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# Modular synthesis of 1,2-azaborines via ring-opening BN-isostere benzannulation

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1,2-Azaborines represent a unique class of benzene isosteres that have attracted interest for developing pharmaceuticals with better potency and bioavailability. However, it remains a long-standing challenge to prepare monocyclic 1,2-azaborines, particularly multi-substituted ones, in an efficient and modular manner. Here we report a straightforward method to directly access diverse multi-substituted 1,2-azaborines from readily available cyclopropyl imines/ketones and dibromoboranes under relatively mild conditions. The reaction is scalable, shows a broad substrate scope, and tolerates a range of functional groups. The utility of this method is demonstrated in the concise syntheses of BN isosteres of a PD-1/PD-L1 inhibitor and pyrethroid insecticide, bifenthrin. Combined experimental and computational mechanistic studies suggest that the reaction pathway involves boron-mediated cyclopropane ring-opening and base-mediated elimination, followed by an unusual low-barrier 6$\pi$-electrocyclization accelerated by the BN/CC isomerism. This method is anticipated to find applications for the synthesis of BN-isostere analogues in medicinal chemistry, and the mechanistic insights gained here may guide developing other boron-mediated electrocyclizations.

As a consequence of the prevalence of arenes in small-molecule drugs, incorporating arene isosteres or bioisosteres has become an emerging strategy in medicinal chemistry for identifying candidates with enhanced performance without substantially altering the structures of lead compounds[1]. 1,2-Azaborines, a class of boron–nitrogen (BN) heterocycles with substantial aromaticity, are viewed as unique BN isosteres of benzene (Fig. 1a)[2–6]. They are generally more polar than benzene, leading to more localized electron distributions and better aqueous solubility[7]. Compared to the original carbonaceous compounds, improved biological activity and bioavailability have been observed in the 1,2-azaborine analogues[8–13]. For example, as shown in a 2017 report by Liu and colleagues, replacement of a phenyl group with a simple 1,2-azaborine moiety in a cyclin-dependent kinase 2 (CDK2) inhibitor led to a two- to fourfold increase in efficacy[7]. Similarly, Janssen Pharmaceuticals has disclosed systematic in vitro and in vivo profiling of 1,2-azaborine analogues of several drug candidates, with comparable or even better biological activity and ADMET (absorption, distribution, metabolism, excretion and toxicity) properties being observed[14]. These studies further suggest that 1,2-azaborines are stable under physiological, mildly basic, or oxidative conditions, serving as viable pharmacophores[15].

Despite the great promise of using 1,2-azaborines as arene bioisosteres in drug discovery, only a limited number of bioactive BN analogues have been reported so far, and it is still not a trivial task to access multi-substituted 1,2-azaborines[2–6]. In particular, unlike those in a fused a polyaromatic system[2,4], preparation of monocyclic 1,2-azaborines remains a substantial challenge[3]. The state-of-art synthesis employs allyl Molander salt and allyl amine as substrates to access *B*-alkoxy-1,2-azaborines in 25% yield over four steps, featured by a ring-closing metathesis with Schrock's catalyst and a Pd-catalysed dehydrogenative aromatization (Fig. 1b, left)[16]. Although this is a remarkable improvement over earlier approaches[17–19], extension of this

