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Azaborine benzylic ion stability and reactivity in ionic polymerization†

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Benzylic cations and anions are implicated in the mechanism of critical organic transformations, such as styrene polymerization. We investigate the influence of BN for CC bond substitution on the reactivity of benzylic ions and the effect on BN 2-vinylnaphthalene (BN2VN) ionic polymerization. Calculations suggest that the proximity of a N donor to a cation influences the stability of a BN benzylic cation, rationalizing unsuccessful protonation of BN2VN. Organolithium reagents undergo clean nucleophilic aromatic substitution with BN2VN and related BN naphthalenes *via* a hypothesized associative mechanism. These results suggest design principles for main group aromatic substitution.

Introduction

Aromatic vinyl monomers like styrene and 2-vinylnaphthalene are highly versatile: polymerization by coordination–insertion, radical, cationic, and anionic mechanisms are all well-established. Key to this versatility is the unique ability of the benzylic position to stabilize a variety of reactive intermediates (Fig. 1a). Our research group has developed an interest in understanding how well organometallic styrene mimics, such as azaborine derivatives, may intercept the unique versatility of styrene in polymerization chemistry. Herein, we investigate cationic and anionic polymerization of an aromatic organoborane vinyl monomer. We find that the polarization of the aromatic ring results in elimination or substitution reactions on the BN naphthalene side chain instead of vinyl polymerization. Potential mechanisms are described, as well as the consequences for postpolymerization functionalization.

1,2-azaborine is the aromatic heterocycle arising from the substitution of a CC bond in benzene with the isoelectronic boron–nitrogen (BN) bond.^{1–3} While BN aromatic rings were first described more than a half century ago by Dewar,⁴ recent years have seen a surge of new synthetic approaches⁵ and molecular insights.⁶ Efforts in the synthesis and polymerization of BN mimics of styrene and other aromatic monomers have focused almost exclusively on radical mechanisms (Fig. 1b).⁷ Ashe reported the first synthesis of a BN styrene, which was used as a ligand in transition metal complexes.⁸ Liu and Jäkle reported the first polymerization of a BN styrene by free and controlled radical polymerization, although much

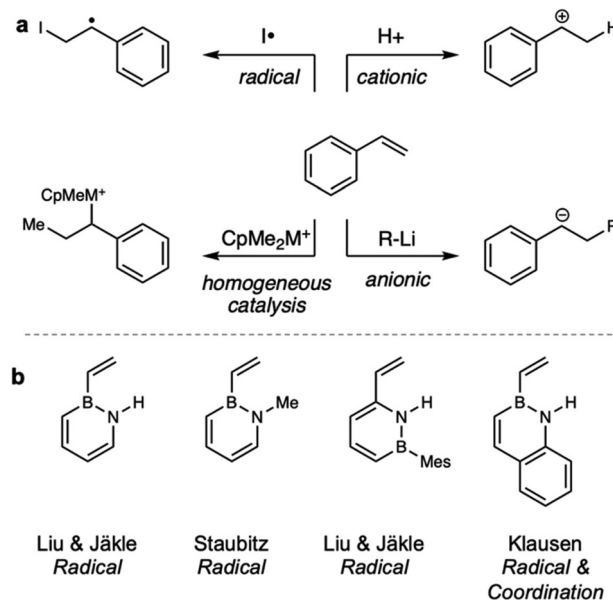


Fig. 1 (a) Benzylic reactive intermediates implicated in styrene polymerization under several distinct mechanistic platforms. (b) Examples of BN styrene mimics and polymerization mechanism.

Table 1 Lewis acid catalysts evaluated for BN2VN cationic polymerization

Entry	Catalyst (mol%)	Solvent	Conversion ^a (%)
1	AlCl ₃	CH ₂ Cl ₂	0
2	BF ₃ ·OEt ₂	CH ₂ Cl ₂	0
3	SnCl ₄	CH ₂ Cl ₂	0

^a Determined by ¹H NMR analysis. See Fig. 2a and Fig. S1–S3.†

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lower degrees of polymerization were found for BN styrene relative to a biphenyl monomer in which the vinyl group was attached to carbon (M_n 1.9 vs. 19.2 kDa).⁹ This was followed by

a report from Staubitz on N-protected BN styrenes, which afforded higher molecular weight polymers upon free radical polymerization (16.5 kDa).¹⁰ BN styrene structural isomers in

