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Design and synthesis of stable four-coordinated benzotriazole-borane with tunable fluorescence emission†

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A new class of stable four-coordinated benzotriazole-borane compounds was developed *via* gold-catalyzed alkyne hydroboration. The application of polymeric $(BH_2CN)_n$ reagent gave the formation of cyano-amine-boranes (CAB) complexes with less basic N-heterocyclic amines and anilines. Various new CABs were investigated in catalytic hydroboration to synthesize N–B cycles. The 1,2,3-benzotriazoles were identified as the only feasible N-source, giving the four coordinated borane N–B cycles (BTAB) in excellent yields (up to 90%) with good functional group tolerability. This new class of polycyclic N–B compounds showed excellent stability toward acid, base, high temperature, and photo-irradiation. The facile synthesis, excellent stability, strong and tunable fluorescence emission make BTAB interesting new fluorescent probes for future chemical and biological applications.
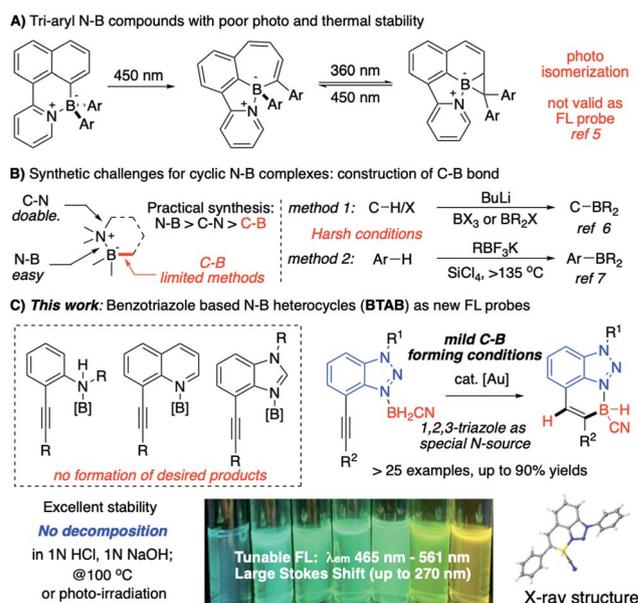
Introduction

With the good binding affinity between nitrogen lone-pair electrons and boron's empty orbital, the amine–borane complexes have been widely applied as versatile synthetic reagents.[1] Recently, discovering interesting photo/electronic properties associated with the cyclic N–B compounds makes them an important class of heterocycles in chemical, material, and biomedical research.[2] With the discovery of BODIPY and its derivatives, the four-coordinate boron "ate" complexes have received great attention due to their interesting fluorescence (FL) properties.[3] Recently, the discovery of aryl-modified boron complexes (containing C–B–N moiety) led to a new direction for developing molecular probes with novel structural skeletons.[4] However, with labile B–Ar bonds, these compounds undergo rapid photo-initiated isomerization (Scheme 1A), impeding them from being valid FL probes.[5]

The synthesis of N–B heterocycles could be challenging. As shown in Scheme 1B, N–B heterocycle formation involves the selected construction of N–B, C–N, and C–B bonds. Compared

with N–B and C–N bonds, the C–B bond construction is the most challenging due to limited available methods. Currently, strategies for cyclic N–B complex synthesis include (A) carbon anion (from *n*-BuLi C–H deprotonation) nucleophilic addition[6] and (B) LA promoted aryl C–H activation.[7] The lack of effective practical approaches for large-scale synthesis and the strong need to access new N–B modified polycyclic molecular skeletons

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Scheme 1 N–B heterocycles as new molecular probes.

make developing a new synthetic strategy toward the N–B modified polycyclic system highly desirable.[8] In this work, we report the preparation of benzotriazole borane (BTAB) as a new class of stable four-coordinate N–B heterocycles through gold-catalyzed alkyne hydroboration. These new N–B heterocycles give strong and tunable FL emission ($\lambda_{max} = 465$ nm to 561 nm) with excellent stability toward acid (1 N HCl), base (1 N NaOH), thermal (100 °C, 24 h), and photo radiation (254 nm and 365 nm, 24 h), making them promising new molecular probes for chemical research (Scheme 1C).

