4 Hz, 1 H, 1-H), 3.45 (m, 1 H, 3-H), 2.85 (dt, J_1 = 9.6 Hz, J_2 = 7.1 Hz, 1 H, 3-H), 2.33 (s, 3 H, CH_3), 2.26 (m, 1 H, 2-H), 2.14 (quin, *J* = 8.9 Hz, 1 H, 2-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.99 (Ar-C), 128.46 (2 C, Ar-C), 127.39 (Ar-C), 126.71 (2 C, Ar-C), 71.30 (1-C), 53.06 (3-C), 44.61 (CH_3), 27.01 (2-C).

This method was also used for the synthesis of enantiopure azetidine, (*R*)-**14**, employing (*S*)-3-chloro-1-phenylpropanol-1-ol [(*S*)-**23**] as starting material.[14b] The absolute configuration of enantioenriched azetidine (*R*)-**14** was assigned assuming retention of configuration in the reaction with $SOCl_2$ and inversion of configuration in the cyclisation step with $MeNH_2$. The ee value for (*R*)-**14** was determined by chiral GC (Cycloβdex, iso: 90 °C, length: 30 m, i.d.: 0.25). For enantioenriched material, the result was t_R (*S*) = 35.21 (area% 13), t_R (*R*) = 35.57 (area% 87).

1,1-Dimethyl-2-phenylazetidin-1-ium Trifluoromethanesulfonate (3b)

Following a modified procedure by Couty,[15b] azetidine **14** (515.3 mg, 3.5 mmol) was dissolved in dry Et_2O (30 mL). After cooling to 0 °C, methyl trifluoromethanesulfonate (830 µL, 7.3 mmol) was added. The mixture was stirred for 1 h, then all the volatiles were removed under vacuum to afford azetidinium triflate **3b** (1.075 g, >95%) as an orange oil.

IR (neat): 1465, 1254, 1223, 1152, 1028, 975, 830, 770, 756, 706 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.47 (m, 5 H, Ar-H), 5.84 (dd, J_1 = 10.5 Hz, J_2 = 8.6 Hz, 1 H, 1-H), 4.59 (ps q, J = 9.3, 1 H, 3-H), 4.07 (ps td, J_1 = 10 Hz, J_2 = 3.5 Hz, 1 H, 3-H), 3.29 (s, 3 H, CH_3), 3.24 (m, 1 H, 2-H), 2.78 (m, 1 H, 2-H), 2.59 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.85 (Ar-C), 129.86 (2 C, Ar-C), 129.71 (2 C, Ar-C), 128.80 (Ar-C), 122.40 (CF_3), 79.05 (1-C), 62.62 (3-C), 52.50 (CH_3), 45.67 (CH_3), 18.96 (2-C).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –78.31.

HRMS (ESI): m/z [M – SO_3CF_3]$^+$ calcd for $C_{11}H_{16}N$: 162.1277; found: 162.1283.

***N,N*-Dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (2ba)**

According to general procedure GP2, diisopropylamine (561 µL, 4 mmol), *n*-BuLi (2.5 mL, 4 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (622.6 mg, 2 mmol) and 2-ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5a**) (374.5 mg, 2.4 mmol) in anhydrous THF (35 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), γ-dimethylamino boronic ester **2ba** (437.5 mg, 69%) as a colourless oil.

IR (neat): 2973, 2936, 1460, 1370, 1350, 1308, 1260, 1143, 1031, 967, 851, 759 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.29 (m, 2 H, Ar-H), 7.27–7.23 (m, 2 H, Ar-H), 7.11 (tt, J_1 = 6.8 Hz, J_2 = 1.3 Hz, 1 H, Ar-H), 2.20 [s, 6 H, N-$(CH_3)_2$], 2.19–2.13 (m, 2 H, 1-H), 2.04–1.91 (m, 2 H, 2-H), 1.91–1.75 (m, 2 H, CH_2-CH_3), 1.20 (s, 6 H, 2 × C-CH_3), 1.17 (s, 6 H, 2 × C-CH_3), 0.70 (t, J = 7.4 Hz, 3 H, CH_2-CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.53 (Ar-C), 128.07 (2 C, Ar-C), 127.68 (2 C, Ar-C), 125.10 (Ar-C), 83.22 (2 C, 2 × B-O-C), 56.46 (1-C), 45.96 [2 C, N-$(CH_3)_2$], 31.93 (2-C), 29.85 (3-C), 28.10 (CH_2-CH_3), 24.98 (2 C, 2 × C-CH_3), 24.96 (2 C, 2 × C-CH_3), 9.27 (CH_2-CH_3).