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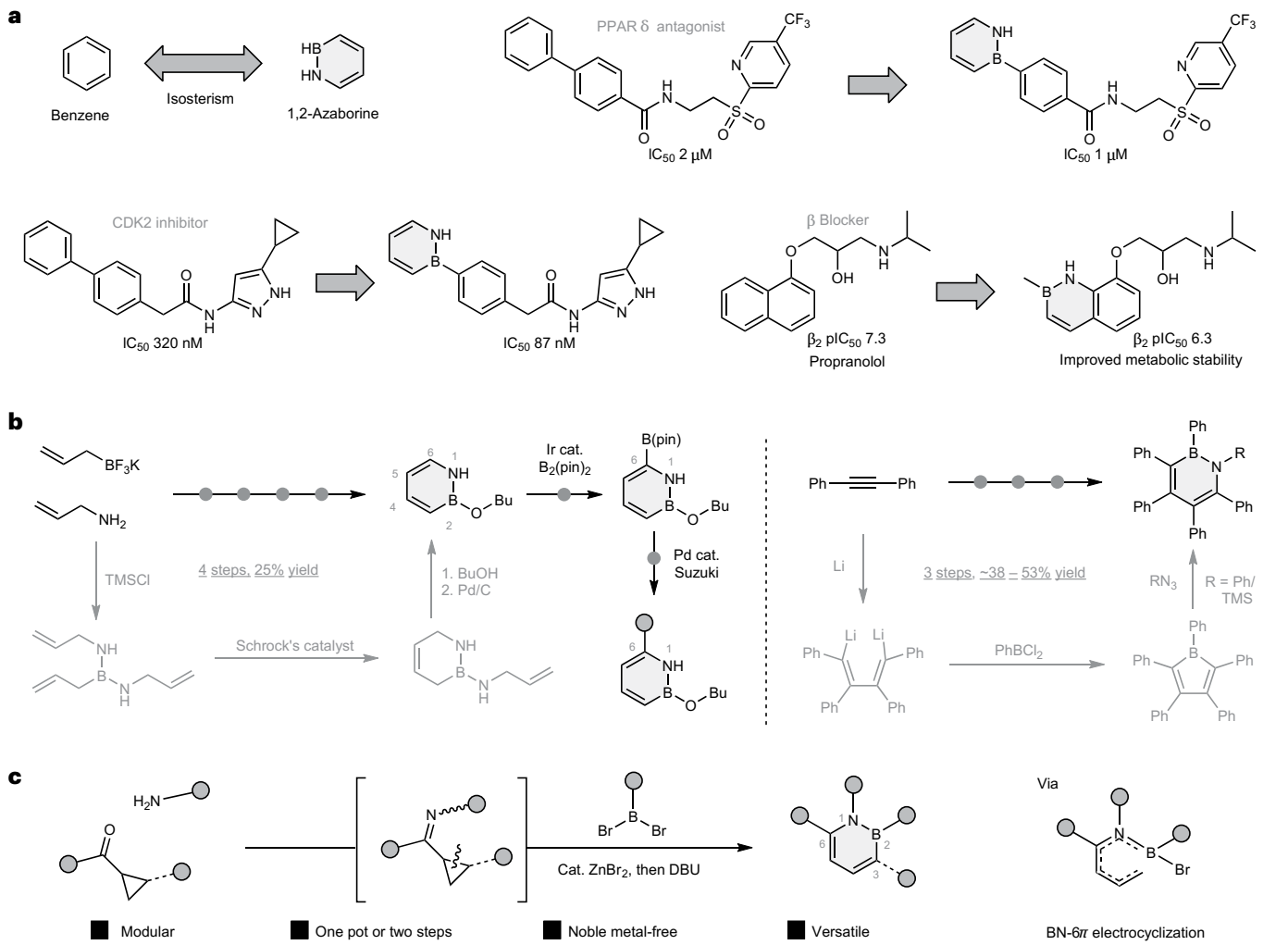


**Fig. 1 | Synthetic methods to access 1,2-azaborines. a**, Isosterism between benzene and 1,2-azaborine and their applications in medicinal chemistry. Improved biological activity and efficacies have been observed in the 1,2-azaborine analogues. $IC_{50}$, half-maximum inhibitory concentration; $pIC_{50}$, $-\log(IC_{50})$. **b**, Representative syntheses of monocyclic 1,2-azaborines. Left, B-alkoxy-1,2-azaborines are prepared from the reaction of allyl Molander salt and allyl amine, followed by ring-closing metathesis and dehydrogenative aromatization. Extension of this strategy to access C-substituted 1,2-azaborines is challenging. Right, poly-substituted 1,2-azaborines can be prepared from boroles, in which a divinyl lithium intermediate is involved. TMS, trimethylsilyl. **c**, This work: a two-step or one-pot modular synthesis of multi-substituted 1,2-azaborines from simple building blocks. DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene.

strategy to directly prepare C-substituted 1,2-azaborines has been elusive. For example, synthesis of C6-substituted 1,2-azaborines required an overall six-step sequence[20]. Alternatively, Braunschweig et al. disclosed a distinct approach to access poly-substituted 1,2-azaborines through either insertion of a nitrene into boroles (generated from a divinyl lithium intermediate; Fig. 1b, right)[21] or via a Rh-catalysed/mediated cyclization between iminoboranes and alkynes[22,23]. These reactions show limited scopes with moderate yields. To harness the full potential of the BN/CC isomerism for medicinal chemistry research, we recognized that it would be necessary to conceive of a more direct BN-benzannulation strategy to access monocyclic 1,2-azaborines. Ideally, this strategy can (1) use easily accessible substrates, (2) operate under mild conditions, (3) tolerate a broad range of functional groups, (4) give good overall yield, (5) avoid expensive noble metals, (6) be easily scalable and (7) be modular to access multi-substituted 1,2-azaborines with diverse structures in a straightforward manner. In this Article we describe the development of a general 1,2-azaborine-synthesis method that meets all the above criteria (Fig. 1c).

## Results and discussion

### Reaction discovery and optimization

From the outset, we questioned whether 1,2-azaborines could be synthesized from readily available cyclopropyl imines and a boron electrophile via a 'ring-opening-then-rebound' strategy[24]. It was initially hypothesized that a tandem boron-mediated C–C bond cleavage[25]/reductive C–B bond formation should generate the six-membered BN-heterocycle, which then gives the 1,2-azaborines after oxidative aromatization (Fig. 2a). Although this proposal was indeed feasible (details are provided in Supplementary Fig. 1), to our surprise, a more straightforward and redox-neutral method to prepare 1,2-azaborines was realized simply by treating the ring-opened intermediate with a base in a one-pot manner (Fig. 2b). For example, when cyclopropyl phenyl imine **1a** was employed as the model substrate, its reaction with (*o*-tolyl)$BBr_2$ **2a** in the presence of 10 mol% $ZnBr_2$ at 60 °C for 4 h, followed by in situ addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), gave the desired 1,2-azaborine **3a** in 84% yield. This protocol avoids oxidation and reduction and is easy to operate. The role of the Lewis acid was likely to activate the imine/dibromoborane adduct so