One effective strategy for vinyl-C–B bond synthesis is alkyne hydroboration.[9e] Though this method has been applied for many B-containing compound preparation, it could not be feasible in the N–B heterocycles synthesis. As shown in Fig. 1A, cis-addition of alkyne in most catalytic system leads to a "wrong" regioisomer against the sequential endo-type cyclization.[10] Although Wang and coworkers reported an interesting route to N–B heterocycles with the assistance of directing nitrogen (Fig. 1B),[11] it only works with 9-BBN as borane source, and the resulting 5-membered N–B heterocycles have poor stability, even decomposing upon the separation. To test whether this method would be valid for broader N–B heterocycles synthesis, we prepared alkynes 1a–1e (Fig. 2C) to react with 9-BBN using Wang's condition. No cyclic N–B compounds were observed in any cases. This result, again, highlighted the challenges associated with the synthesis of polycyclic four-coordinated N–B compounds.

Our group recently reported that the triazole-gold (TA-Au) catalyzed alkyne hydroboration to synthesize cyclic N–B compounds (N as aliphatic amine).[12] As we reported previously, triazole gold [L-Au-TA]$^+$ showed significantly improved stability over [L-Au]$^+$. However, treating TA-Au with [N]–BH$_3$ still led to rapid gold decomposition, highlighting the challenge of applying gold catalysis under a reductive environment. Fortunately, the cyano-amino-borane (CAB, N–BH$_2$CN) was identified as the valid hydride source, giving hydroboration with TA-Au as the catalyst ([L-Au]$^+$ gave rapid decomposition). The initial preparation of CABs could be tricky by treating the aliphatic amine HCl salts with NaBH$_3$CN in THF. As a result, this protocol could not be used for the polycyclic N–B compound synthesis
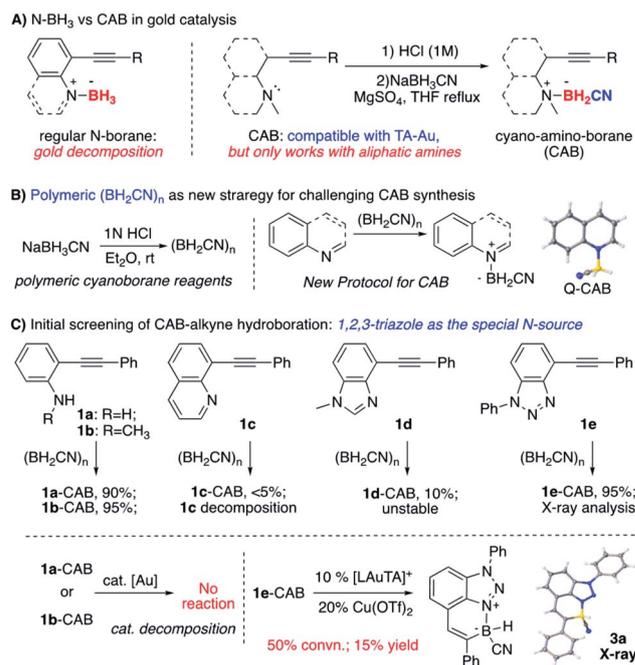

Fig. 2 New CAB synthesis strategy and hydroboration.

since both aniline and N-heterocycles failed to produce CABs using the initial conditions (Fig. 2A).

Over the past several years, we have devoted efforts to exploring new strategies for plausible CAB synthesis with aniline or N-heterocycles as the N-source. After many attempts, we identified polymeric cyano-borane $(BH_2CN)_n$ as a new reagent in CAB synthesis.[13] As shown in Fig. 2B, this polymeric $(BH_2CN)_n$ reagent could be readily prepared by treating NaBH$_3$CN with 1 N HCl (see ESI†). The resulting THF solution can be used directly to react with quinoline, giving the desired **Q-CAB** in 90% yields. With this new reagent, the desired CABs of aniline **1a** or **1b** were prepared in excellent yields. Other N-heterocycles were also tested. Both quinoline alkyne **1c** and benzimidazole alkyne **1d** gave low yields of CAB due to poor stability (substrate decomposition). Interestingly, the 1,2,3-benzotriazole alkyne **1e** gave the desired CAB with excellent yield (95%).