^{11}B NMR (128 MHz, $CDCl_3$): δ = 31.77.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{33}BNO_2$: 318.2602; found: 318.2608.

***N,N*-Dimethyl-3,5-diphenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (2bb)**

According to general procedure GP2, diisopropylamine (140 µL, 1 mmol), *n*-BuLi (625 µL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155 mg, 0.5 mmol) and 4,4,5,5-tetramethyl-2-phenethyl-1,3,2-dioxaborolane (**5b**) (139 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), γ-dimethylamino boronic ester **2bb** (97 mg, 50%) as an orange solid.

IR (neat): 2936, 1459, 1138, 1111, 1096, 1079, 1069, 1052, 1022, 988, 839, 757 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.39 (d, J = 7.6 Hz, 2 H, Ar-H), 7.31 (t, J = 7.5 Hz, 2 H, Ar-H), 7.23 (t, J = 7.5 Hz, 2 H, Ar-H), 7.18–7.09 (m, 4 H, Ar-H), 2.42–2.37 (m, 2 H, 5-H), 2.30–2.26 (m, 2 H, 1-H), 2.23 [s, 6 H, N-$(CH_3)_2$], 2.13–2.02 (m, 4 H, 2-H + 4-H), 1.26 (s, 6 H, 2 × C-CH_3), 1.25 (s, 6 H, 2 × C-CH_3).

^{13}C NMR (101 MHz, CD_3OD): δ = 146.14 (Ar-C), 144.35 (Ar-C), 129.36 (2 C, Ar-C), 129.23 (2 C, Ar-C), 129.20 (2 C, Ar-C), 128.52 (2 C, Ar-C), 126.67 (Ar-C), 126.48 (Ar-C), 84.72 (2 C, 2 × B-O-C), 57.34 (1-C), 45.77 [2 C, N-$(CH_3)_2$], 39.42 (2-C), 33.10 (5-C), 32.81 (4-C), 25.34 (4 C, 4 × C-CH_3); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 31.62, 13.02.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{25}H_{37}BNO_2$: 394.2916; found: 394.2933.

***N,N*,5-Trimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-1-amine (2bc)**

According to general procedure GP2, diisopropylamine (140 µL, 1 mmol), *n*-BuLi (625 µL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155.7 mg, 0.5 mmol) and 2-isobutyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5c**) (110.5 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), γ-dimethylamino boronic ester **2bc** (79.5 mg, 46%) as a colourless oil.

IR (neat): 2952, 1447, 1371, 1143, 701 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.39 (d, J = 8.0 Hz, 2 H, Ar-H), 7.26 (t, J = 7.6 Hz, 2 H, Ar-H), 7.12 (t, J = 7.3 Hz, 1 H, Ar-H), 2.19 [s, 6 H, N-$(CH_3)_2$], 2.17–1.99 (m, 4 H, 1-H + 2-H), 1.77 (m, 2 H, 4-H), 1.56 (sept, J = 6.7 Hz, 1 H, CH), 1.21 (s, 6 H, 2 × C-CH_3), 1.19 (s, 6 H, 2 × C-CH_3), 0.82 (d, J = 6.7 Hz, 3 H, CH-CH_3), 0.78 (d, J = 6.7 Hz, 3 H, CH-CH_3).

^{13}C NMR (101 MHz, CD_3OD): δ = 146.53 (Ar-C), 129.05 (2 C, Ar-C), 128.56 (2 C, Ar-C), 126.30 (Ar-C), 84.66 (2 C, 2 × B-O-C), 57.09 (1-C), 45.64 [2 C, N-$(CH_3)_2$], 45.45 (4-C), 33.00 (2-C), 26.78 (CH), 25.30 (2 C, 2 × C-CH_3), 25.20 (2 C, 2 × C-CH_3), 24.85 (CH-CH_3), 24.61 (CH-CH_3); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 32.36, 19.17, 16.11.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{21}H_{37}BNO_2$: 346.2916; found: 346.2911.

3-Cyclohexyl-*N,N*-dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-amine (2bd)

According to general procedure GP2, diisopropylamine (140 µL, 1 mmol), *n*-BuLi (625 µL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (159 mg, 0.51 mmol) and 2-cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5d**) (126.1 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), γ-dimethylamino boronic ester **2bd** (84.2 mg, 44%) as a colourless oil.