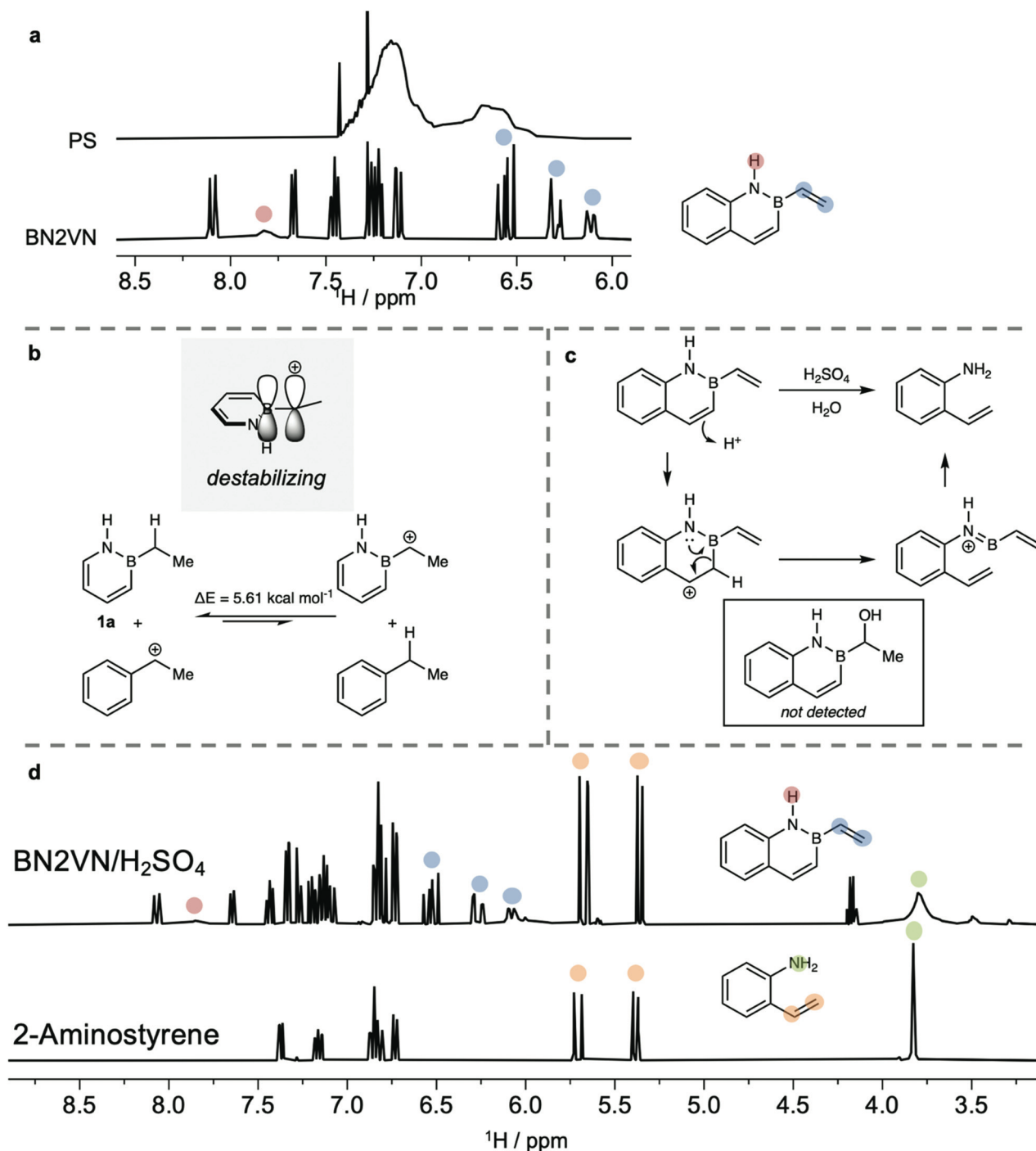


Fig. 2 (a) Cropped ^1H NMR spectra comparing the results of AlCl_3 promoted cationic polymerization of styrene (top) and BN2VN (bottom) after 16 hours. Complete consumption of styrene was observed, while only unreacted BN2VN was observed under the same conditions. The vinyl protons of BN2VN are as indicated. (b) Hypothesis: the benzylic cation could be destabilized by an adjacent empty p-orbital on boron. A hydride transfer reaction provides a computational estimate of the difference in stability between hydrocarbon and BN aromatic benzylic cations. (c) An acid-catalyzed hydration of BN2VN yielded the protodeborination product 2-aminostyrene instead of the targeted secondary alcohol. Geometry optimization and energy calculation were performed at the B3LYP/6-31G(d,p) level of theory.²¹ (d) Superimposed cropped ^1H NMR spectra (400 MHz, CDCl_3) of the unpurified reaction mixture from attempted BN2VN hydration compared to 2-aminostyrene.

which the vinyl group was attached to a carbon atom are also amenable to free radical polymerization.¹¹

Our own group has focused on BN 2-vinylnaphthalene (BN2VN), which has the advantage of a short 2-step synthesis relative to the six-step synthesis of BN styrenes.¹² We have reported gram-scale free radical polymerization, as well as copolymerization with 2-vinylnaphthalene.¹² In subsequent work, we reported free radical copolymerization with activated monomers (*e.g.*, styrene¹³ and methyl methacrylate¹⁴) and postpolymerization oxidative conversion of the BN naphthalene side chain to hydroxyl groups. In support of the aromatic-like reactivity of BN2VN, we reported a close agreement in reactivity ratios between styrene and BN2VN.¹⁵ We also reported the first example of polymerization of a BN aromatic monomer by a non-radical mechanism; we observed highly syndiospecific coordination–insertion polymerization by the action of the cationic complex arising from Cp*TiMe₃/B(C₆F₅)₃.¹⁶ Later work by Cui *et al.* found that Sc-complexes were also effective for syndiospecific polymerization of BN2VN.¹⁷ The stability of BN2VN to coordination polymerization is notable, given the use of highly Lewis acidic complexes such as B(C₆F₅)₃ or methylalumoxane (MAO), and suggested the potential viability of cationic polymerization.

