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Azaborine Isomer Effects on Benzylic Ion Stability and Reactivity: Consequences for BN2VN Ionic Polymerization

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ARTICLE

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 (Figure 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 approaches[5] 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 (Figure 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 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 which the vinyl group was attached to a carbon atom are also amenable to free radical polymerization.[11]

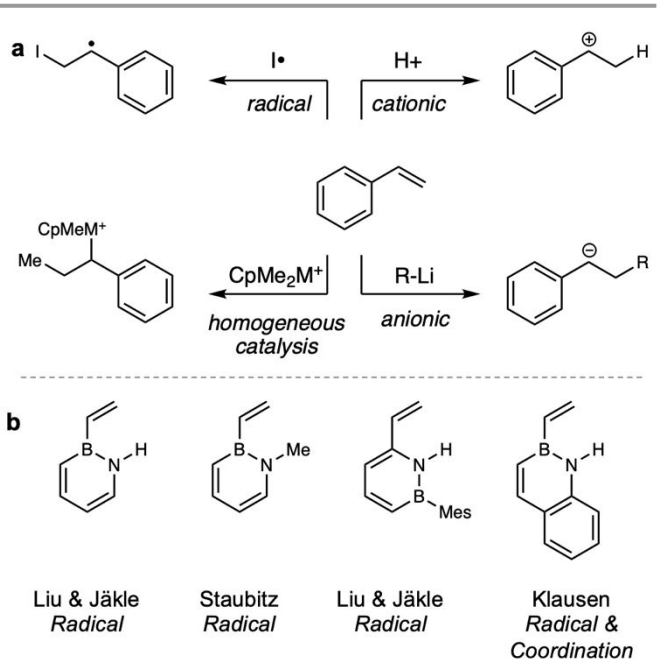

Figure 1. a) Benzylic reactive intermediates implicated in styrene polymerization under several distinct mechanistic platforms. b) Examples of BN styrene mimics and polymerization mechanism.

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., styrene[13] and methyl methacrylate[14]) and

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postpolymerization oxidative conversion of the BN naphthalene side chain to hydroxyl groups. In support of the aromatic-like