IR (neat): 2926, 2852, 1450, 1371, 1350, 1300, 1269, 1141, 1036, 852 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.35 (d, J = 7.5 Hz, 2 H, Ar-H), 7.24 (t, J = 7.5 Hz, 2 H, Ar-H), 7.13 (t, J = 7.3 Hz, 1 H, Ar-H), 2.24–2.10 (m, 2 H, 3-H + *c*Hex-H), 2.17 [s, 6 H, N-$(CH_3)_2$], 2.02–1.93 (m, 2 H, 1-H + *c*Hex-H), 1.89 (m, 1 H, *c*Hex-H), 1.76–1.48 (m, 5 H, 3 × *c*Hex-H + 2 × 2-H), 1.33 (s, 6 H, 2 × C-CH_3), 1.32 (s, 6 H, 2 × C-CH_3), 1.29–0.91 (m, 5 H, 5 × *c*Hex-H).

^{13}C NMR (101 MHz, CD_3OD): δ = 144.80 (Ar-C), 130.16 (2 C, Ar-C), 128.65 (2 C, Ar-C), 126.47 (Ar-C), 84.80 (2 C, 2 × B-O-C), 58.26 (1-C), 48.01 (2-C), 45.45 [2 C, N-$(CH_3)_2$], 33.92 (*c*Hex-C), 31.54 (*c*Hex-C),

30.20 (*c*Hex-C), 28.42 (*c*Hex-C), 28.23 (*c*Hex-C), 27.96 (*c*Hex-C), 25.68 (2 C, 2 × C-CH_3), 25.37 (2 C, 2 × C-CH_3); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 33.25.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{39}BNO_2$: 372.307254; found: 372.309094.

3-Cyclopropyl-*N*,*N*-dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-amine (2be)

According to general procedure GP2, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155.7 mg, 0.5 mmol) and 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5e**) (100.8 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), γ-dimethylamino boronic ester **2be** (108.2 mg, 66%) as a colourless oil.

IR (neat): 2976, 1371, 1306, 1142, 853, 700 cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.42 (dd, J_1 = 7.9 Hz, J_2 = 1.2 Hz, 2 H, Ar-H), 7.26 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.13 (t, *J* = 7.3 Hz, 1 H, Ar-H), 2.35 (t, *J* = 8.2 Hz, 2 H, 1-H), 2.20 [s, 6 H, N-$(CH_3)_2$], 2.01 (m, 2 H, 2-H), 1.22 (s, 6 H, 2 × C-CH_3), 1.20 (s, 6 H, 2 × C-CH_3), 1.03 (m, 1 H, 4-H), 0.59–0.48 (m, 3 H, 5-H/6-H), 0.32 (m, 1 H, 5-H/6-H).

^{13}C NMR (101 MHz, CD_3OD): δ = 146.86 (Ar-C), 128.98 (2 C, Ar-C), 128.90 (2 C, Ar-C), 126.39 (Ar-C), 84.65 (2 C, 2 × B-O-C), 57.54 (1-C), 45.52 [2 C, N-$(CH_3)_2$], 36.08 (2-C), 25.20 (2 C, 2 × C-CH_3), 25.08 (2 C, 2 × C-CH_3), 18.09 (4-C), 4.10 (5-C/6-C), 3.43 (5-C/6-C); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 31.68.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{33}BNO_2$: 330.2603; found: 330.2607.

N,*N*-Dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-amine (2bf)

According to general procedure GP2, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155 mg, 0.5 mmol) and 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5f**) (101 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), dimethylamino boronic ester **2bf** (67 mg, 45%) as a colourless oil.

IR (neat): 2975, 1457, 1371, 1143, 1057, 700 cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.32–7.24 (m, 4 H, Ar-H), 7.11 (ps t, *J* = 7.2 Hz, 1 H, Ar-H), 5.62 (tdd, J_1 = 17.3 Hz, J_2 = 10.2 Hz, J_3 = 7.2 Hz, 1 H, 5-H), 5.03 (dd, J_1 = 17.1 Hz, J_2 = 2.2 Hz, 1 H, 6-H_{trans}), 4.95 (dd, J_1 = 10.2 Hz, J_2 = 2.2 Hz, 1 H, 6-H_{cis}), 2.57 (d, *J* = 7.2 Hz, 2 H, 4-H), 2.26–2.17 (m, 2 H, 1-H), 2.19 [s, 6 H, N-$(CH_3)_2$], 2.02–1.97 (m, 2 H, 2-H), 1.20 (s, 6 H, 2 × C-CH_3), 1.19 (s, 6 H, 2 × C-CH_3).

^{13}C NMR (101 MHz, CD_3OD): δ = 146.00 (Ar-C), 136.91 (5-C), 129.10 (2 C, Ar-C), 128.35 (2 C, Ar-C), 126.34 (6-C), 117.34 (Ar-C), 84.58 (2 C, 2 × B-O-C), 56.82 (1-C), 45.79 [2 C, N-$(CH_3)_2$], 40.46 (4-C), 32.26 (2-C), 25.36 (2 C, 2 × C-CH_3), 25.32 (2 C, 2 × C-CH_3); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 30.73.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{33}BNO_2$: 330.2603; found: 330.2604.