Results and discussion

Encouraged by the synthesis of aniline and triazole CABs, the alkyne-CAB complexes were charged with gold-catalyzed hydroboration under various conditions. After exploring various gold-catalyzed conditions, the aniline CABs (**1a** and **1b**) failed to give any hydroboration products with rapid gold decomposition, likely due to the more reactive B–H. Interestingly, under previously optimal conditions, 10 mol% [(ArO)$_3$-PAu(TA-Ph)]OTf and 20 mol% Cu(OTf)$_2$ at 60 °C, benzotriazole modified **1e-CAB** successfully generated the desired cyclic N–B product **3a**, though in low yields (Fig. 2C, 50% conversion, 15% yields). To our surprise, this new N–B heterocycle **3a** was very stable toward air, moisture, and even elevated temperature (vide
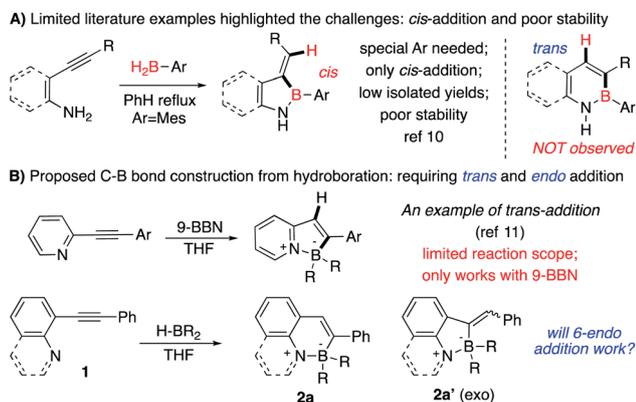

Fig. 1 Challenges of hydroboration toward N–B cycle construction.

infra). Therefore, the low yield results from gold catalyst decomposition (low conversation) and **1e-CAB** decomposition (formation of **1e**). This result was exciting since it confirmed that 1,2,3-benzotriazole, as a special N-heterocycle, could be successfully applied to construct the N–B heterocycle as a new molecular skeleton. Comprehensive condition screening was performed, and RuPhosAuNTf$_2$ (10 mol%) in DCE at 80 °C was identified as the optimal one, giving the BTAB **3a** in 87% isolated yields. Comparison with selected alternative conditions is summarized in Table 1 (see detailed conditions screening in ESI†).

As shown in Table 1, among various tested metal complexes (including Ag, Cu, Zr, Zn *etc.* entry 12), the cationic gold is the only one that gives desired hydroboration products, which highlighted the critical role of gold catalyst for this transformation. The primary ligand on gold plays a crucial role by providing balanced reactivity and catalyst stability. The Buchwald type bis-aryl ligands increased conversion with the improved gold cation stability (entries 5–6). Notably, while triazole helps to improve gold stability, TA-Au gave low conversion (entry 7), likely due to the competing TA-borane coordination. Reducing reaction temperature to 60 °C caused a slow reaction rate with gold decomposition over time. With the optimal condition in hand, the substrate scope was evaluated.

As shown in Table 2, this new transformation works well with aromatic and aliphatic substituted alkynes, giving the desired BTAB in good yields. Both EDG and EWG modified aryl alkynes work well (**3a**–**3g**), except *ortho*-substituted benzene (**3h**, slow conversion, likely due to the combination of electronic effect and steric hindrance). Impressively, thiophene substituted alkynes (**3l**–**3n**) are suitable substrates for this reaction, albeit the potential Au–S binding. Terminal alkyne (**3p**) and aliphatic alkyne (**3o**) give slightly reduced yields. The

Table 2 Reaction scope and BTAB derivatization^{a,b,c}
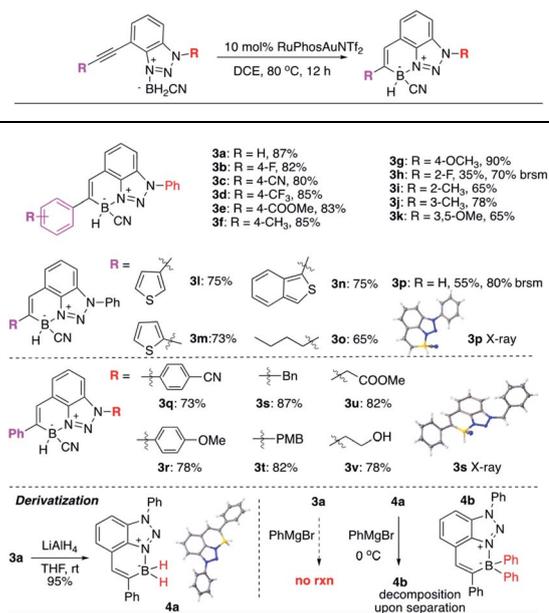
^{a} Conditions: **4a** (0.2 mmol), Au cat. (0.01 mmol), DCE (2 mL), 80 °C, 12 h. ^{b} Isolated yields. ^{c} brsm = based on recovered starting material.

substituted group on the N-1 position of benzotriazole was also tested. Both *N*-aryl (**3q**) and *N*-alkyl (**3s**) substituted benzotriazole are suitable substrates. In addition, both EDG and EWG modified *N*-aryl triazoles gave the desired N–B heterocycles in good yields (**3q**, **3r**). Various *N*-alkyl substituted triazoles (**3s**–**3u**) were applied, giving the BTABs in good yields, suggesting the