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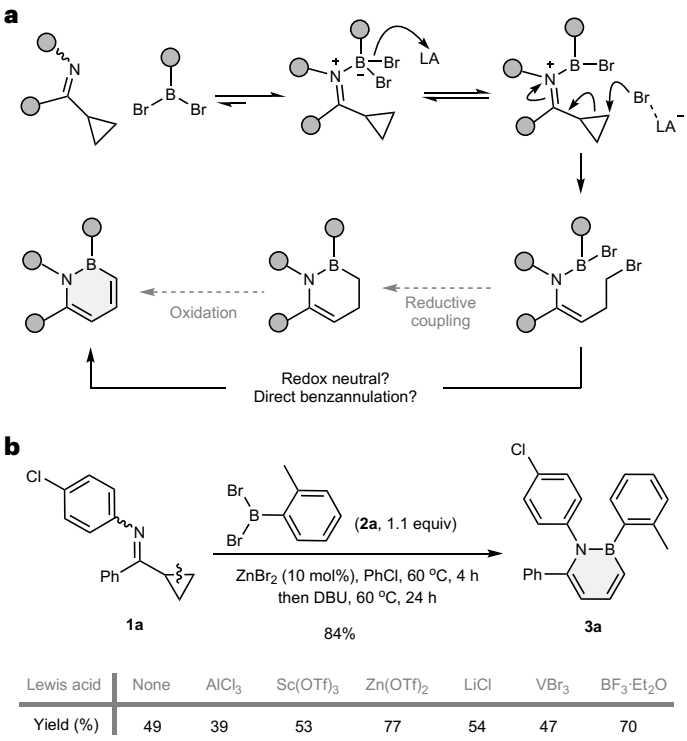


| Lewis acid | None | $AlCl_3$ | $Sc(OTf)_3$ | $Zn(OTf)_2$ | LiCl | $VBr_3$ | $BF_3{\cdot}Et_2O$ |
|---|---|---|---|---|---|---|---|
| Yield (%) | 49 | 39 | 53 | 77 | 54 | 47 | 70 |

**Fig. 2 | Proposed strategy and reaction discovery. a**, The original proposal involved a tandem Lewis acid (LA)-catalysed boron-mediated C–C bond cleavage/reductive C–B bond formation, followed by an oxidative aromatization. **b**, A redox-neutral condition was discovered with $ZnBr_2$ as the Lewis acid. Upon ring-opening of the cyclopropane, treatment with DBU in situ directly gave the desired 1,2-azaborine in good yield. Bottom: optimization of various Lewis acids shows that $ZnBr_2$ is optimal. The role of the Lewis acid is to promote the cyclopropane ring-opening by activating the imine/dibromoborane adduct.

as to promote the cyclopropane ring-opening. Among the various Lewis acids examined, $ZnBr_2$ proved to be optimal (Fig. 2b). Although $Zn(OTf)_2$ and $BF_3$ also offered good yields, other Lewis acids were less efficient. DBU was found to be the most suitable base. Weaker amines or inorganic bases were not effective for this transformation (details are provided in Supplementary Table 1).

## Substrate scope and synthetic applications

Given that (1) cyclopropyl imines/ketones are readily accessible from the corresponding carboxylic-acid derivatives and (2) dibromoboranes can be in situ-generated from $BBr_3$ and silanes, the scope of the reaction appears to be quite broad (Table 1). First, diverse anilines can efficiently condense with cyclopropyl ketones, and they all generated the desired 1,2,6-trisubstituted 1,2-azaborines in good yields. The reaction temperature was increased to 80 °C for some challenging substrates to enhance the overall efficiency. In addition, alkylamine-derived products can also be produced efficiently (**3p**–**3y** and **3aw**). Both aryl- and alkyl-substituted dibromoboranes, including the one derived from α-pinene (**3aq**), were suitable coupling partners. Notably, a *B*-silylmethyl 1,2-azaborine (**3ao**) was effectively obtained and the silyl group could serve as a handle for further functionalization. Furthermore, various C6 substitutents, including aryl, alkenyl and alkyl groups, can be installed. It is noteworthy that 1,2-azaborine with alkyl substituents at both C6 and N1 positions (**3am**) can be obtained. Finally, complex substrates derived from drug molecules, such as benzocaine, dapsone, ibuprofen and naproxen, as well as natural products such as lithocholic acid and leelamine, smoothly underwent the BN-isostere benzannulation reaction to deliver the desired products **3ar**–**3aw** in moderate to good yields. It is attractive that a range of functional groups were tolerated with this method. In particular, moieties reactive under various transition-metal catalysis conditions, such as halogens (-F, -Cl, -Br and -I, **3a**–**3f**) and pinacol boronate (**3o**), remained intact. Electrophilic groups, such as esters (**3l** and **3ar**), amide (**3al**) and sulfones (**3as**), as well as Lewis basic groups, such as ethers (**3i**, **3n**, **3v** and **3ab**), tertiary amines (**3j** and **3am**) and silyl ethers (**3au**), were also compatible.