3-(4-Methoxyphenyl)-*N*,*N*-dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-amine (2bg)

According to general procedure GP2, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (153 mg, 0.5 mmol) and 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5g**) (140.5 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), dimethylamino boronic ester **2bg** (145 mg, 75%) as a yellow oil.

IR (neat): 2969, 1509, 1461, 1341, 1297, 1245, 1181, 1141, 1035, 852, 827 cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.26–7.10 (m, 7 H, Ar-H), 6.80 (d, *J* = 8.7 Hz, 2 H, Ar-H), 3.76 (s, 3 H, O-CH_3), 2.36–2.28 (m, 2 H, 1-H), 2.20 [s, 6 H, N-$(CH_3)_2$], 2.10 (ps t, *J* = 7.8 Hz, 2 H, 2-H), 1.15 (s, 6 H, 2 × C-CH_3), 1.14 (s, 6 H, 2 × C-CH_3).

^{13}C NMR (101 MHz, CD_3OD): δ = 159.08 (Ar-C), 147.75 (Ar-C), 139.18 (Ar-C), 131.32 (2 C, Ar-C), 130.28 (2 C, Ar-C), 128.82 (2 C, Ar-C), 126.54 (Ar-C), 114.25 (2 C, Ar-C), 84.80 (2 C, 2 × B-O-C), 58.82 (1-C), 55.60 (O-CH_3), 45.44 [2 C, N-$(CH_3)_2$], 35.85 (2-C), 24.89 (2 C, 2 × C-CH_3), 24.88 (2 C, 2 × C-CH_3); C attached to boron not observed.

^{11}B NMR (128 MHz, CD_3OD): δ = 32.02, 18.66, 15.54.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{35}BNO_3$: 396.2709; found: 396.2718.

3-(Dimethylamino)-1,1-diphenylpropan-1-ol (15bh)

According to general procedure GP3a, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (153 mg, 0.49 mmol) and 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**5h**) (122.5 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5), tertiary alcohol **15bh** (88 mg, 70%) as a white solid.

IR (neat): 2830, 2783, 1446, 1204, 1064, 1019, 963, 891, 841, 777, 751, 716 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (ps d, *J* = 8.0 Hz, 4 H, Ar-H), 7.32 (ps t, *J* = 7.4 Hz, 4 H, Ar-H), 7.20 (ps t, *J* = 7.2 Hz, 2 H, Ar-H), 2.42 (s, 4 H, 2-H + 1-H), 2.23 [s, 6 H, N-$(CH_3)_2$].

^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.07 (2 C, Ar-C), 128.01 (4 C, Ar-C), 126.31 (2 C, Ar-C), 125.84 (4 C, Ar-C), 79.17 (3-C), 56.32 (1-C), 45.10 [2 C, N-$(CH_3)_2$], 35.99 (2-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}NO$: 256.1696; found: 256.1697.

3-(Dimethylamino)-1-phenyl-1-(thiophen-2-yl)propan-1-ol (15bi)

According to general procedure GP3b, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155.7 mg, 0.5 mmol) and 4,4,5,5-tetramethyl-2-(thiophen-2-yl)-1,3,2-dioxaborolane (**5i**) (126.1 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5), tertiary alcohol **15bi** (63.5 mg, 49%) as a white solid.

IR (neat): 2779, 1178, 1068, 847, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 7.4 Hz, 2 H, Ar-H), 7.33 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.22 (t, *J* = 7.1 Hz, 1 H, Ar-H), 7.18 (d, *J* = 5.0 Hz, 1 H, 5-H), 6.92 (t, *J* = 3.6 Hz, 1 H, 6-H), 6.89 (d, *J* = 3.5 Hz, 1 H, 7-H), 2.52 (m, 1 H, 1-H), 2.47–2.30 (m, 3 H, 1-H + 2-H), 2.24 [s, 6 H, N-$(CH_3)_2$].

^{13}C NMR (101 MHz, $CDCl_3$): δ = 154.41 (4-C), 147.37 (Ar-C), 128.22 (2 C, Ar-C), 126.84 (Ar-C), 126.62 (6-C), 125.54 (2 C, Ar-C), 124.30 (5-C), 122.75 (7-C), 78.53 (3-C), 56.55 (1-C), 45.19 [2 C, N-$(CH_3)_2$], 38.10 (2-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}NOS$: 262.1260; found: 262.1267.