We therefore investigated the polymerization of BN2VN by cationic or anionic initiators. We were motivated to understand both fundamental reactivity – how well do BN aromatic rings stabilize adjacent reactive intermediates – as well as to expand the scope of applicable polymerization methodology and possible polymer architectures. Controlled cationic polymerization can afford well-defined, narrow dispersity polymers and more recently has offered access to highly isotactic polymers.^{18,19} Living anionic polymerization is also well-suited for block copolymer synthesis and control of molecular weight distribution. However, under the conditions tested, we observed instead of vinyl polymerization elimination and substitution reactions of the BN naphthalene ring. The results reported herein expand our understanding of BN aromaticity and the reactivity of azaborine derivatives.

Results and discussion

Cationic polymerization

Initial efforts focused on Lewis acid catalysts, given the observed stability of BN2VN to Lewis acidic coactivators in coordination polymerization.^{16,17} However, a screen of several Al- and B-based Lewis acids known to promote styrene cationic polymerization failed to initiate BN2VN polymerization (Table 1). In contrast to styrene polymerizations conducted as control reactions, only unreacted starting material was observed by ¹H NMR spectroscopy (Fig. 2a).

We hypothesized that cationic polymerization was inhibited by the destabilization of the benzylic cation by the adjacent electron-poor boron atom. We obtained computational support for this hypothesis by calculating the reaction enthalpy of the hydride transfer reaction between ethyl 1,2-aza-

borine **1a** and a benzylic cation (Fig. 2b), which indicated that direct attachment of a 1,2-azaborine to the ethyl group destabilized the benzylic carbocation by 5.61 kcal mol^{−1}.

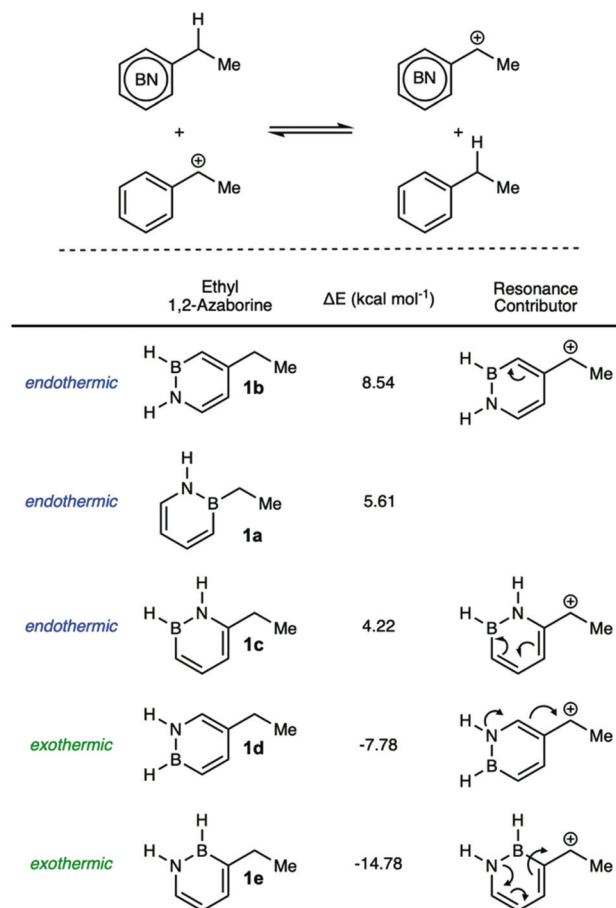


Fig. 3 Enthalpies of reaction for hydride transfer between a benzylic cation and isomeric ethyl 1,2-azaborines. Resonance structures that contribute to cation stabilization or destabilization are shown. Geometry optimization and energy calculation were performed at the B3LYP/6-31G(d,p) level of theory.²¹

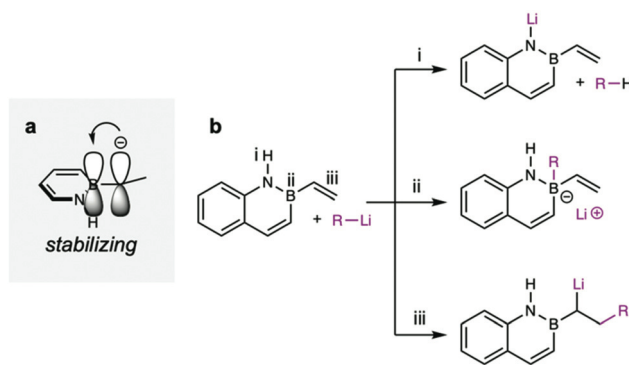
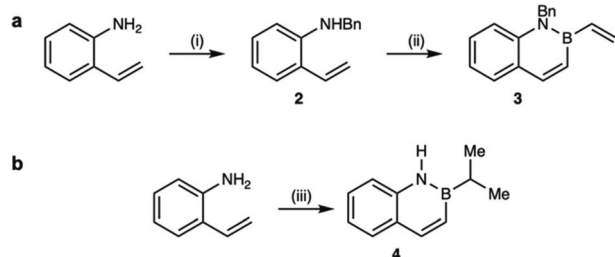


Fig. 4 (a) Hypothesized stabilizing interaction between benzylic anion and a 1,2-azaborine ring. (b) Competitive (i) NH deprotonation and (ii) B-coordination in the anionic polymerization (iii) of BN2VN initiated by an alkyl lithium reagent R-Li.

