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Borylation directed borylation of N-alkyl anilines using iodine activated pyrazaboles

A doubly electrophilic pyrazabole derivative (pyrazabole $= [\text{H}_2\text{B}(\mu-\text{C}_3\text{N}_2\text{H}_3)]_2$), activated with I$_2$, was found to effect the ortho-borylation of N-alkyl-anilines in the presence of Et$_3$N. This methodology represents a metal free transiently directed C-H borylation approach to form N-alkyl-2-BPin-aniline derivatives. In addition, this work includes mechanistic studies of doubly electrophilic pyrazabole systems that led us to use the aforementioned.
Borylation directed borylation of N-alkyl anilines using iodine activated pyrazaboles†


Doubly electrophilic pyrazabole derivatives (pyrazabole = [H2B(µ-πN3H3)]2) combined with one equiv. of base effect the ortho-borylation of N-alkyl anilines. Initial studies found that the bis(trifluoromethane) sulfonimide ([NTf2]2) pyrazabole derivative, [H(NTf2)B(µ-πN3H3)]2, is highly effective for ortho-borylation, with this process proceeding through N–H borylation and then ortho C–H borylation. The activation of pyrazabole by I2 was developed as a cheaper and simpler alternative to using HNTf2 as the activator. The addition of I2 forms mono or ditopic pyrazabole electrophiles dependent on stoichiometry. The ditopic electrophile [H[I]B(µ-πN3H3)]2 was also effective for the ortho-borylation of N-alkyl-anilines, with the primary C–H borylation products readily transformed into pinacol boronate esters (BPin) derivatives. Comparison of borylation reactions using the di-NTf2– and the diiodopyrazabole congeners revealed that more forcing conditions are required with the latter. Furthermore, the presence of iodide leads to competitive formation of side products, including [H[B(µ-πN3H3)]2]BH+†, which are not active for C–H borylation. Using [HI]B(µ-πN3H3)2 and 0.2 equiv. of [Et3NH][NTf2] combines the higher yields of the NTf2 system with the ease of handling and lower cost of the iodide system generating an attractive process applicable to a range of N-alkyl-anilines. This methodology represents a metal free and transiently directed C–H borylation approach to form N-alkyl-2-BPin-aniline derivatives.

Introduction

C–H borylation is a powerful methodology for generating synthetically ubiquitous organoboranes in an efficient manner.1 The use of directing groups (DGs) in C–H borylation reactions enables access to organoboranes with a distinct regiochemistry to that formed from non-directed transformations.2 One specific example of this is in the synthesis of ortho-borylated anilines, which are useful for accessing ortho substituted anilines prevalent in pharmaceuticals, agrochemicals and organic materials.3 Directing groups generally are required for this ortho C–H borylation as in the absence of DGs the electrophilic C–H borylation of anilines leads to para-functionalisation,4 while iridium and cobalt catalysed C–H borylations generally lead to mixtures of meta- and para-borylated products.5 To date, the ortho C–H borylation of anilines has been dominated by approaches requiring the separate installation and removal of a directing group (resulting in “multiple pot” processes).6,7 For example, the electrophilic ortho C–H borylation of aniline derivatives using N-pivaloyl DGs and BBr3 (Fig. 1a, top)8 requires the installation and removal of pivaloyl in separate processes, the latter under forcing conditions.8 The use of transient DGs is preferable as these are installed, direct the C–H borylation and then are removed all in one pot.9 In notable work, the ortho-borylation of anilines using transient DGs has been reported using iridium catalysts and B2Eg2 (Eg = ethylene glycolato).10 This proceeds via in situ formation of an ArylN(H) BEg species (Fig. 1b, inset) that then directs the ortho C–H borylation. The N-BEg unit is then readily cleaved during work-up. While this methodology is highly effective for ArylNH2 species, much lower yields (<30%) are obtained with N-alkyl-anilines.11,12 Given the prevalence of ortho-functionalised N-alkyl-anilines in pharmaceuticals (e.g. Flutemetamol, Entrectinib and Agratroban), the development of a higher yielding, transient DG approach for the ortho-borylation of N-alkyl-anilines is desirable, particularly if the process is precious metal-free.13

Recently, we reported the borylation directed borylation (BDB) of indoles using pyrazabole electrophile A (Fig. 1c) as a method to install boron units at the C7 position.14,15 In this process reduction of indole to indoline occurs first, with the spectroscopic data indicating that this led to an N-borylated indoline intermediate (e.g. B). The N–B bond and the pyrazabole structure in compound B positions the second boron centre appropriately to borylate the proximal sp2 C–H leading to C, a C7