Interestingly, apart from simple cyclopropyl, β-phenyl-substituted cyclopropyl imines were also competent substrates (Fig. 3a), delivering 1,2,3,6-tetrasubstituted azaborines **3ax** or **3ay** in moderate yield with complete selectivity of cleaving the more substituted C–C bond. Both the *trans* and *cis* isomers of the substrate (**1ax**) gave the same product (**3ax**) in comparable yield, suggesting that the reactivity is not substantially affected by the cyclopropane stereochemistry. The relatively low yield was probably due to steric hindrance of the β-phenyl group during the annulation process. The structure of **3ay** was further confirmed by X-ray crystallography. Note that synthesis of 1,2,3,6-tetrasubstituted azaborines has been very rare[2–6,26]. Alternatively, such compounds can be prepared more efficiently via site-selective bromination of trisubstituted azaborine **3b** followed by cross-couplings to introduce various functional groups at the C3 position (Fig. 3b)[26–29]. To show the synthetic utility of this method, a BN isostere of a PD-1/PD-L1 inhibitor[30] was first synthesized (Fig. 3c). Starting from imine **1az** (prepared from the corresponding commercially available ketone and methylamine), the benzannulation with $PhBBr_2$ provided the 1,2-azaborine intermediate (**3az**), which then underwent a Pd-catalysed formylation[31] and reductive amination to deliver the target BN isostere analogue **7**. Compound **7** is stable to air and moisture and can be purified via silica gel chromatography. In addition, 1,2-azaborine **3p** can be converted to a BN isostere (**8**) of the insecticide bifenthrin[32] via a boryl diazo intermediate[33] (**3p-CN$_2$**) in a four-step sequence (Fig. 3d). Note that the aryl group on the boron can be easily converted to a more reactive alkoxy group that can be further transformed to other moieties[34]. Bio-evaluation and pharmacological profiling of these BN-isostere analogues will be carried out in the future. Moreover, a one-pot protocol of preparing 1,2-azaborine **3a** directly from commercially available cyclopropyl phenyl ketone was realized in good efficiency (Fig. 3e). Finally, the synthesis of 1,2-azaborine **3n** is readily scalable; good yield can be retained in a gram-scale reaction (Fig. 3f).

## Mechanistic studies

To gain some insights into the reaction mechanism, efforts were first made to isolate the intermediates from different reaction stages. After imine **1a** reacted with (*o*-tolyl)$BBr_2$ **2a** in the presence of $ZnBr_2$ (without adding DBU), the proposed dibromo intermediate **4a** after the C–C cleavage was formed in high yield based on NMR analysis. Although **4a** was not isolatable, the corresponding hydrolysis product **4a′** can be purified and fully characterized (Fig. 4a), which suggests intermediacy of such an alkyl bromide in the ring-opening stage. This observation is consistent with a Lewis acid-promoted ring-opening pathway for cyclopropyl imines[35] and our previous understanding of the bromide anion abstraction/ring-opening process in the $ArBBr_2/ZnBr_2$ system (Fig. 4d)[24]. When imine **1l** was used as the substrate, shortening the DBU treatment time to 1 h led to isolation of a diene intermediate (**5l′**) in 75% yield along with 8% 1,2-azaborine product **3l** (Fig. 4b). In contrast, when the reaction was allowed to stir for 24 h after the addition of DBU, **5l′** almost fully disappeared and was converted to 1,2-azaborine **3l**. This observation indicates that a diene intermediate, generated via a base-mediated elimination of HBr, is probably involved in the cyclization stage[36–38]. As a control experiment, the use of homoallylamine **1ba** (mono alkene) as the substrate did not yield any cyclized product under the standard conditions, implying the important role of such a conjugate diene structure in the C–B bond-forming stage (Fig. 4c).

To understand how 1,2-azaborine is generated from the putative diene intermediate, density functional theory (DFT) calculations

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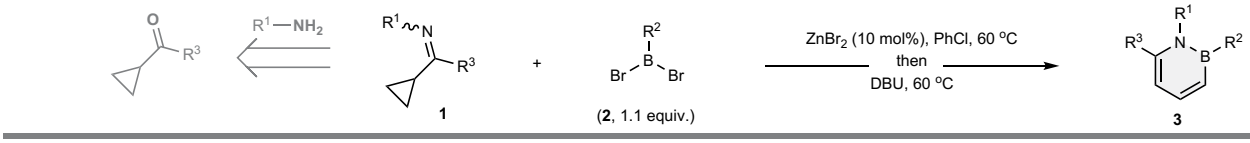
**Table 1 | Substrate scope**




Scope of $R^1$

$R^1$ = Ar

$R^2$ = *o*-tolyl

**3a**, 83%

**3b**, 74%

**3c**, 56%[a]

**3d**, R = F, 71%
**3f**, R = I, 42%
**3g**, R = H, 81%
**3h**, R = Me, 76%
**3i**, R = OMe, 61%
**3j**, R = $N(Me)_2$, 73%
**3k**, R = Ph, 82%