To further test the hypothesis that the aromatic ring in BN2VN does not afford the same level of stabilization as an aromatic hydrocarbon we attempted the sulfuric acid-catalyzed hydration of BN2VN (Fig. 2c). Instead of the targeted secondary alcohol, we observed protodeborination to 2-aminostyrene, as well as unreacted BN2VN (Fig. 2d). We suggest that protodeborination proceeded by preferential protonation of a C–C bond within the BN naphthalene ring over the vinyl group.



Scheme 1 (a) Synthesis of **3**. (i) PhCHO, NaBH₄, MeOH, rt, 62%; (ii) CH₂CHBF₃K, SiCl₄, 1:1 CPME-toluene, 60 °C, 54%. (b) Synthesis of **4**. (iii) i-PrBF₃K, SiCl₄, NEt₃, 1:1 CPME-toluene, 60 °C, 18 h, 83%. rt = room temperature; CPME = cyclopentyl methyl ether.

Subsequent elimination and hydrolysis provide 2-aminostyrene and an unidentified vinyl boronic acid derivative.

These efforts rationalize the low cationic polymerization reactivity of BN2VN. This may be a general effect for vinyl boron compounds, as Ouchi *et al.* reported that treatment of isopropenyl pinacol boronate with catalytic BF₃·OEt₂ resulted in *ca.* 2% conversion in 24 hours.²⁰

While placement of a boron atom directly adjacent to a vinyl group inhibited cationic polymerization, isomeric BN aromatic rings might favorably position a nitrogen lone pair to stabilize carbocationic character. The difficulty of synthesizing all possible 1,2-azaborine analogs of styrene suggested that computation would be an effective approach for initial evaluation of this hypothesis. Using a similar approach as in Fig. 2b, we investigated the enthalpy of reaction for hydride transfer between a benzylic cation and four additional isomeric ethyl 1,2-azaborines **1b–e**.

We found an extraordinary >20 kcal mol^{−1} range of estimated hydride transfer enthalpies across all isomers (Fig. 3). The isomers **1b** and **1c** were predicted to have endothermic hydride transfer enthalpies, with magnitudes comparable to or greater than the vinyl borane. In both these isomers, resonance structures suggest that the boron position deactivated the benzylic cation by increasing partial positive charge at the

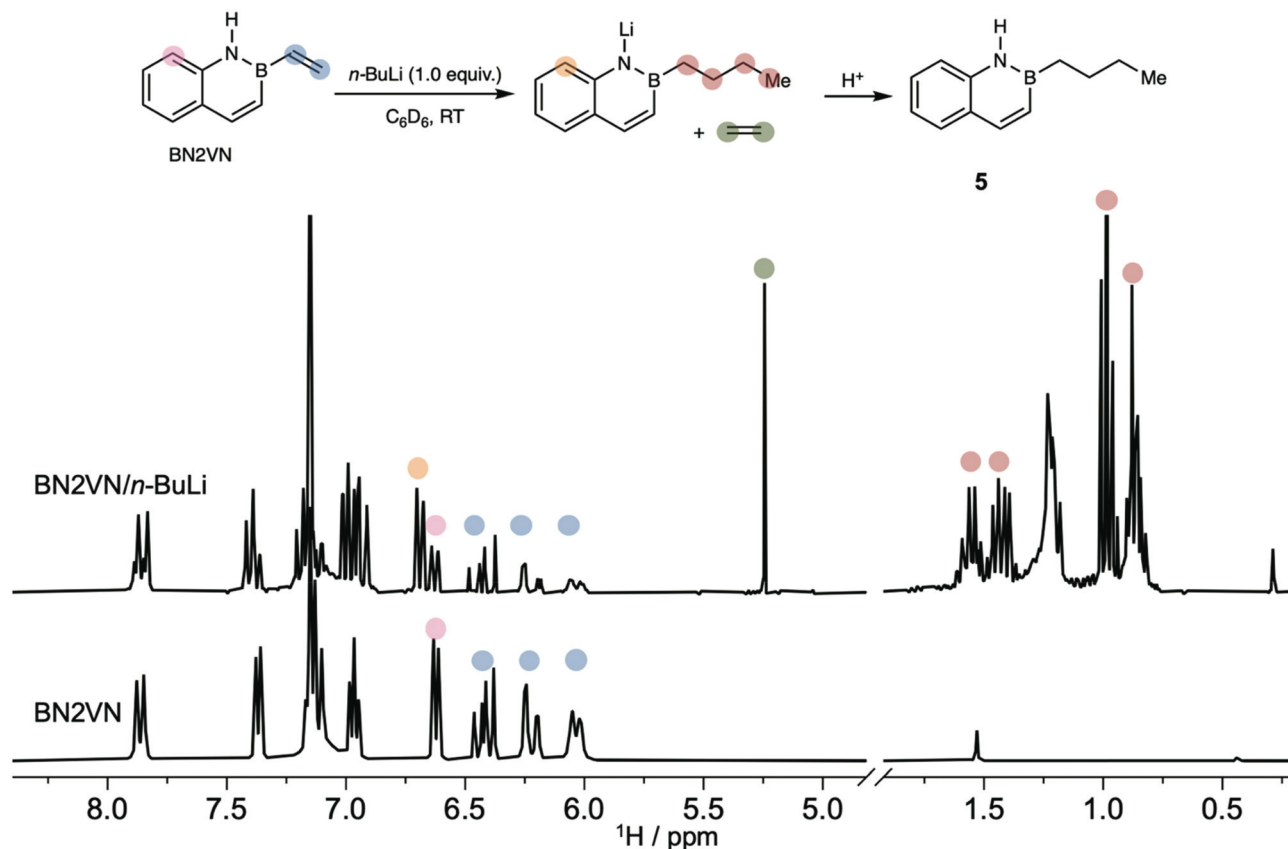
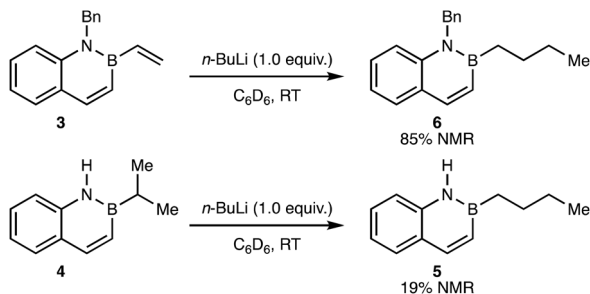