3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-phenylpropan-1-amine (16bj)

According to general procedure GP4, diisopropylamine (120 μL, 0.88 mmol), *n*-BuLi (550 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (137 mg, 0.44 mmol), 2-(4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5j**) (138.3 mg, 0.58 mmol), CsF (99.8 mg, 0.66 mmol) and H_2O (9 μL, 0.48 mmol) in anhydrous THF (8 mL) afforded, after purification by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5), protodeboronated compound **16bj** (85.2 mg, 71%) as a colourless oil.

IR (neat): 2942, 2765, 1489, 1092, 1014, 821, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.24 (m, 8 H, Ar-H), 7.15 (m, 1 H, Ar-H), 3.93 (t, *J* = 6.0 Hz, 1 H, 3-H), 2.27–2.20 (m, 4 H, 1-H + 2-H), 2.19 [s, 6 H, N-$(CH_3)_2$].

^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.52 (Ar-C), 144.96 (Ar-C), 132.94 (Ar-C), 130.36 (2 C, Ar-C), 129.63 (2 C, Ar-C), 129.51 (2 C, Ar-C), 128.73 (2 C, Ar-C), 127.47 (Ar-C), 59.06 (1-C), 49.87 (3-C), 45.43 [2 C, N-$(CH_3)_2$], 33.96 (2-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{21}ClN$: 274.1357; found: 274.1363.

1-(Dimethylamino)-3-phenylpentan-3-ol (15ba)

According to general procedure GP3a, diisopropylamine (140 μL, 1 mmol), *n*-BuLi (625 μL, 1 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155.7 mg, 0.5 mmol) and 2-ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5a**) (93.6 mg, 0.6 mmol) in anhydrous THF (6 mL) afforded, after purification by flash chromatography on silica gel (CH_2Cl_2/MeOH/Et_3N = 100:0.5:0.5), tertiary alcohol **15ba** (60.4 mg, 58%) as a white solid.

IR (neat): 2936, 2823, 2781, 1464, 1445, 1174, 1042, 1024, 773 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.39 (m, 2 H, Ar-H), 7.34–7.30 (m, 2 H, Ar-H), 7.20 (ps tt, J_1 = 8.4 Hz, J_2 = 0.9 Hz, 1 H, Ar-H), 2.28 (td, J_1 = 12.5 Hz, J_2 = 2.6 Hz, 1 H, 1-H), 2.19 (m, 1 H, 1-H), 2.18 [s, 6 H, N-$(CH_3)_2$], 2.08 (ddd, J_1 = 14.7 Hz, J_2 = 12.0 Hz, J_3 = 3.12 Hz, 1 H, 2-H), 1.84–1.74 (m, 3 H, CH_2-CH_3 + 2-H), 0.72 (t, *J* = 7.3 Hz, 3 H, CH_2-CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.04 (Ar-C), 128.01 (2 C, Ar-C), 126.06 (Ar-C), 125.86 (2 C, Ar-C), 78.21 (3-C), 56.23 (1-C), 45.15 [2 C, N-$(CH_3)_2$], 37.15 (2-C), 36.69 (CH_2-CH_3), 7.73 (CH_2-CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{22}NO$: 208.1696; found: 208.1702.

N,*N*-Dimethyl-3-phenylpentan-1-amine (16ba)

N,*N*-Dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (**2ba**) (63.5 mg, 0.2 mmol) was dissolved in dry THF (2 mL) and TBAF·3H_2O (95 mg, 0.3 mmol) was added at r.t. The reaction mixture was allowed to stir at reflux for 2 h, then H_2O (5 mL) was added. The mixture was partitioned between H_2O and CH_2Cl_2 and the aq phase was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude residue was purified by flash chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford **16ba** (28 mg, 73%) as a colourless oil.

IR (neat): 2929, 1453, 1042, 755, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (m, 2 H, Ar-H), 7.22–7.15 (m, 3 H, Ar-H), 2.47 (sept, *J* = 5.0 Hz, 1 H, 3-H), 2.23 (m, 1 H, 1-H), 2.21 [s, 6 H, N-$(CH_3)_2$], 2.09 (td, J_1 = 10.3 Hz, J_2 = 5.1 Hz, 1 H, 1-H), 1.87 (m, 1 H, 2-H), 1.80–1.65 (m, 2 H, 2-H + 4-H), 1.59 (m, 1 H, 4-H), 0.78 (t, *J* = 7.4 Hz, 3 H, 5-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.41 (Ar-C), 128.42 (2 C, Ar-C), 127.80 (2 C, Ar-C), 126.13 (Ar-C), 58.10 (1-C), 45.97 (3-C), 45.48 [2 C, N-$(CH_3)_2$], 34.25 (2-C), 30.03 (4-C), 12.21 (5-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{22}N$: 192.1747; found: 192.1755.