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The reactive electrophile N-substrate, combinations that achieved the process, with transient DGs underexplored in electrophilic C-borylation. Therefore, pyrazabole is acting as a transient DG in this BDB process, with transient DGs underexplored in electrophilic C-H borylation. Our initial BDB study utilised stoichiometric amounts of bistriflimidic acid ([2]NTf2) to form the reactive electrophile A. However, [2]NTf2 is relatively expensive,12 and it, and NTf2-analogous pyrazaboles (e.g. A), have to be handled within a glovebox. Therefore, extending the BDB of N-alkyl-aniline derivatives beyond indoline while using an inexpensive and more readily handled activator would be attractive. Herein we report our studies addressing this challenge. This led to the development of iodine as a cheap and easy to handle activator for pyrazaboles that forms ditopic electrophiles that are effective in the transient DG mediated ortho-borylation of N-alkyl-anilines.

Results and discussion

Our first focus was identifying electrophilic pyrazabole – base combinations that achieved the ortho-borylation of our model substrate, N-Me-aniline. Initially, the previously reported 1 (Scheme 1) was added to N-Me-aniline in the presence of 2,6-di-tert-butyl-4-methylpyridine (DBP) as base. At room temperature this led to slow BDB, but on heating to $\geq 70^\circ C$ the BDB product [2]NTf2 was formed as the major product within 18 h. [2]NTf2 was fully characterised, which revealed protonation of the aniline nitrogen occurs during this BDB. A modified (shorter reaction time)14 N-B cleavage/pinacol installation process then led to formation of 3a.

DBP is an expensive Brønsted base that was used to simplify initial studies as it does not coordinate to boron electrophiles. In contrast, other Lewis bases (e.g. MeCN) can displace NTf2 anions from 1, and base coordination to boron could retard the BDB reaction.14 Given the aniline substrate also functions as a Brønsted base during BDB (as indicated by the formation of [2]NTf2) only one equivalent of exogenous base is required. Therefore, one equivalent of the inexpensive bases Et3N and Hüning base were trialled in place of DBP in the BDB of N-Me-aniline using 1. On heating both of these reactions led to the formation of [2]NTf2 and [baseH][NTf2] as a by-product. Pinacol installation/work-up enabled 3a to be isolated in 62 and 65% yield using Et3N and Hüning base, respectively. Thus cheaper (than DBP) bases can be used in the BDB of N-alkyl-anilines. Our attention turned next to replacing HNTf2 with a simpler to handle and cheaper activator.

Based on the established reactivity of L→BH3 with iodine, which forms reactive boron electrophiles of general formula L→BH2I,18 diido-pyrazabole was targeted as an alternative to 1. While dibromo- and dichloro-pyrazaboles are known,8 our knowledge no B-I containing pyrazaboles have been reported to date. The latter are desirable as iodine is inexpensive, easy to handle and is less coordinating to boron than the lighter halides. Furthermore, L→BH2I species have been demonstrated to react with nucleophiles to form C–B bonds in a related manner to L→BH3([2]NTf2) species.19 Therefore, one equivalent of iodine, pyrazabole and Et3N were combined and found to be viable for the BDB of N-Me-aniline (Scheme 2), albeit requiring heating to 100 °C for significant BDB to occur. In contrast, attempts using dibromo-pyrazabole under identical conditions led to no BDB reaction (Scheme 2), indicating that the less coordinating nature of iodide towards boron is vital for this transformation. Despite extensive optimisation studies using iodine activated pyrazabole (see Table S2†) the isolated yield of 3a remained <50% (based on N-Me-aniline) – with Et3N providing the best outcome from the bases explored. Notable points from this optimisation study included: use of 1 equiv. of Et3N retarding the BDB reaction, while using two equiv. of N-Me-aniline and no other base gave only trace amounts of 3a. Given the lower yields of 3a using iodine activated pyrazabole...
relative to using 1, both systems were analyzed further to determine the origin(s) of this disparity.