Fig. 5 Reaction of BN2VN with *n*-BuLi. Bottom: BN2VN (400 MHz, C₆D₆, RT); top: *in situ* reaction showing evolution of dissolved ethylene (300 MHz, C₆D₆, RT).



Scheme 2 Nucleophilic aromatic substitution of BN naphthalenes **3** and **4**.

adjacent position. In contrast, the isomers **1d** and **1e** were predicted to have highly exothermic hydride transfers (-7.78 and -14.78 kcal mol $^{-1}$, respectively), indicating that the azaborine ring stabilized the benzylic carbocation relative to a phenyl ring. In contrast to the endothermic reactions, resonance structures suggested a pathway for nitrogen lone pair donation to the carbocation.

These calculations suggest not only design principles for the synthesis of BN styrene mimics amenable to cationic polymerization, but may also have predictive value in other reactions implicating cation character, such as S_N2 reactions of

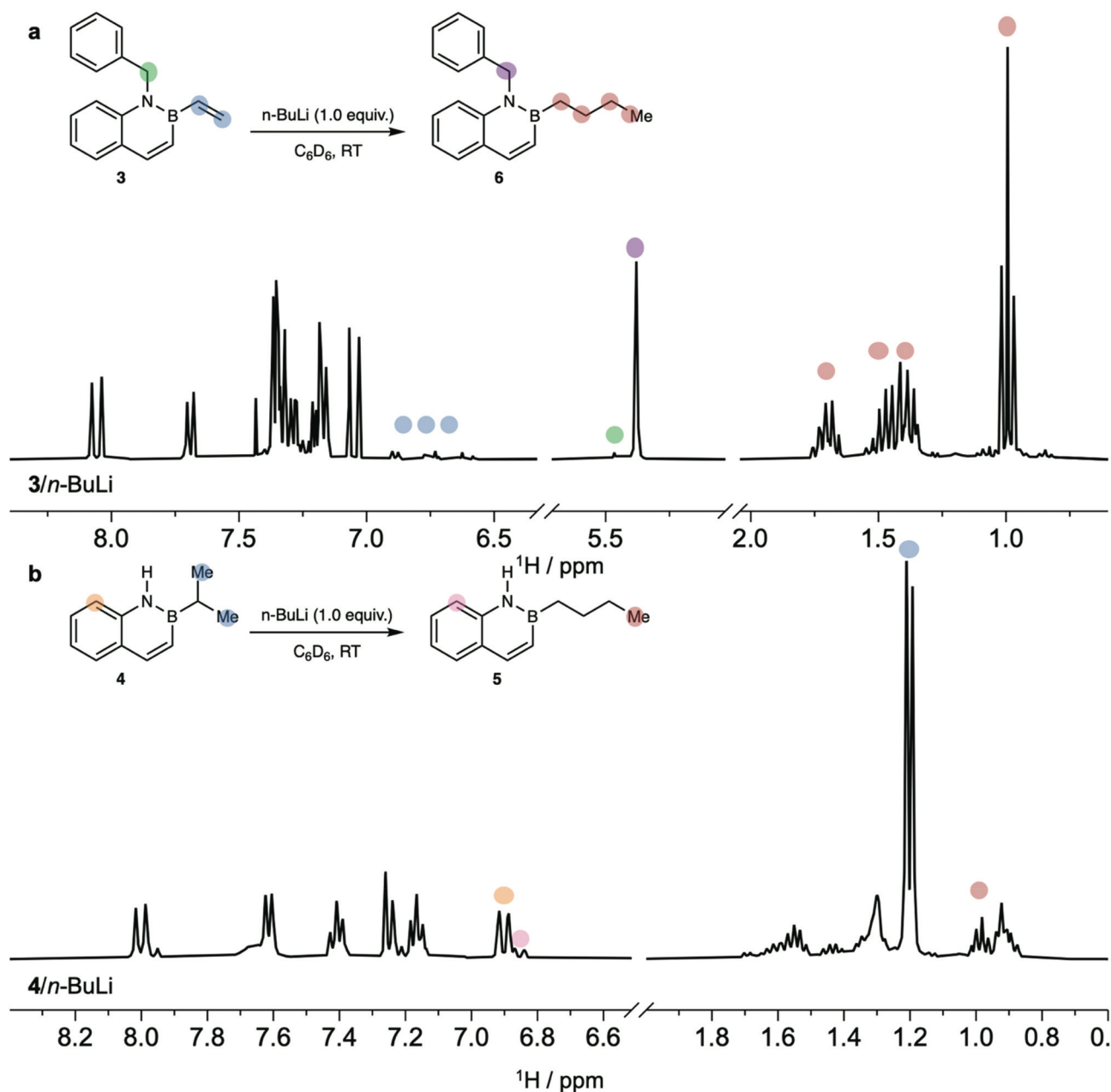


Fig. 6 (a) Cropped 1H NMR spectrum (400 MHz, $CDCl_3$) of the unpurified reaction between **3** and *n*-BuLi showing formation of compound **6**. (b) Cropped 1H NMR spectrum (400 MHz, $CDCl_3$) of the unpurified reaction between **4** and *n*-BuLi showing formation of compound **5**.

benzylic halides. We suggest that any characterization of a Hammett-like parameter must consider BN bond placement within an aromatic framework in considering electrophilicity.

Anionic polymerization

While our experimental and computational data indicated that benzylic cations are destabilized by BN for CC substitution proximal to the cation, a benzylic anion might be stabilized by interaction with a boron acceptor (Fig. 4a). In styrene anionic polymerization, benzylic anions are generated by alkyllithium β -vinyl addition. Extrapolation to BN2VN polymerization seems promising but could be complicated by competing pathways unique to the azaborine structure: NH deprotonation and direct coordination to boron (Fig. 4b). NH-deprotonation of monocyclic 1,2-azaborines has previously