3-Ethyl-*N*,*N*-dimethyl-3-phenylpent-4-en-1-amine (17ba)

Following a modified literature procedure,[5d] *n*-BuLi (1.5 mmol, 940 μL) was added dropwise at r.t. to neat tetravinyltin (0.75 mmol, 140 μL) under an N_2 atm. The reaction mixture was stirred for 30 min; the white solid formed was allowed to settle and the colourless solution was removed by syringe under N_2. The solid (vinyl lithium) was washed with dry pentane (3 × 1 mL), every time adding and removing the solvent by syringe under N_2, and then dissolved in dry THF (1 mL). *N*,*N*-Dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (**2ba**) (0.3 mmol, 95.2 mg) was dissolved in dry THF (3 mL) and the vinyl lithium solution was added dropwise at –78 °C. The reaction mixture was stirred for 30 min at –78 °C, warmed to –42 °C and then stirred at that temperature for an additional 20 min. After that time, ^{11}B NMR analysis of the crude reaction mixture showed complete boronate complex formation. The solution was cooled to –78 °C and a solution of I_2 (1.5 mmol, 380.7 mg) in dry MeOH (2.4 mL) was added dropwise. After stirring for 15 min at –78 °C, a suspension of NaOMe (3 mmol, 126.1 mg) in dry MeOH (1.2 mL) was added. The reaction mixture was allowed to warm to r.t. and stirred for 1 h; then an aq solution of $Na_2S_2O_3$ (10 mL) was added. The layers were separated, the organic layer was washed with brine (2 × 5 mL) and the combined aq layers were extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford alkene **17ba** (33.7 mg, 52%) as a colourless oil.

IR (neat): 2937, 2815, 2763, 1462, 1041, 912, 759, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.28 (m, 4 H, Ar-H), 7.18 (m, 1 H, Ar-H), 5.91 (dd, J_1 = 17.7 Hz, J_2 = 11.0 Hz, 1 H, 4′-H), 5.20 (dd, J_1 = 10.9 Hz, J_2 = 1.0 Hz, 1 H, 5′-H_{cis}), 5.11 (dd, J_1 = 17.7 Hz, J_2 = 1.0 Hz, 1 H, 5′-H_{trans}), 2.19 [s, 6 H, N-$(CH_3)_2$], 2.10 (m, 2 H, 1-H), 1.97 (m, 2 H, 2-H), 1.80 (m, 2 H, 4-H), 0.72 (t, *J* = 7.4 Hz, 3 H, CH_2-CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.67 (Ar-C), 145.19 (4′-C), 128.15 (2 C, Ar-C), 127.37 (2 C, Ar-C), 125.98 (Ar-C), 113.15 (5′-C), 55.23 (1-C), 47.03 (3-C), 45.67 [2 C, N-$(CH_3)_2$], 34.48 (2-C), 30.25 (4-C), 8.56 (5-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{24}N$: 218.1903; found: 2218.1910.

3-Ethyl-2,2-difluoro-1,1-dimethyl-3-phenyl-1λ^4,2λ^4-azaborolidine (18ba)

Following a literature reported procedure,[33] to a rapidly stirred solution of *N*,*N*-dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (**2ba**) (95.2 mg, 0.3 mmol) in MeOH (3 mL) was added dropwise a solution of KHF_2 (105.4 mg, 1.35 mmol) in H_2O (700 μL) at r.t. The resulting mixture was stirred for 30 min and then concentrated under reduced pressure. The residue was redissolved in a mixture of MeOH/H_2O (1:1 v/v, 6 mL) and evaporated to dryness. This concentration–dissolution cycle was repeated 6 times,

after which ^{1}H NMR analysis of an aliquot of the reaction mixture showed no presence of pinacol (δ = 1.14) in acetonitrile-d_3. The solid residue was then triturated with dry acetone (5 mL); the liquid phase was carefully decanted and the residual inorganic salts were additionally washed with acetone (3 × 1 mL). The combined washings were collected and concentrated in vacuo to give a 2:1 mixture of the desired tetrafluoroborate salt and azaborolidine **18ba** (82% overall yield). A portion of the mixture (45 mg) was dissolved in dry MeCN (3 mL) and the solution was heated at reflux for 5 h. The reaction mixture was then filtered through a pad of SiO_2 and washed with CH_2Cl_2 to give azaborolidine **18ba** (26.4 mg, 68%) as a white solid.