Mechanistic studies

On analysing the reaction of 1 and one equiv. base (base = DBP or Et$_3$N) with N-Me-aniline by in situ NMR spectroscopy an intermediate was observed. This intermediate, termed 4, could be obtained cleanly by the combination of 1 and the independently synthesised di(N-Me-anilide)-pyrazabole 5 (Scheme 3, see ESI Section 2 and Fig. S14†). Compound 4 displayed two pyrazabole C–H resonances in the $^1$H NMR spectrum in 2:1 ratio indicating a symmetrically substituted pyrazabole. Further insight into the structure of 4 came from $^{19}$F NMR spectroscopy, which revealed NTf$_2$ is not coordinated to boron ($\delta_{	ext{19F}}$ = −78.7, whereas for B-NTf$_2$ systems $\delta_{	ext{19F}}$ = −69).$^{22}$ and DOSY NMR studies (see ESI, Section 5.3†) which indicated 4 is dimeric. The dimeric structure for 4 presumably is related to the previously reported oxo-bridged dimer D (Scheme 3),$^{22}$ with an analogous structure fully consistent with the NMR data for 4 (as a single isomer with a cis arrangement of the aniline-N substituents). Compound 4 converted into the BDB product [2]NTf$_2$ slowly at ambient temperature, but more rapidly and in high conversion on heating. While 4 could not be isolated as single crystals suitable for diffraction studies the structure of the dicaticonic portion of 4 (termed [4]$^{2+}$) was calculated at the MN15/6-311G(d,p)/PCM (PhCl, PCM = polarizable continuum model) level (inset Scheme 3, note all calculations are performed at this level herein, with the LANL2DZ basis set used for iodide). While the B–N distances in the calculated structure (1.615–1.618 Å) are comparable to related borocations,$^{23}$ there is evidence for significant distortion in [4]$^{2+}$ due to steric interactions between the pyrazole rings and the N-Me and N-Ph substituents. For example, the Ph–C–N–C$_{Me}$ angle is small (102.7° in [4]$^{2+}$) while the B$_2$N$_4$ core is twisted (in the B$_2$N$_4$ core of D the four nitrogens are co-planar, however in [4]$^{2+}$ they deviate by up to 0.11 Å above and below the plane made by the four nitrogens). These distortions will destabilise dimeric [4]$^{2+}$ presumably enabling dissociation into a monomeric form that is required to effect ortho C–H borylation.

Moving to the iodo-pyrazaboles, the reaction of pyrazabole and iodine was investigated first as iodo-pyrazaboles have not been reported previously to our knowledge. The addition of 0.5 equiv. of I$_2$ to pyrazabole led to the rapid formation of the mono-iodo pyrazabole, 6 (Scheme 4) at room temperature (by in situ NMR spectroscopy, Fig. S44†). Addition of a further 0.5 equiv. of iodine led to the full conversion of 6 into the diiodo pyrazabole, 7. Compound 7 is formed as a ca. 1:1 mixture of isomers as indicated by two doublets in the $^{11}$B NMR spectrum along with two sets of 2:1 relative integral pyrazole resonances in the $^1$H NMR spectrum, which is consistent with two symmetrically substituted pyrazaboles. These isomers are assigned as the cis and trans isomers of 7 based on previous reports from the groups of Trofimenko and Nöh on cis and trans isomers being formed for the lighter dihalo pyrazaboles.$^{24,25}$ Calculations also indicated that the cis and trans isomers of 7 are close in energy (ca. 1 kcal mol$^{-1}$ calculated free energy difference), consistent with the two species observed in solution being the cis and trans isomers of 7. The addition of one equiv. of I$_2$ in one portion to pyrazabole also led to the formation of 7 and it was isolated in 75% yield. The cis isomer formed single crystals suitable for X-ray diffraction studies. The solid-state structure of the cis isomer of 7 has a B$_2$N$_4$ 6-membered core in a flattened boat conformation with the iodide substituents located in the flagpole positions. In 7 the B···B distance of 3.031(8) Å is in the expected region and is comparable to a related dihalogenated pyrazabole [H(Br)B($\mu$-C$_2$N$_2$H$_4$Cl)$_2$] (3.05 Å).$^{25}$ The B–I bond distances of 2.290(6) and 2.302(6) Å are at the lower end of B–I bond lengths reported for
L → BH$_3$I compounds (L = N-heterocyclic carbenes or PR$_3$).\textsuperscript{28} Notably, combining equimolar 7 and pyrazabole in chlorobenzene led to formation of the mono-iodo pyrazabole 6 at ambient temperature (by \textit{in situ} NMR spectroscopy - Fig. S48†), indicating that intermolecular H/I exchange occurs in iodo-pyrazaboles. Finally, it should be noted that 7 has appreciable thermal stability: heating 7 at 100 °C in PhCl for 3 days led to minimal decomposition (<5% by multinuclear NMR spectroscopy), with the only observable new $^{11}$B NMR resonance consistent with formation of an L-B$_2$I$_3$ compound (based on the $\delta_{11B}$ = −34.6, see Fig. S46 and S47†).