$R^1$ = alkyl

$R^2$ = *o*-tolyl

**3p**, $R^1$ = Me, 77%[a]
**3q**, $R^1$ = butyl, 80%[a]
**3r**, $R^1$ = benzyl, 76%[a]
**3t**, $R^1$ = propyl, 77%[a]
**3u**, $R^1$ = $(CH_2)_3Ph$, 70%[a]
**3w**, $R^1$ = cyclohexyl, 50%[a]
**3x**, $R^1$ = *iso*-propyl, 66%[a]

**3e**, 77%

**3l**, 76%

**3m**, 82%

**3n**, 80%

**3o**, 52%

**3s**, 70%[a]

**3v**, 45%[a]

**3y**, 36%[a]

Scope of $R^3$

$R^3$ = Ar

$R^1$ = OPh

$R^2$ = *o*-tolyl

**3z**, R = Ph, 79%
**3aa**, R = OPh, 72%
**3ac**, R = $CF_3$, 82%
**3af**, R = F, 79%

**3ab**, 49%

**3ad**, 55%

**3ae**, 53%

**3ag**, 57%[a]

**3ah**, 51%[a]

**3ai**, $R^3$ = Me, 46%[a]
**3aj**, $R^3$ = $(CH_2)_2Ph$, 41%[a]
**3ak**, $R^3$ = cyclohexyl, 62%[a]

**3al**, 45%[a]

**3am**, 33%[a]

**3an**, 32%[a]

Scope of $R^2$

$R^1$ = OPh

**3ap**, $R^2$ = hexyl, 42%[a]

**3ao**, 68%[a]

**3aq**, 61%

From leelamine
**3aw**, 71%[a]

Drug and natural product derivatives

$R^2$ = *o*-tolyl

From benzocaine
**3ar**, 81%

From dapsone
**3as**, 20%[a,b]

From ibuprofen
**3at**, 48%[a]

From lithocholic acid
**3au**, 28%[a]

From naproxen
**3av**, 25%[a]

Conditions: all reactions were conducted with 0.2 mmol substrate, 0.22 mmol $R^2BBr_2$ and 0.02 mmol $ZnBr_2$ in 1 ml of PhCl at 60 °C under nitrogen for 4 h, followed by the addition of 0.6 mmol DBU, and stirred at the same temperature for 24 h. All yields are isolated yields after silica gel chromatography. [a]The reaction was run at 80 °C. [b]0.44 mmol $R^2BBr_2$, 0.04 mmol $ZnBr_2$ and 1.2 mmol DBU were used. DBU, 1,8-diazabicyclo(5.4.0)undec-7-ene; TMS, trimethylsilyl.

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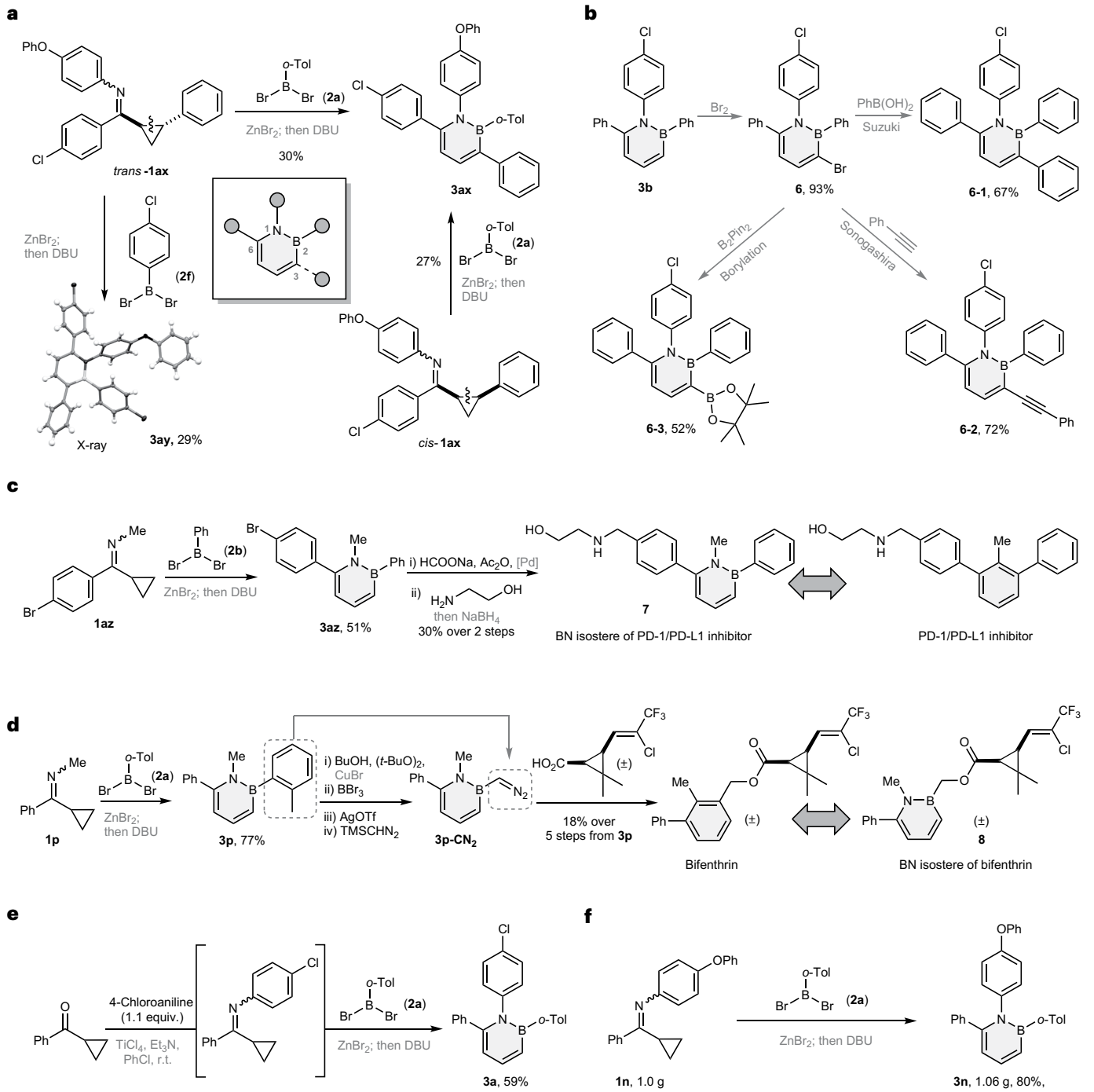