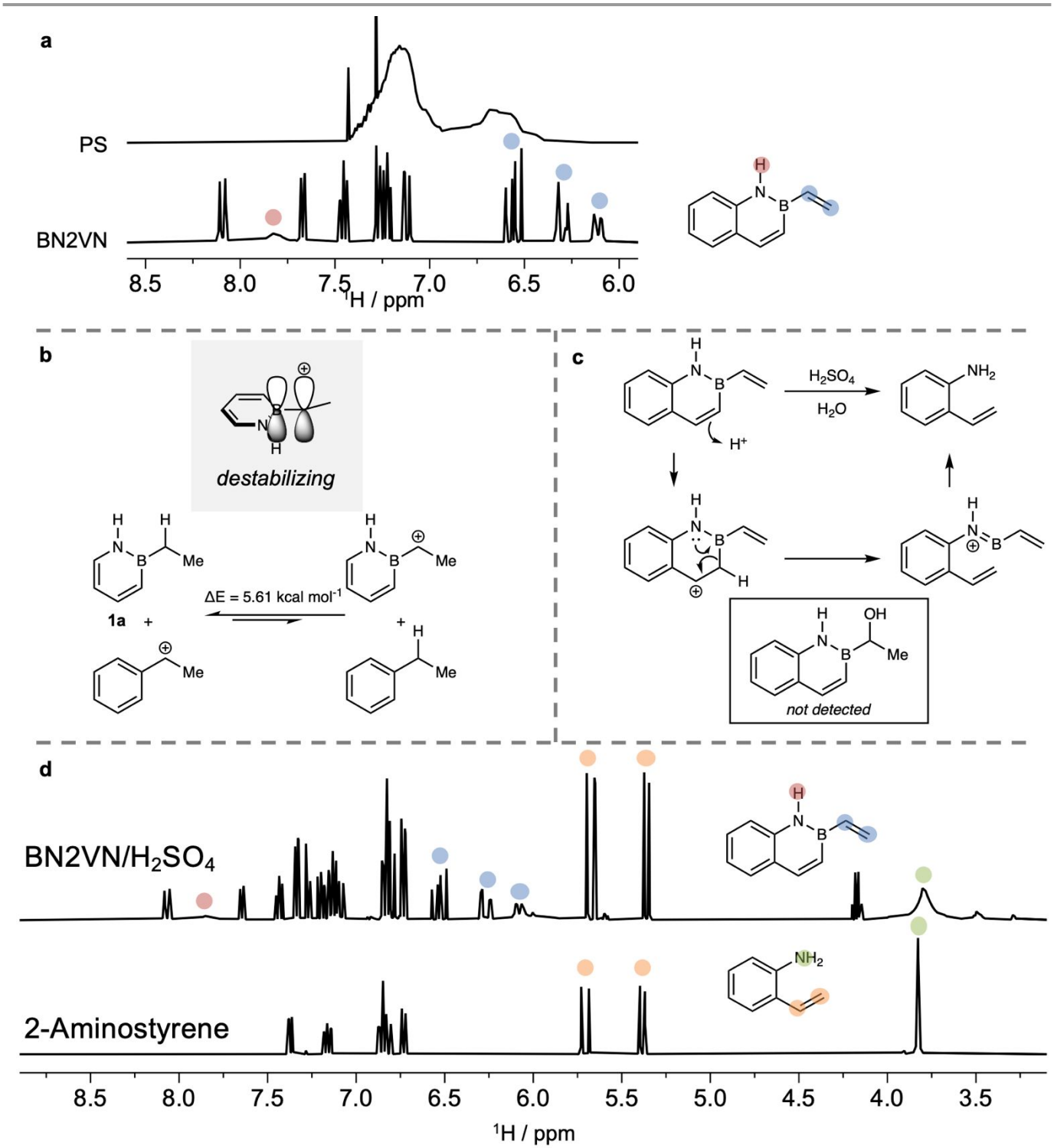


Figure 2. a) Cropped ^{1}H NMR spectra comparing the results of $AlCl_3$ promoted cationic polymerization of styrene (top) and BN2VN (bottom) after 16 hours. Complete consumption of styrene was observed, while only unreacted BN2VN was observed under the same conditions. The vinyl protons of BN2VN are 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 ^{1}H NMR spectra (400 MHz, $CDCl_3$) of the unpurified reaction mixture from attempted BN2VN hydration compared to 2-aminostyrene.

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 syndioselective coordination-insertion polymerization by the action of the cationic complex arising from $Cp^*TiMe_3/B(C_6F_5)_3$.[16] Later work

by Cui et al. found that Sc-complexes were also effective for syndioselective polymerization of BN2VN.[17] The stability of BN2VN to coordination polymerization is notable, given the use of highly Lewis acidic complexes such as $B(C_6F_5)_3$ 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 ^{1}H NMR spectroscopy (Figure 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-azaborine **1a** and a benzylic cation (Figure 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}.

Table 1. Lewis acid catalysts evaluated for BN2VN cationic polymerization.

Entry	Catalyst (mol%)	Solvent	Conversion (%)[a]
1	$AlCl_3$	CH_2Cl_2	0
2	BF_3•OEt_2	CH_2Cl_2	0
3	SnCl4	CH_2Cl_2	0

[a] Determined by ^{1}H NMR analysis. See Figure 2a and Figures S1-S3.

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 (Figure 2c). Instead of the targeted secondary alcohol, we observed protodeborination to 2-aminostyrene, as well as unreacted BN2VN (Figure 2d). We suggest that protodeborination proceeded by preferential protonation of a C–C bond within the BN naphthalene ring over the vinyl group. 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 BF_3•OEt_2 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 Figure 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 (Figure 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 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 benzylic halides. We suggest that any characterization of a Hammett-like parameter must consider BN bond placement within an aromatic framework in considering electrophilicity.