With an understanding of the products formed from combining iodine and pyrazabole in hand the reactivity of 7 towards Et$_3$N was explored, Et$_3$N was selected as it gave the best outcome in our initial optimisation study (see Table S2†). The addition of one equivalent of Et$_3$N to 7 led to formation of the mono-cation 8 (Scheme 5). The identity of 8 was confirmed by single crystal X-ray diffraction analysis (inset, Scheme 5). The solid-state structure of 8 also has a flattened boat conformation for the B$_2$N$_4$ core with the iodide and Et$_3$N moieties being \textit{cis} in the flagpole positions. The steric demand of Et$_3$N in 8 causes a distortion in the geometry with an increase of the Y-B-Centroid angles (Y = I or N$_{Et_3}$; centroid = calculated centroid of the B$_2$N$_4$ ring) observed on comparing 7 (I-B-centroid = 113.3(3)$^\circ$ and 112.6(3)$^\circ$) and 8 (I-B-centroid = 118.6(12)$^\circ$; Et$_3$N–B-centroid = 122.1(14)$^\circ$). Compound 8 also has a longer B–I bond of 2.36(2) Å vs. the B–I bonds in 7 (2.290(6) and 2.302(6) Å), consistent with greater steric crowding in 8 relative to 7. However, the B–N$_{Et_3}$ bond length in 8 (1.62(2) Å) is in the range of previously reported Et$_3$N–BR$_3$ adducts (1.60–1.69 Å).\textsuperscript{27}

In contrast to the di-NTf$_2$ analogue 1 (where both NTf$_2$ anions are displaced by Lewis bases to form dicaticonic products),\textsuperscript{14} the addition of further Et$_3$N to 8 did not displace the second iodide (Fig. S49†). This is consistent with the more coordinating nature of iodide relative to [NTf$_2$]$^-$\textsuperscript{−}. However, the addition of both N-Me aniline and Et$_3$N (in either order of addition) to 7 led to substitution of both iodides to form the dianilide product 5 as the major boron containing species. This indicates that Et$_3$N coordination to boron in 8 does not irreversibly block N-Me-aniline from reacting with boron. Next, diido-pyrazabole 7 and dianilide-pyrazabole 5 were combined to determine if the iodide analogue of the dimer 4 forms. This led to slow and complex reactivity at room temperature with no iodide analogue of 4 observed. In contrast, the di-NTf$_2$ pyrazabole 1 and compound 5 are completely consumed within minutes of mixing to form 4 cleanly. In the \textit{in situ} monitored BDB reactions using diido-pyrazabole 7, 5 is the only major new pyrazabole product observed, again there is no evidence for the iodide analogue of 4 (by NMR spectroscopy). From the \textit{in situ} monitoring experiments \textsuperscript{[2]**} it forms as one of the major products on heating, but this occurs along with the formation of two other major products. The first of these was assigned as (MePh)N$_2$BH (\(\delta_{11B} = 29.0, ^1J_{B-I} = 126\) Hz) by comparison to the previous report.\textsuperscript{28} The second was identified as compound 9 (Scheme 6), which precipitated from the BDB reactions mixtures (along with some [Et$_3$NH][I] precipitating). Compound 9 was independently synthesised and crystallised with X-ray diffraction studies confirming its formulation (inset Scheme 6). These results combined indicate that heating diido-pyrazabole 7 in the presence of Et$_3$N/N-Me-aniline leads to competitive (to BDB) break-up of the pyrazabole core and the formation of species that are non-productive for BDB (e.g.}

**Scheme 4** Left, formation of mono- (6) and diido-pyrazabole (7). Inset right, the solid state structure of \textit{cis}-7, ellipsoids at 50% probability. Blue = nitrogen, pink = boron, purple = iodine, grey = carbon, white = hydrogen.