**Fig. 3 | Derivatization and synthetic applications. a**, One-step synthesis of 1,2,3,6-tetrasubstituted 1,2-azaborines from disubstituted cyclopropanes. The X-ray structure of compound **3ay** is shown. **b**, Synthesis of 1,2,3,6-tetrasubstituted azaborines from 3-bromo-1,2,6-triarylated azaborine via Pd-catalysed Suzuki coupling, borylation and Sonogashira coupling. **c**, Synthesis of a BN isostere of a PD-1/PD-L1 inhibitor. **d**, Synthesis of a BN isostere of the insecticide bifenthrin. *o*-Tol, *o*-tolyl. OTf, triflate. **e**, One-pot synthesis from cyclopropyl phenyl ketone. **f**, The gram-scale reaction gave good yield.

were conducted, which support an unusual 6$\pi$-electrocyclization mechanism (Fig. 4d). The diene intermediate is an isostere of 1,3,5-trienes that are known to undergo 6$\pi$-electrocyclization. However, 6$\pi$-electrocyclization of unactivated trienes bearing two terminal substituents suffers from relatively low reactivity[39,40]. For example, the reaction of triene **11**, the CC isostere of the BN-diene intermediate (**9**), requires a relatively high activation free energy of 34.9 kcal mol$^{-1}$ (Fig. 4e). By contrast, our calculations indicated that diene **9** undergoes a much more facile 6$\pi$-electrocyclization via **TS1** to form cyclic *N*-borylated iminium **10**, which, upon DBU-mediated elimination of HBr, forms azaborine **3g′**. The 6$\pi$-electrocyclization requires a low activation free energy of 20.8 kcal mol$^{-1}$ with respect to the s-*trans* conformer of **9**, which is consistent with the mild reaction conditions observed for the 1,2-azaborine formation. The reactivity of diene **9** is promoted by the polarization of the B–N bond[41,42] as well as the smaller torsional strain to rotate the B–N bond, compared to rotation of the C=C double bond in 1,3,5-trienes, for example, **11** (Fig. 4e). In **TS1**, the B–N bond is rotated to a more non-planar geometry, as