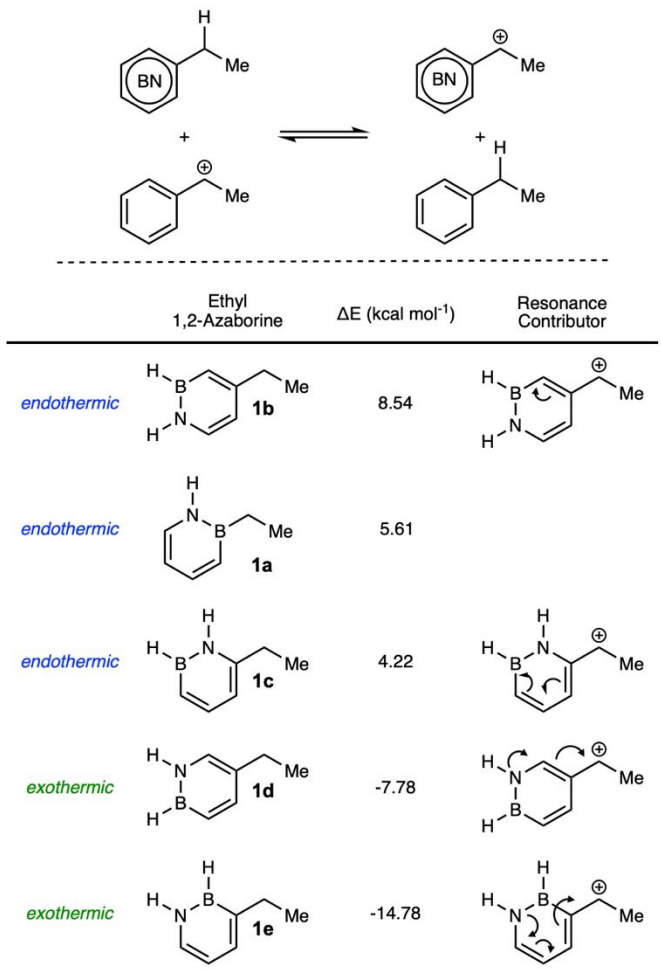


Figure 3. Enthalpies of reaction for hydride transfer between a benzylic cation and isomeric ethyl 1,2-azaborines. Resonance structures that contribute to cation stabilization or destabilization are shown. Geometry optimization and energy calculation were performed at the B3LYP/6-31G(d,p) level of theory.[21]

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 (Figure 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 (Figure 4b). NH-deprotonation of monocyclic 1,2-azaborines has previously been reported by Ashe (pKa ca. 26)[22] and Liu[5] 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 deportation and quaternization (pathways I and ii).[23]

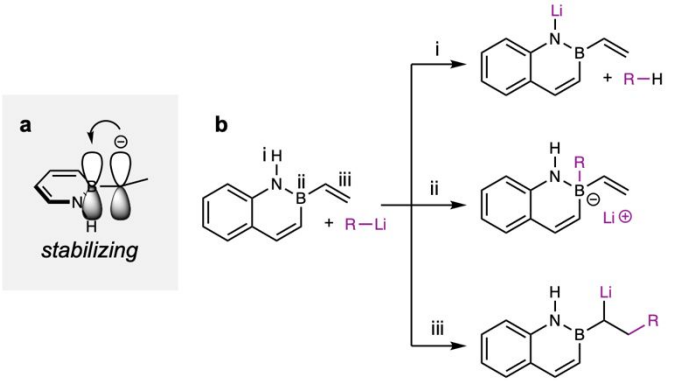
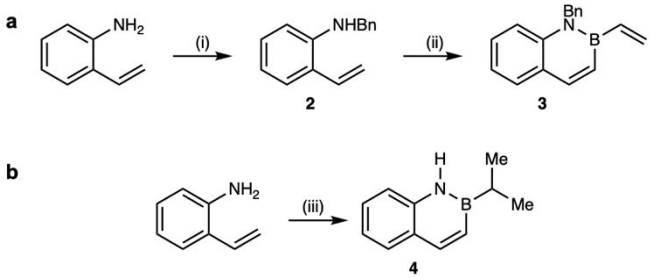


Figure 4. a) Hypothesized stabilizing interaction between benzylic anion and a 1,2-azaborine ring. b) Competitive (i) NH deprotonation and (ii) B-coordination in the anionic polymerization (iii) of BN2VN initiated by an alkyllithium reagent R–Li.

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 ^{1}H NMR spectrum the growth of a sharp singlet at δ 5.23 consistent with dissolved ethylene (Figure 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).



Scheme 1. (a) Synthesis of **3**. (i) PhCHO, $NaBH_4$, MeOH, rt, 62%; (ii) CH_2CHBF_3K, $SiCl_4$, 1:1 CPME-toluene, 60 °C, 54%. (b) Synthesis of **4**. (iii) *i*-$PrBF_3K$, $SiCl_4$, NEt_3, 1:1 CPME-toluene, 60 °C, 18 h, 83%. rt = room temperature; CPME = cyclopentyl methyl ether.