IR (neat): 2959, 2927, 1467, 1053, 950, 755, 724, 701, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 4 H, Ar-H), 7.12 (m, 1 H, Ar-H), 3.00 (m, 1 H, 1-H), 2.90 (m, 1 H, 1-H), 2.61 (s, 3 H, N-CH_3), 2.39 (s, 3 H, N-CH_3), 2.30 (quin, J = 7.6 Hz, 1 H, 2-H), 1.89 (m, 2 H, 4-H), 1.59 (quin, J = 6.9 Hz, 1 H, 2-H), 0.57 (t, J = 7.2 Hz, 3 H, 5-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.68 (Ar-C), 137.72 (4 C, Ar-C), 124.39 (Ar-C), 60.41 (1-C), 46.76 (d, J = 9.1 Hz, N-CH_3), 46.55 (d, J = 10.1 Hz, N-CH_3), 30.94 (4-C), 29.56 (2-C), 9.05 (5-C); C attached to boron not observed.

^{11}B NMR (96 MHz, $CDCl_3$): δ = 7.36 (t, J = 67.4 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –152.44, –157.32.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{13}H_{20}BF_2NNa$: 262.1551; found: 262.1551.

1-Methyl-2-phenylpyrrolidine (24)

Following a procedure reported by Turner,[34] commercially available 2-phenylpyrrolidine (3.4 mmol, 500 mg) was suspended in H_2O (4 mL) in a microwave test tube and formic acid (3.7 mmol, 141 µL) and formaldehyde (35% solution in H_2O, 3.7 mmol, 320 µL) were added at r.t. The tube was sealed and was heated using microwave irradiation at 150 °C for 5 min. The reaction mixture was allowed to cool to r.t., then it was basified to pH 14 using an aq solution of NaOH (2.0 M) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by Kugelrohr distillation to afford the pure tertiary amine (396 mg, 72%) as a colourless liquid.

IR (neat): 2968, 2775, 1454, 1044, 754, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.29 (m, 4 H, Ar-H), 7.23 (m, 1 H, Ar-H), 3.24 (td, J_1 = 9.4 Hz, J_2 = 1.8 Hz, 1 H, 4-H), 3.03 (t, J = 8.8 Hz, 1 H, 1-H), 2.28 (m, 1 H, 4-H), 2.17 (m, 1 H, 2-H), 2.17 (s, 3 H, CH_3), 1.95 (m, 1 H, 3-H), 1.78 (m, 2 H, 2-H + 3-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.40 (Ar-C), 128.47 (2 C, Ar-C), 127.62 (2 C, Ar-C), 127.12 (Ar-C), 71.79 (1-C), 57.22 (4-C), 40.62 (CH_3), 35.29 (2-C), 22.63 (3-C).

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{16}N$: 162.127726; found: 162.127190.

1,1-Dimethyl-2-phenylpyrrolidin-1-ium Trifluoromethanesulfonate (19a)

Following a modified version of a procedure by Couty,[15b] pyrrolidine **24** (358 mg, 2.22 mmol) was dissolved in dry Et_2O (19 mL). After cooling to 0 °C, methyl trifluoromethanesulfonate (500 µL, 4.45 mmol) was added. The mixture was stirred for 1 h at r.t.; then the volatiles were removed under vacuum to afford pyrrolidinium triflate **19a** (721 g, >99%) as a purple oil.

IR (neat): 2972, 1475, 1256, 1152, 754, 706, 635 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, J = 6.6 Hz, 2 H, Ar-H), 7.45 (t, J = 8.6 Hz, 3 H, Ar-H), 4.87 (dd, J_1 = 11.5 Hz, J_2 = 7.8 Hz, 1 H, 1-H), 3.82 (t, J = 7.7 Hz, 2 H, 4-H), 3.07 (s, 3 H, CH_3), 2.69 (s, 3 H, CH_3), 2.60 (m, 1 H, 2-H), 2.49 (m, 1 H, 2-H), 2.31 (m, 2 H, 3-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.36 (Ar-C), 130.85 (2 C, Ar-C), 129.47 (2 C, Ar-C), 128.41 (Ar-C), 120.72 (q, J = 322.2 Hz, CF_3), 78.69 (1-C), 65.84 (4-C), 50.59 (CH_3), 45.18 (CH_3), 26.13 (2-C), 19.25 (3-C).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –78.37.

HRMS (ESI): m/z [M – SO_3CF_3]$^+$ calcd for $C_{12}H_{18}N$: 176.1434; found: 176.1440.