Table 1 Optimization of reaction conditions^{a,b}
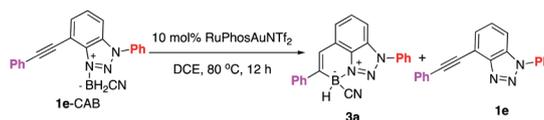
Entry	Variation from "standard conditions"	Convn. (%)	**3a** (%)	**1e** (%)
1	None	100	90 (87)	<5
2	[Au] = PPh$_3$AuNTf$_2$	<5	n.d.	n.d.
3	IPrAuNTf$_2$	70	20	38
4	JohnPhosAuNTf$_2$	80	45	24
5	(ArO)$_3$PAuNTf$_2$	52	10	35
6	SPhosAuNTf$_2$	95	78	10
7	TA-Au: RuPhosAu(TA-H)OTf	43	8	30
8	[Au] + [Cu]: RuPhosAu(TA-H)OTf + Cu(OTf)$_2$	20	<5	n.d.
9	Other solvents (CH$_3$CN, THF, tol, MeOH. See details in ESI)	<89	<71	—
10	5% [Au]	65	54	<5
11	60 °C	65	30	—
12	Other metal cat. (Ag, Cu, Zr, Zn *etc.* See ESI)	<10%	n.d.	—

^{a} Conditions: **1e-CAB** (0.1 mmol), Au cat. (0.01 mmol), DCE (2 mL), 80 °C, 12 h. ^{b} ^{1}H NMR yields using 1,3,5-tribromobenzene as an internal standard (isolated yields).

excellent functional group tolerability and easy modification for future applications (with N-1 position as the synthetic handle).

Treating BTAB **3a** with $LiAlH_4$ gave the dihydro borane **4a** (R_2BH_2) in excellent yield, confirming the feasibility of sequential modification on boron after cyclization. However, the reaction of **3a** with Grignard reagents gave no CN substitution. Instead, the reaction between **4a** (R_2BH_2) and excess PhMgBr gave the formation of diphenyl substituted borane **4b** (decomposition upon separation, based on crude NMR).[14] The polyaromatic hydrocarbon (PAH) compounds have received tremendous attention over the past decades due to their interesting photo and electronic properties.[15] With the incorporation of "electron" and "hole" pair, the NB modified PAH is undoubtedly one interesting modification of typical PAH. As a six-membered N–B heterocycle, one question is whether this new class BTAB would transform into three-coordinated azaborine as polyaromatic hydrocarbons, especially with active B–H bond (losing hydride).

To explore this idea, BTAB **3a** was treated by various RCOOH. As shown in Fig. 3, while acetic acid and PhCOOH gave no reaction, treating **3a** with TFA gave the rapid formation of TFA substituted BTAB **4c** in excellent yield (structure confirmed by singles crystal X-ray structure determination). Interestingly, the hydroxy modified BTAB **3v** could give the [2 + 2] cycloaddition product **4d** (X-ray) over a long period (10 days) without N–B bond dissociation in the hexane and ethyl acetate solvent mixture. These results suggested the excellent N–B bond stability of this four-coordinated BTAB polycycles.

Comprehensive photophysical properties evaluations of these new stable N–B polycyclic molecular skeletons were performed. As expected, strong photoluminescence activity was observed. The detailed excitation (λ_{ex}), emission (λ_{em}), adsorption (ε), Stokes shift, quantum yield (φ_F), and fluorescence lifetime (FLT) date are summarized in SI. Some representative data are highlighted in Fig. 4. First, all BTABs gave strong fluorescence emission in the solid-state and in the solution with emission λ_{max} between 465 nm and 561 nm (Fig. 4A). In addition, this N–B polycyclic skeleton showed impressive stability with no decomposition in acid (1 N HCl, 24 h), base (1 N NaOH, 24 h), thermal (100 °C, 24 h), and photo-irradiation (254 nm, 24 h). Both N-substituted group R^1 and alkyne C-substitute group R^2 would influence the overall fluorescence performance, giving
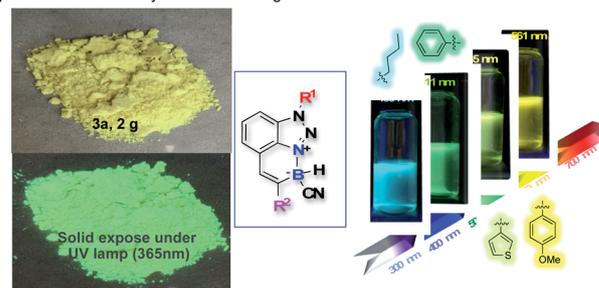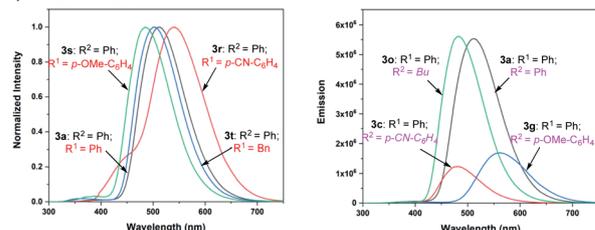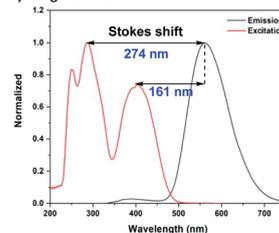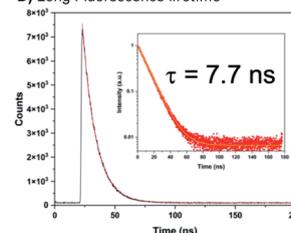