been reported by Ashe (pK_a ca. 26)²² and Liu⁵ using lithium diisopropylamide (LDA) and lithium tetramethylpiperidine (LiTMP). Liu and Dixon also investigated the reaction of monocyclic 1,2-dihydro-1,2-azaborines with alkyllithiums, which underwent substitution at boron *via* a mechanism hypothesized to involve both deprotonation and quaternization (pathways I and ii).²³

To account for potential deprotonation, we therefore also synthesized **3**, an *N*-benzyl protected analog of BN2VN (Scheme 1). The synthesis proceeded by reductive amination of 2-aminostyrene to yield *N*-Bn **2**, followed by borylation with

vinyl potassium trifluoroborate using a protocol adapted from Molander to give **3**.²⁴ We also synthesized isopropyl-functionalized **4**.

We began investigation of the ionic reactivity of BN2VN using a stoichiometric equivalent of *n*-butyllithium in an NMR-scale reaction (*n*-BuLi (1.0 equiv.), C_6D_6). We observed in the 1H NMR spectrum the growth of a sharp singlet at δ 5.23 consistent with dissolved ethylene (Fig. 5).²⁵ Residual BN2VN was observed (31.4%), as well as a new BN naphthalene lacking vinylic peaks (68.5% NMR yield). The alkyl region showed butyl-containing fragments. After an aqueous work-up and column chromatography, compound **5** was isolated (33% yield).

Ethylene likely arose from the decomposition of a quaternary boronate intermediate (Fig. 4b, pathway ii). This was surprising as the addition of *n*-butyllithium to vinylboronic pinacol ester results in a stable quaternary boronate complex²⁶ that can be employed in subsequent palladium-catalyzed 1,2-metallate rearrangements²⁷ or radical-polar crossover reactions.²⁶ The quaternary BN2VN/*n*-BuLi adduct may be destabilized relative to pinacol esters as quaternization dearomatizes the 1,2-azaborine motif.

To shed further light on the mechanism of ethylene elimination, we also investigated the reactivity of **3** and **4** with *n*-BuLi (Scheme 2). After aqueous workup, we observed that substi-