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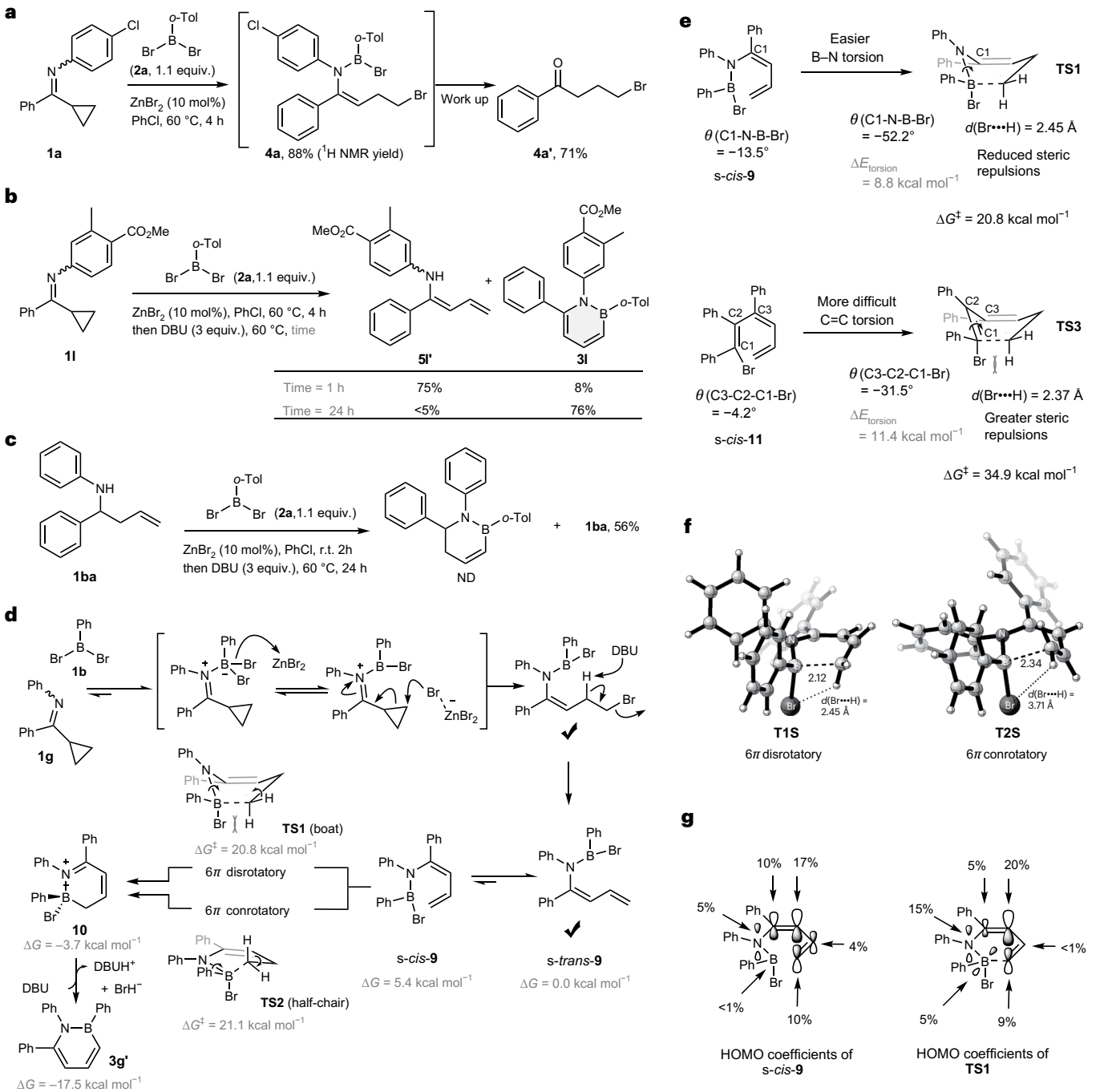


**Fig. 4 | Preliminary mechanistic studies. a**, The ring-opening intermediate before the addition of DBU is identified. Isolation of the hydrolysed alkyl bromide **4a'** supports the intermediacy of **4a** in the ring-opening stage. **b**, The reaction intermediate in the base-mediated cyclization step is identified. **c**, A control experiment shows the importance of the diene structure in the cyclization stage. ND, not detected. **d**, Proposed mechanism and the energy of the 6$\pi$-electrocyclization pathway to form 1,2-azaborines. Check marks mean identified intermediates. **e**, Torsion-promoted electrocyclization of intermediate **9**, in comparison with a triene substrate **11**. *d* means the distance between the two atoms. **f**, Transition-state structures of **TS1** and **TS2**. **g**, Unique nodal properties of the $\pi$-system of intermediate **9** lead to the small energy difference between the symmetry-allowed (**TS1**) and -forbidden (**TS2**) electrocyclization pathways. DFT calculations were performed at the M06-2X/6-311+G(d,p)/SMD(chlorobenzene)//M06-2X/6-31G(d) level of theory. All energies are with respect to *s-trans*-**9**.

evidenced by the larger dihedral angle of $\theta$(C1–N–B–Br) (−52.2°). For comparison, the corresponding dihedral angle of $\theta$(C3–C2–C1–Br) (−31.5°) in the 6$\pi$-electrocyclization transition state of triene **11** is much smaller. The non-planar geometry of the B–N terminus leads to attractive interactions of the electron-rich dienamine moiety with the vacant B orbital on the borane terminus, and also reduces the steric repulsions between these two termini in the boat-like transition state (Fig. 4e). Notwithstanding the greater rotation, a smaller torsional energy is required to distort the B–N bond in **9** to the corresponding transition-state geometry compared to the rotation of the terminal C=C bond in **11** ($\Delta E_{torsion}$ = 8.8 and 11.4 kcal mol$^{-1}$ for **9** and **11**, respectively). As a result, the 6$\pi$-electrocyclization of diene **9** requires a much lower activation free energy than the corresponding reaction with triene **11** ($\Delta\Delta G^{\ddagger}$ = 14.1 kcal mol$^{-1}$).