**Scheme 5** Top, the reaction of 7 towards Et$_3$N. Inset bottom, the solid-state structure of the cationic portion of 8, ellipsoids at 30% probability. Blue = nitrogen, pink = boron, purple = iodine, grey = carbon, white = hydrogen.
To combine the best of the NTf₂ (higher yields) and iodide (which are much cleaner by lower conversions to under these conditions. This is presumably the origin of the anion plays a crucial role in the cleavage of the pyrazabole core <5% formation of other pyrazole containing products by NMR compared to conversions to pyrazabole, Scheme 7). This is consistent with the addition of NTf₂ exchange initially was explored computationally which Optimisation of the BDB of N-alkyl-anilines using iodo-pyrazaboles

To combine the best of the NTf₂ (higher yields) and iodide (cheaper/easier to handle) systems we considered an in situ anion exchange process that could convert iodo-pyrazaboles into more reactive NTf₂-pyrazaboles. The feasibility of iodide/NTf₂ exchange initially was explored computationally which indicated that the displacement of iodide from pyrazabole by triflimide is endergonic (by +7.5 kcal mol⁻¹ for the mono-pyrazabole, Scheme 7). This is consistent with the addition of 5 equiv. of [Et₃NH][NTf₂] to 7 resulting in no observable anion exchange (by NMR spectroscopy). Nevertheless, as the BDB process has a significantly lower overall barrier for the NTf₂ system relative to the iodide analogue (1 performs BDB at room temperature, albeit slowly, while 7 requires heating to ≥70 °C for BDB) anion exchange may still lead to an enhanced BDB outcome. Note, a related anion exchange process facilitating an electrophilic C–H borylation with B-trypticenes has been reported recently using stoichiometric Na[B(C₆F₅)₄].

An initial experiment to assess for any anion exchange derived enhancement in yield used a 0.9 : 0.1 mix of 7 : 1 in the BDB of N-Me-aniline with one equiv. of Et₃N as base. Notably, this led to comparable yields for the formation of 3a (Scheme 8) to that using 1 equiv. of 1. A significant yield enhancement was also observed using a 0.9 : 0.1 mix of 7 and 1 in the BDB of tetrahydroquinoline to form 3b after pinacol installation/work-up (Scheme 8). The significant yield enhancement observed using 0.9 : 0.1 mixtures of 7 and 1 indicates it is not just due to compounds 7 and 1 reacting separately in the BDB process. We tentatively attribute this enhancement to a degree of metathesis of an iodo-pyrazabole with [Et₃NH][NTf₂] (formed during BDB) leading to a more reactive NTf₂-pyrazabole electrophile. Note, during these reactions in chlorobenzene solid precipitates, which on analysis was found to be [Et₃NH][I]. Thus the lower solubility of [Et₃NH][I] relative to the NTf₂ salt under these conditions may be assisting anion exchange. The precipitation of [Et₃NH][I] also will reduce the iodide concentration in solution, potentially slowing the formation of decomposition species. This is consistent with the observation that compound 9 is not observed during the reactions using 0.9 : 0.1 of 7 and 1.

Overall, these observations suggested that combining 7 with sub-stoichiometric [cation][NTf₂] could result in a similar enhancement in yield. This hypothesis was confirmed by the use of one equiv. of 7 and 0.2 equiv. of [Et₃NH][NTf₂] in the BDB process leading to a 60% yield of 3a and a 78% yield of 3b (comparable to outcomes from conditions B and C in Scheme 8). This is a notable improvement over the yields reported using iridium catalysed transient DG approaches to form ortho-BPin-
N-alkyl-anilines. Note, the use of 0.2 equiv. of LiNTf₂ with 7 gave lower yields relative to using [Et₃NH][NTf₂] under otherwise identical conditions, therefore the latter salt is used hereon. With conditions identified that avoided expensive bases and stoichiometric amounts of anhydrous HNTf₂ ([Et₃NH][NTf₂] can be stored on the bench and is readily accessible from commercial LiNTf₂ and [Et₃NH][Cl]) a substrate scope exploration was performed (Scheme 9). The scoping study revealed that in addition to 3a and 3b the conditions were amenable to larger alkyl substituents on nitrogen, with the N-Pr derivative, 3c, isolated in 52% yield. Alongside 3b, the seven (3d) and five (3e) membered analogues were also amenable to BDB, indicating the change in positioning of the N-bound pyrazabole unit enforced by the different ring sizes does not significantly influence this BDB reaction. Notably, neither 3d nor any other C9 borylated benzo[b]azepines have been reported previously to our knowledge. This is despite the significant importance of substituted benzo[b]azepines in pharmaceuticals and agro-chemicals, including C9-substituted derivatives (e.g. zilpaterol). In contrast, the ortho-methyl derivative, 2,N-Me₂-aniline, was not amenable to this process. We attribute this to the ortho methyl forcing an orientation that disrupts conjugation between the aniline phenyl ring and the nitrogen lone pair. This was supported by calculations on analogues of 5 containing 2,N-Me₂-aniline (twisted away from co-planarity by 44°) and indoline and tetrahydroquinoline (see Table S4†) — with the latter two compounds and 5 having close to co-planar N and phenyl units that maximise conjugation and thus increase the nucleophilicity of the 7 system (thereby favouring S_NAr).