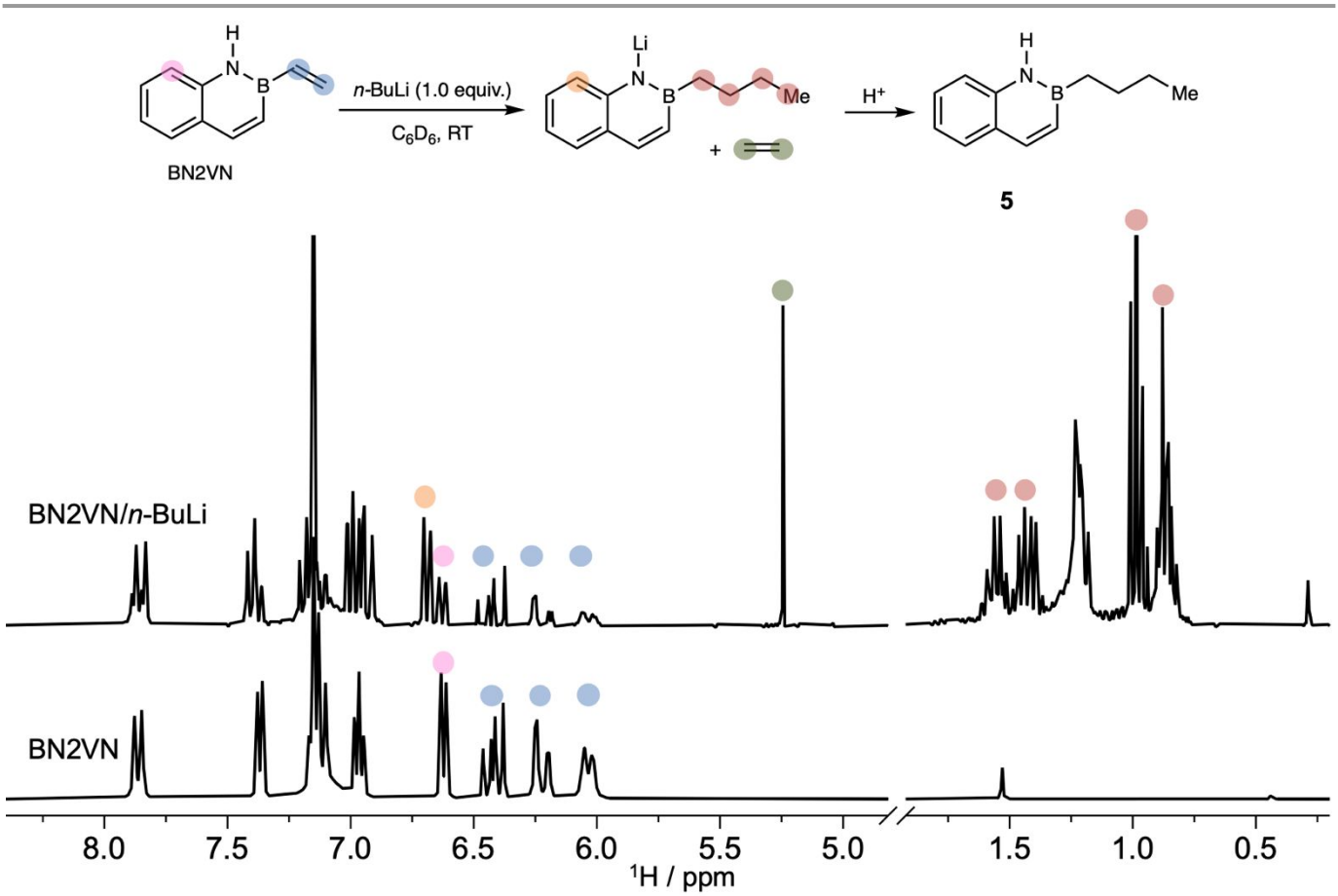
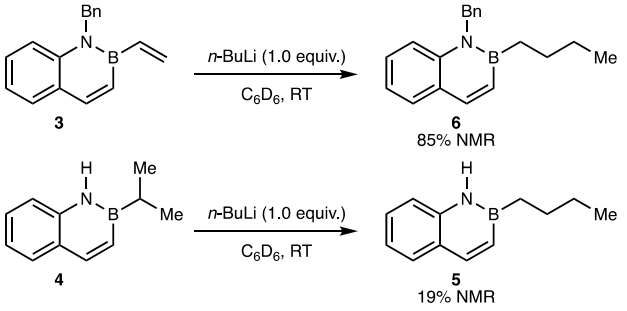


Figure 5. Reaction of BN2VN with *n*-BuLi. Bottom: BN2VN (400 MHz, C_6D_6, RT); top: *in situ* reaction showing evolution of dissolved ethylene (300 MHz, C_6D_6, RT).