(*Z*)-2-Methyl-1,2,3,4,5,10a-hexahydrobenzo[*c*]azocine (20a)

To a solution of diisopropylamine (140 µL, 1 mmol) in anhydrous THF (500 µL) was added *n*-BuLi (625 µL, 1 mmol) at –78 °C. After stirring for 20 min at –78 °C and 10 min at r.t., the solution was added dropwise to a mixture of pyrrolidinium salt **19a** (162.7 mg, 0.5 mmol) and 2-ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5a**) (93.6 mg, 0.6 mmol) in dry THF (12 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm to r.t. The solvent was removed in vacuo and the crude residue was taken up with H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to afford the crude product, which was purified by chromatography on silica gel (EtOAc/Et_3N = 100:0.5) to afford the pure azocine **20a** (42.2 mg, 48%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.05 (d, J = 9.5 Hz, 1 H, 6-H), 5.94 (dd, J_1 = 9.4 Hz, J_2 = 5.3 Hz, 1 H, 8-H), 5.77–5.68 (m, 3 H, 4-H, 7-H, 9-H), 3.51 (br s, 1 H, 10-H), 2.70–2.46 (m, 4 H, 2 × 1-H, 3-H, 11-H), 2.42 (s, 3 H, CH_3), 2.21 (m, 1 H, 3-H), 2.04 (m, 1 H, 11-H), 1.87 (m, 1 H, 2-H), 1.47 (m, 1 H, 2-H).

(*Z*)-2-Methyl-1,2,3,4,5,10a-hexahydrobenzo[*c*]azocine (**20a**) was found to rapidly rearrange at r.t. to give 2-methyl-1,2,3,4,5,6-hexahydrobenzo[*c*]azocine (**21a**), which could be fully characterised.

2-Methyl-1,2,3,4,5,6-hexahydrobenzo[*c*]azocine (21a)

IR (neat): 2922, 1448, 1044, 753, 613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (m, 4 H, Ar-H), 3.78 (s, 2 H, 1-H), 2.85 (t, J = 5.8 Hz, 2 H, 5-H), 2.46 (t, J = 4.8 Hz, 2 H, 2-H), 2.39 (s, 3 H, CH_3), 1.71 (quin, J = 5.8 Hz, 2 H, 4-H), 1.61 (quin, J = 5.6 Hz, 2 H, 3-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.14 (Ar-C), 134.45 (Ar-C), 131.00 (Ar-C), 129.57 (Ar-C), 127.84 (Ar-C), 125.95 (Ar-C), 55.93 (1-C), 54.08 (2-C), 43.61 (CH_3), 33.11 (5-C), 30.97 (4-C), 23.70 (3-C).

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{18}N$: 176.143376; found: 176.143020.

2-[1,2-Diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropyl]-*N*,*N*-dimethylethan-1-amine (22)

According to general procedure GP2, diisopropylamine (140 µL, 1.0 mmol), *n*-BuLi (625 µL, 1.0 mmol), 1,1-dimethyl-2-phenylazetidin-1-ium trifluoromethanesulfonate (**3b**) (155 mg, 0.5 mmol) and 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**5k**) (138 mg, 0.6 mmol) in anhydrous THF (12 mL) afforded, after purification on silica gel (EtOAc/Et_3N = 100:0.5), cyclopropane **22** (47 mg, 24%) as a colourless oil.

IR (neat): 2976, 1599, 1448, 1372, 1144, 849, 766, 697 cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.06–6.78 (m, 10 H, Ar-H), 2.54 (ps td, J_1 = 12.4 Hz, J_2 = 4.4 Hz, 1 H, 1-H), 2.32 (ps td, J_1 = 11.5 Hz, J_2 = 4.4 Hz, 1 H, 1-H), 2.17 [s, 6 H, N-$(CH_3)_2$], 2.15 (m, 1 H, 2-H), 1.99 (br s, 1 H, 5-H), 1.87 (ps td, J_1 = 12.3 Hz, J_2 = 4.3 Hz, 1 H, 2-H), 1.36 (d, J = 4.8 Hz, 1 H, 5-H), 1.26 (s, 6 H, 2 × C-CH_3), 1.22 (s, 6 H, 2 × C-CH_3).

^{13}C NMR (101 MHz, CD_3OD): δ = 141.43 (Ar-C), 141.31 (Ar-C), 131.42 (2 C, Ar-C), 130.56 (2 C, Ar-C), 128.60 (2 C, Ar-C), 128.05 (2 C, Ar-C), 126.83 (Ar-C), 125.81 (Ar-C), 84.96 (2 C, 2 × B-O-C), 58.67 (1-C), 45.27 [2 C, N-$(CH_3)_2$], 37.60 (3-C), 36.77 (2-C), 25.34 (2 C, 2 × C-CH_3), 25.20 (2 C, 2 × C-CH_3), 20.41 (5-C); C attached to boron not observed.

^{11}B NMR (96 MHz, $CDCl_3$): δ = 30.66, 21.12.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{25}H_{35}BNO_2$: 392.2760; found: 392.2768.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562447.

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