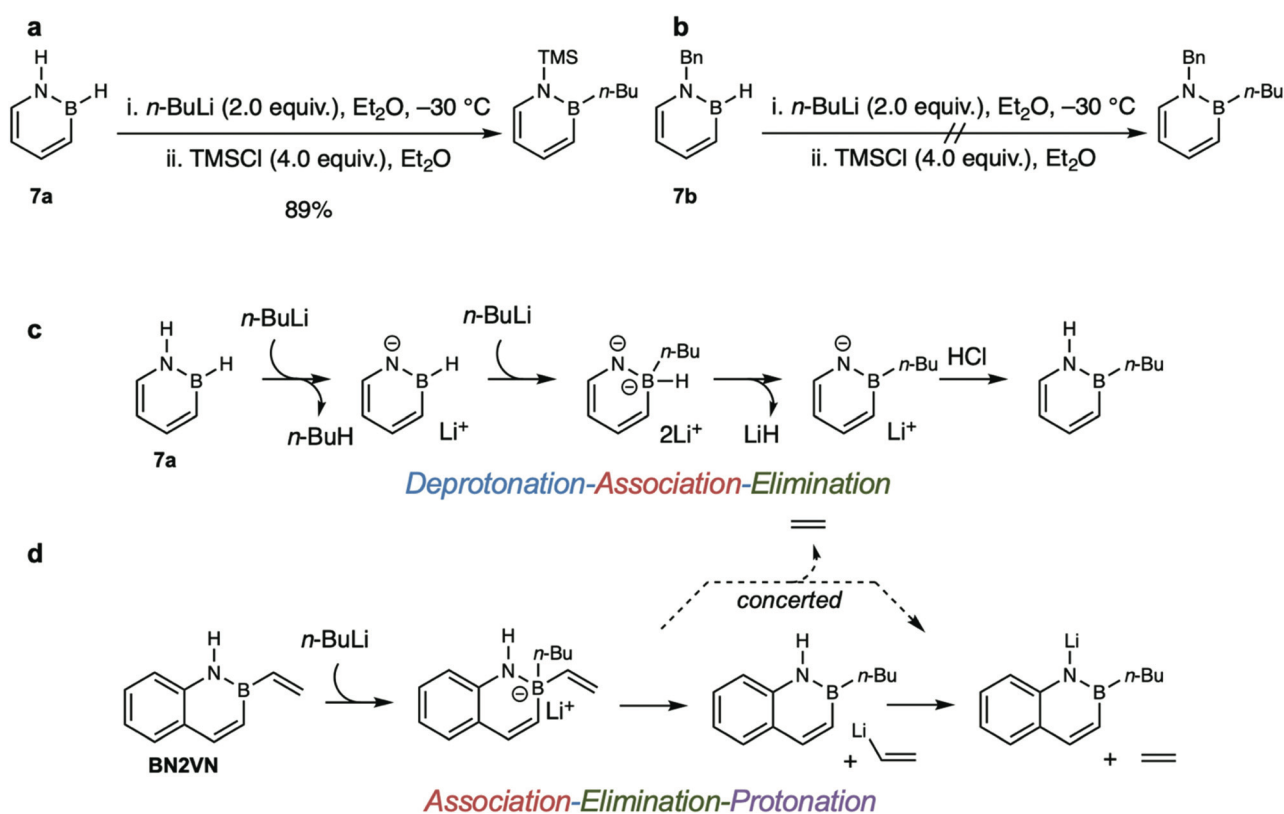


Fig. 7 Prior work by Liu. (a) Nucleophilic aromatic substitution of 1,2-dihydro-1,2-azaborine **6a**.²³ (b) Failed nucleophilic aromatic substitution of *N*-Bn **6b**.²³ (c) Hypothesized mechanism for nucleophilic aromatic substitution of 1,2-azaborines. (d) Proposed mechanism of nucleophilic aromatic substitution of BN2VN.

tution had occurred, with the vinyl group of **3** replaced with a butyl group (85% NMR yield, Fig. 6a) and the isopropyl group of **4** replaced with a butyl group (19% NMR yield, Fig. 6b). Mass spectrometry confirmed formation of the substitution products **6** and **5** (Fig. S4†).

These observations are distinct from the closely related work by Liu on the reaction of 1,2-dihydro-1,2-azaborine with *n*-butyllithium.²³ For 1,2-dihydro-1,2-azaborine **7a**, nucleophilic aromatic substitution was found to occur with selective functionalization at boron and nitrogen (Fig. 7a). In contrast, the N-Bn protected compound **7b** did not undergo nucleophilic aromatic substitution (Fig. 7b); a non-aromatic quaternary borane was identified by ¹¹B NMR spectroscopy (δ -3.9). Interestingly, nucleophilic aromatic substitution of **7a** also proceeded with alkoxide nucleophiles (e.g. NaOt-Bu), which are insufficiently basic to deprotonate the NH (1,2-dihydro-1,2-azaborine, pK_a ca. 26 vs. *t*-BuOH pK_a ca. 29 in DMSO). For alkyl-lithiums, Liu and Dixon suggested a mechanism involving first NH-deprotonation then an associative substitution mechanism proceeding through a stepwise addition-elimination sequence (Fig. 7c). Calculations indicated that formation of a benzyne-like intermediate was significantly uphill. However, the result with alkoxides demonstrated that deprotonation is not required for nucleophilic aromatic substitution.

Given our observation of successful BN2VN substitution with only one equivalent *n*-BuLi and with N-protected systems, we suggest that for BN naphthalenes, the associative mechanism proceeds without initial NH deprotonation (Fig. 7d). Formation of ethylene could proceed *via* concerted or stepwise elimination and deprotonation. A stepwise sequence is suggested based on the successful nucleophilic aromatic substitution of N-Bn **3**, which cannot directly eliminate ethylene. The BN2VN NH is proposed as a proton source for the vinyl-lithium $\rightarrow$ ethylene process; in the case of **3**, vinyl-lithium protonation could occur during work-up. The substitution reaction with B-*i*Pr **4** showed that elimination is not limited to C(sp²) carbanions, as 2-lithiopropene would be formed.^{28,29}

We suggest that the outcomes herein may reflect kinetic phenomena. As the pK_a of BN2VN is likely similar to 1,2-dihydro-1,2-azaborine **7a**, boron quaternization may be faster than the acid-base reaction between BN2VN and *n*-butyllithium. Elimination of a carbanion from the quaternary boronate may be accelerated by a drive to restore BN aromaticity, rationalizing the distinction from well-developed pinacol borane lithiation-rearrangement chemistry. Future work will investigate if changes in alkyl-lithium structure may decelerate the quaternization pathways relative to vinyl addition.