Fig. 4 BTAB photophysical properties.

tunable emissions. As shown in Fig. 4B, extended conjugation on both C and N positions gave the expected red shift (**3a** vs. **3t**; **3r** vs. **3t**). Similarly, since TA is electron deficient, the electron-withdrawing group (EWG, R^1) modified **3r** gave further redshift compared to the electron-donating group (EDG) modified **3s**. In contrast, EDG modified R^2 substrates cause the red shift compared to the EWG modified R^2 substrates due to this extended conjugation effect (**3g** vs. **3c**). Impressively, a large Stokes shift (193 nm to 274 nm, Fig. 4C) and long fluorescence lifetime (7.7 ns, Fig. 4D) were obtained with these BTABs, suggesting promising application scope as this new FL probe.[16]

Finally, density functional theory (DFT) and time-dependent density functional theory (TD-DFT) calculations were performed to explore the emission mechanism. The calculation of **3a** at PBE0 level shows the first two peaks of absorption are 404 nm and 297 nm, which are very close to the experimental results (375 nm and 287 nm). The calculated energy gap of HOMO and LUMO was 3.8 eV, corresponding to the first absorption peak. The analysis of those orbitals shows that HOMO is majorly located on azaborine moiety while LUMO is majorly located on benzotriazole moiety, suggesting a possible charge transfer process from the azaborine to benzotriazole in the exited process. Based on this computational model, the emission was determined as 522 nm, which was in very good agreement with the experimental data (511 nm), suggesting the good correlation of the computational model in explaining the fluorescence emission mechanism for these new BTAB compounds.
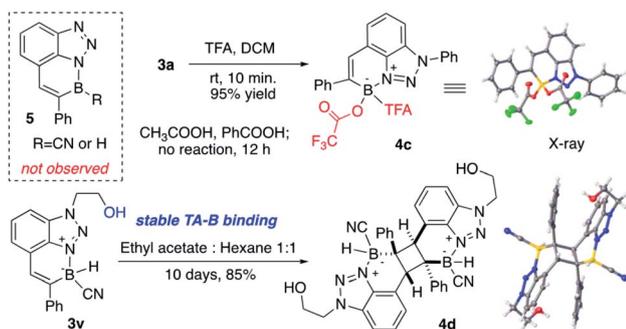

Fig. 3 BTAB derivatization: the extremely stable TA-B coordination.

Conclusions

In summary, with the application of polymeric $(BH_2CN)_n$ reagent to form cyanoborane complexes of less reactive N-heterocycles, we identified 1,2,3-benzotriazole as the critical building block and successfully developed a highly efficient synthesis to achieve a new class of N–B heterocycles BTABs. These new compounds showed strong, tunable fluorescence emission with excellent stability toward acid, base, and photo-irradiation. The combination of easy gram-scale synthesis, long lifetime, and large Stokes shift makes BTABs a promising new fluorophore for future chemical and material applications.

Data availability

All experimental and characterization data, including experiment procedure, NMR spectra, crystallographic data, photophysical spectra, and calculations are available in the ESI.†

Author contributions

X. S. designed and directed the investigations. Q. T. performed the experiments. Q. T., X. Y., T. Y., K. Z., and Y. H. analyzed and discussed the experiment results. S. L. and Y. L. carried out the calculations. C. S. and L. W. carried out the X-ray crystallographic measurements. D. R. collected the ^{19}B NMR spectroscopic data. All authors were involved in the preparation of the manuscript. The final manuscript was approved by all authors.

Conflicts of interest

There are no conflicts to declare.

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