Ethylene likely arose from the decomposition of a quaternary boronate intermediate (Figure 4b, pathway ii). This was surprising as the addition of n-butyllithium to vinylboronic pinacol ester results in a stable quaternary boronate complex[26] that can be employed in subsequent palladium-catalyzed 1,2-metallate rearrangements[27] 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 substitution had occurred, with the vinyl group of **3** replaced with a butyl group (85% NMR yield, Figure 6a) and the isopropyl group of **4** replaced with a butyl group (19% NMR yield, Figure 6b). Mass spectrometry confirmed formation of the substitution products **6** and **5** (Figure S4).



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

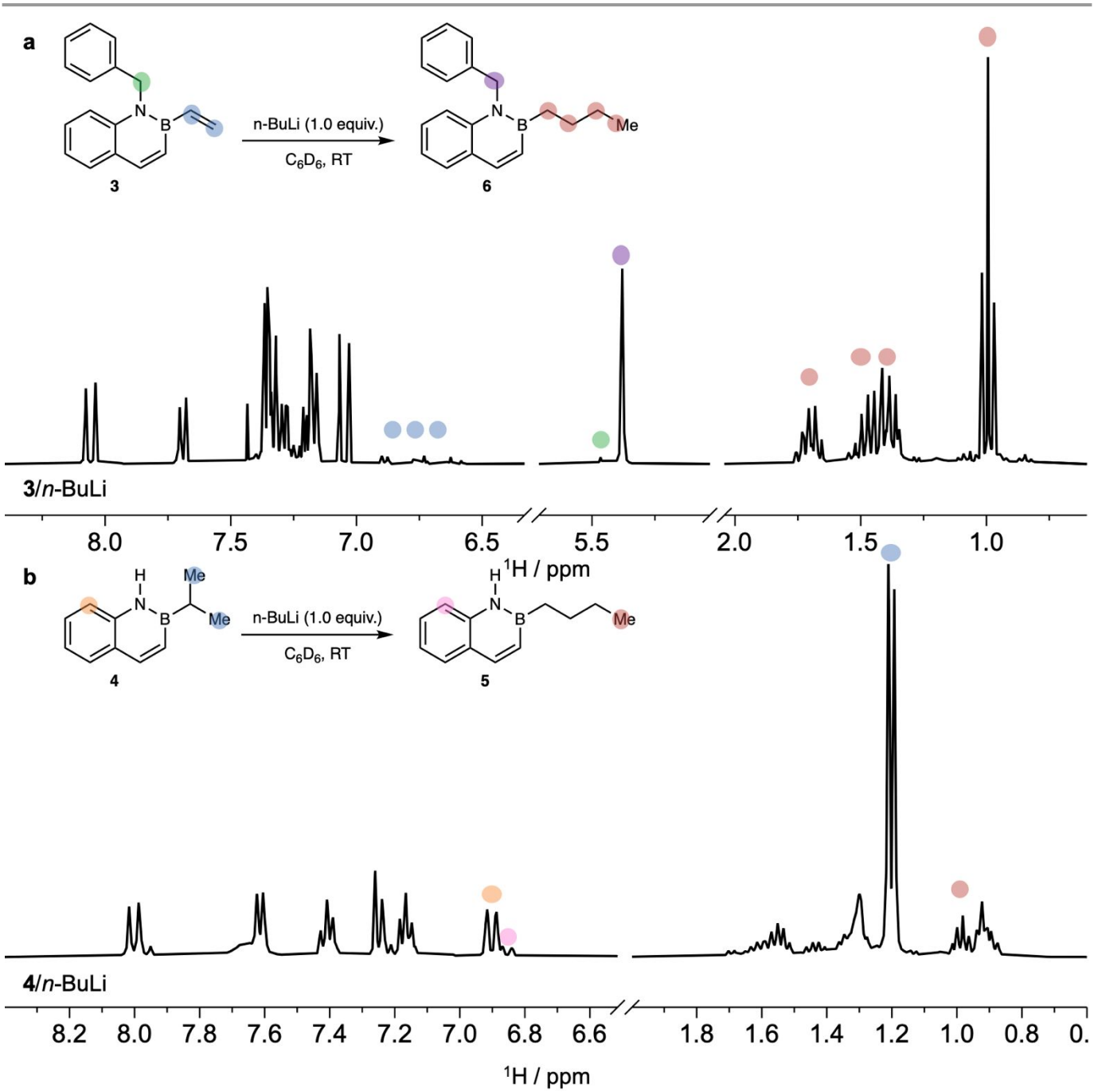


Figure 6. a) Cropped ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of the unpurified reaction between **3** and *n*-BuLi showing formation of compound **6**. b) Cropped ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of the unpurified reaction between **4** and *n*-BuLi showing formation of compound **5**.