Conclusions

Herein, we described the ionic reactivity of BN2VN and related BN naphthalenes with a goal of exploring the influence of BN for CC bond substitution on the fundamental reactivity of benzylic ions. We found that BN2VN did not undergo olefin protonation, either during attempted Lewis acid-catalyzed cat-

ionic polymerization or under acid-catalyzed hydration. Computational studies point to a strong influence of the position of BN for CC bond substitution on the stability of benzylic cations. These results suggest that isomeric BN styrenes may undergo cationic polymerization, although synthetic access to those substitution patterns is not yet straightforward.

The reactivity of BN2VN and two related BN naphthalenes towards *n*-BuLi was also investigated. Instead of deprotonation or vinyl addition, clean addition-elimination resulting in nucleophilic aromatic substitution at boron was observed. Future work will explore the influence of anion steric bulk on the balance between competing anionic reactivity pathways.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- 1 P. G. Campbell, A. J. V. Marwitz and S.-Y. Liu, *Angew. Chem., Int. Ed.*, 2012, **51**, 6074–6092.
- 2 Z. X. Giustra and S. Y. Liu, *J. Am. Chem. Soc.*, 2018, **140**, 1184–1194.
- 3 M. J. D. Bosdet and W. E. Piers, *Can. J. Chem.*, 2009, **87**, 8–29.
- 4 M. J. S. Dewar and R. Dietz, *J. Chem. Soc.*, 1959, 2728–2730.
- 5 E. R. Abbey, A. N. Lamm, A. W. Baggett, L. N. Zakharov and S. Y. Liu, *J. Am. Chem. Soc.*, 2013, **135**, 12908–12913.
- 6 P. G. Campbell, E. R. Abbey, D. Neiner, D. J. Grant, D. A. Dixon and S.-Y. Liu, *J. Am. Chem. Soc.*, 2010, **132**, 18048–18050.
- 7 H. L. van de Wouw and R. S. Klausen, *J. Org. Chem.*, 2019, **84**, 1117–1125.
- 8 J. Pan, J. W. Kampf and A. J. Ashe, *J. Organomet. Chem.*, 2009, **694**, 1036–1040.
- 9 W.-M. Wan, A. W. Baggett, F. Cheng, H. Lin, S.-Y. Liu and F. Jäkle, *Chem. Commun.*, 2016, **52**, 13616–13619.
- 10 B. Thiedemann, P. J. Gliese, J. Hoffmann, P. G. Lawrence, F. D. Sönnichsen and A. Staubitz, *Chem. Commun.*, 2017, **53**, 7258–7261.
- 11 H. Lin, C. R. McConnell, B. Jilus, S. Y. Liu and F. Jäkle, *Macromolecules*, 2019, **52**, 4500–4509.
- 12 H. L. van de Wouw, J. Y. Lee and R. S. Klausen, *Chem. Commun.*, 2017, **53**, 7262–7265.
- 13 H. L. van de Wouw, J. Y. Lee, E. C. Awuyah and R. S. Klausen, *Angew. Chem., Int. Ed.*, 2018, **57**, 1673–1677.
- 14 Y. Ji, T. Zhou, H. L. Van De Wouw and R. S. Klausen, *Macromolecules*, 2020, **53**, 249–255.
- 15 H. L. van de Wouw, E. C. Awuyah, J. I. Baris and R. S. Klausen, *Macromolecules*, 2018, **51**, 6359–6368.

- 16 S. N. Mendis, T. Zhou and R. S. Klausen, *Macromolecules*, 2018, **51**, 6859–6864.
- 17 J. Huang, Y. Jiang, Z. Zhang, S. Li and D. Cui, *Macromol. Rapid Commun.*, 2020, **41**, 2000038.
- 18 A. J. Teator and F. A. Leibfarth, *Science*, 2019, **363**, 1439–1443.
- 19 P. C. Knutson, A. J. Teator, T. P. Varner, C. T. Kozuszek, P. E. Jacky and F. A. Leibfarth, *J. Am. Chem. Soc.*, 2021, **143**, 16388–16393.
- 20 T. Nishikawa and M. Ouchi, *Angew. Chem., Int. Ed.*, 2019, **58**, 12435–12439.
- 21 C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys.*, 1988, **37**, 785–789.
- 22 J. Pan, J. W. Kampf and A. J. Ashe, *Organometallics*, 2004, **23**, 5626–5629.
- 23 A. N. Lamm, E. B. Garner, D. A. Dixon and S.-Y. Liu, *Angew. Chem., Int. Ed.*, 2011, **50**, 8157–8160.
- 24 S. R. Wisniewski, C. L. Guenther, O. A. Argintaru and G. A. Molander, *J. Org. Chem.*, 2014, **79**, 365–378.
- 25 G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176–2179.
- 26 M. Kischewitz, K. Okamoto, C. Mück-Lichtenfeld and A. Studer, *Science*, 2017, **355**, 936–938.
- 27 L. Zhang, G. J. Lovinger, E. K. Edelstein, A. A. Szymaniak, M. P. Chierchia and J. P. Morken, *Science*, 2016, **351**, 70–74.
- 28 R. E. Dessy, W. Kitching, T. Psarras, R. Salinger, A. Chen and T. Chivers, *J. Am. Chem. Soc.*, 1966, **88**, 460–467.
- 29 D. E. Applequist and D. F. O. Brien, *J. Am. Chem. Soc.*, 1963, **85**, 743–748.