It is also remarkable that the 6$\pi$-electrocyclization can occur through either dis- or conrotatory transition states (**TS1** and **TS2**, respectively; Fig. 4f) that have comparable activation free energies. To the best of our knowledge, there has been no known 6$\pi$-electrocyclization that allows both dis- and conrotatory pathways. This finding appears to contradict the Woodward–Hoffmann rules, which predict that for 6$\pi$-electrocyclizations, the disrotatory transition-state barrier should be substantially lower than the barrier for the conrotatory transition state[43]. However, alteration of the nodal properties of the highest occupied molecular orbital (HOMO) shown in Fig. 4g and Supplementary Fig. 6 indicate that the high polarization of this system eliminates the differences between allowed and forbidden processes, as discussed recently in detail for model systems[44]. The polarization of the B–N bond changes the nodal properties of the $\pi$ system in **9**. The diminished orbital coefficient on the terminal boron atom of the HOMO of s-*cis*-**9** essentially reduces the preference for the allowed disrotatory (**TS1**) versus the forbidden conrotatory (**TS2**) electrocyclization. In a normal hydrocarbon triene, the orbital overlap between the termini is favourable for the allowed disrotatory process and unfavourable for the forbidden conrotatory process; when one terminal coefficient, that is, the one of boron, is nearly zero, as shown in the current system, there is no preference.

## Conclusions

In summary, we have developed a general, modular and straightforward method to access diverse multi-substituted monocyclic 1,2-azaborines from readily available staring materials. Owing to the relatively mild conditions, the reaction exhibits a broad substrate scope and good functional-group compatibility. This method is expected to greatly simplify syntheses of diverse BN-isostere analogues and to be readily adoptable in medicinal chemistry. The mechanistic insights gained here should have broad implications for boron-mediated electrocyclization in the preparation of other boron-containing heterocycles.

## Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41557-023-01343-6.

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## Methods

### General procedure for monocyclic 1,2-azaborine synthesis from imine

An oven-dried 4-ml vial was charged with imine **1** (0.2 mmol, 1 equiv.) and $ZnBr_2$ (4.5 mg, 0.02 mmol, 10 mol%) in a nitrogen-filled glovebox. Dry chlorobenzene (1 ml) was then added. After addition of dibromoborane **2** (0.22 mmol, 1.1 equiv.), the vial was tightly sealed and stirred on a pie-block preheated to 60 °C or 80 °C under nitrogen for 4 h. DBU (90 µl, 0.6 mmol, 3 equiv.) was then added and the reaction mixture was stirred at the same temperature for 24 h. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite, washed with ethyl acetate, and concentrated to dryness in vacuo. The crude product was subjected to flash column chromatography to give 1,2-azaborine **3**.

### General procedure for monocyclic 1,2-azaborine synthesis from ketone

An oven-dried 10-ml Schlenk flask was charged with ketone (2 mmol, 1 equiv.), amine (2.2 mmol, 1.1 equiv.), triethylamine (0.56 ml, 4 mmol, 2 equiv.) and dry dichloromethane (8 ml). $TiCl_4$ (1 ml, 1 M solution in dichloromethane, 1 mmol, 0.5 equiv.) was then added dropwise under nitrogen at 0 °C over a period of 15 min. After being stirred at 0 °C for 0.5 h, the reaction mixture was warmed to room temperature and stirred for 12 h. Upon completion, the reaction mixture was filtered through a pad of Celite under nitrogen, washed with dry hexane, and concentrated to dryness under vacuum. The crude product was redissolved with dry hexane and filtered through a pad of Celite and concentrated to dryness again. The obtained imine **1** was directly used in the next step without further purification.

An oven-dried 4-ml vial was charged with imine **1** (0.2 mmol, 1 equiv.) and $ZnBr_2$ (4.5 mg, 0.02 mmol, 10 mol%) in a nitrogen-filled glovebox. Dry chlorobenzene (1 ml) was then added. After addition of dibromoborane **2** (0.22 mmol, 1.1 equiv.), the vial was tightly sealed and stirred on a pie-block preheated to 60 °C or 80 °C under nitrogen for 4 h. DBU (90 µl, 0.6 mmol, 3 equiv.) was then added and the reaction mixture was stirred at the same temperature for 24 h. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite, washed with ethyl acetate and concentrated to dryness in vacuo. The crude product was subjected to flash column chromatography to give 1,2-azaborine **3**.

## Data availability

The data supporting the findings of this study are available within the Article and its Supplementary Information. Crystallographic data for the structure of **3ay** have been deposited at the Cambridge Crystallographic Data Centre, under deposition no. 2150659. Copies of the data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/.

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## Author contributions

H.L. and G.D. conceived and designed the experiments. H.L., Z.C. and Y.W. performed experiments. T.H.T., G.A.K., A.T., K.N.H. and P.L. designed and conducted the DFT calculations. H.L., T.H.T., K.N.H., P.L. and G.D. wrote the manuscript. P.L. and G.D. directed the research.

## Competing interests

A patent application has been filed (applicant: University of Chicago; name of inventor(s): Guangbin Dong, Hairong Lyu, Zhijie Chen, Yifei Wu; application no., 63/376,889; status of application, pending; specific aspect of manuscript covered in patent application, 'New azaborine structures'). The remaining authors declare no competing interests.

## Additional information

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