Moving to other substituents, as this is an electrophilic borylation using borenium cation equivalents and forcing conditions, functional group tolerance will be limited (as indicated by the p-MeO derivative not being amenable to this process), but halides and NR₂ groups are tolerated (vide infra). Furthermore, while the ortho methyl aniline derivative was not amenable to substituents at the meta (3f and 3i) and para (3g and 3h) positions of N-Me-aniline were tolerated. This BDB process was found to be sensitive to aren electronics, with electron withdrawing groups significantly retarding BDB, requiring longer reaction times for 3h and 3i. Consistent with this observation, an N-Me-aniline substrate substituted with an electron donating group, specifically a para-piperidine unit, performed much better in this BDB process, with 3j isolated in 62% yield. Ortho-substituted anilines containing a para-piperidine unit are important as these motifs are found in approved and developmental bioactives, e.g. Brigatinib and ASP3026. Next, we attempted to extend this BDB process to aniline and diphenylamine. However, in both cases no ortho borylated products (3k and 3l) were isolated. While diphenylamine is presumably insufficiently nucleophilic for this BDB reaction (consistent with an S_NAr type process), the origin of the incompatibility of aniline with this BDB reaction is currently unclear. Finally, we assessed the amenability of this methodology to scaling and glovebox free conditions: compound 3a was isolated in 62% yield when the BDB process was scaled up ten-fold, while 3a was isolated in 45% yield under glovebox free conditions (making 7 in situ from bench stable pyrazabole and iodine, note pyrazabole itself is readily accessed from pyrazole and L → BH₃).19

Conclusions

Iodine is an inexpensive activator for pyrazaboles that forms mono- and di-topic pyrazabole electrophiles, with the latter effective in the borylation directed borylation (BDB) of N-alkyl anilines. However, when using diiodo-pyrazabole 7 competitive formation of inactive (for BDB) species occurs that arise from break-up of the B₂N₄ pyrazabole core. This leads to lower BDB conversions using 7 than when using the di-NTf₂ pyrazabole analogue 1 (which reacts with <5% of unwanted side products by NMR spectroscopy). The attractive features of both systems (iodine = cheaper and easy to handle activator, while NTf₂-pyrazaboles = higher conversions in BDB) can be combined by
using the diido-pyrazabole 7 in combination with 0.2. equiv. of [Et₃NH][NTf₂]. This DDB methodology is operationally simple (no glovebox required) and is applicable to a range of N-alkyl anilines. The primary BDB products can be readily transformed into synthetically ubiquitous pinacol boronates esters, thus this process represents a metal-free transient directed C-H borylation methodology to form desirable N-alkyl-2-BPin-anilines.

Data availability

The data supporting this article has been uploaded as part of the ESI† this includes NMR spectra for all new compounds, in situ NMR spectra for catalytic and mechanistic reactions and Cartesian coordinates for all calculated structures.

Author contributions

MI, and CM conceived the research concept and aims and analysed all data. CM performed the majority of the synthetic work and the majority of the analytical components of this project. EN, AS, and JP also performed the synthesis and characterisation of a number of compounds reported in this manuscript. GN and JP collected and solved all the crystal structures. JL performed a number of the calculations. Combined, MI, CM and EN drafted, reviewed and edited the manuscript.

Conflicts of interest

There are no conflicts to declare.

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13 While the ortho-borylation of N-alkyl-anilines is an unmet challenge in electrophilic borylation it should be noted that a number of phenols have been successfully ortho-borylated under electrophilic C-H borylation conditions,


17 A search carried out on 14th August 2023 found >95% purity HNTf2 was available for £139 for 9 mmol on the website of a leading chemical supplier.


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