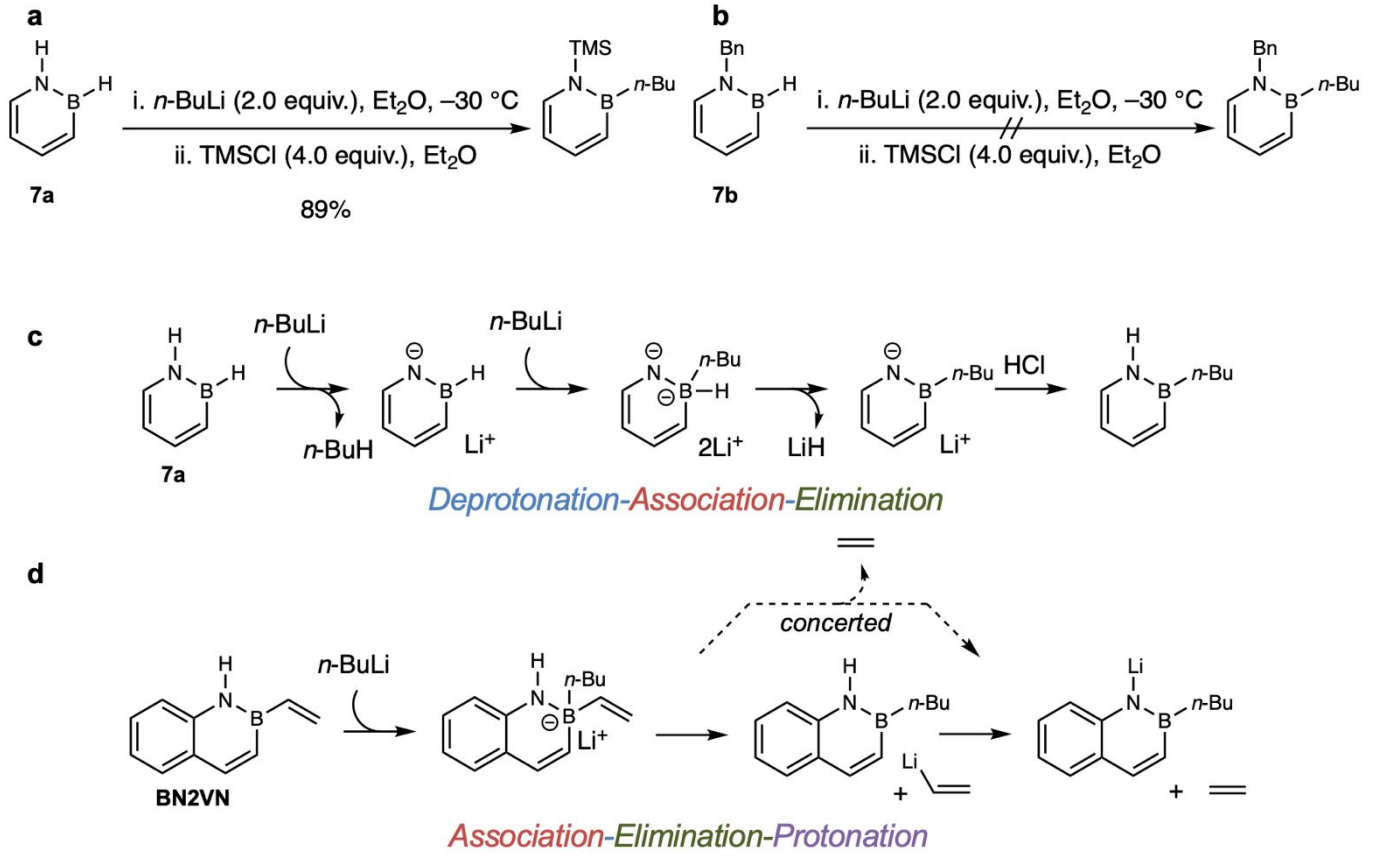


Figure 7. Prior work by Liu. a) Nucleophilic aromatic substitution of 1,2-dihydro-1,2-azaborine **6a**.[23] b) Failed nucleophilic aromatic substitution of N-Bn **6b**.[23]l c) Hypothesized mechanism for nucleophilic aromatic substitution of 1,2-azaborines. d) Proposed mechanism of nucleophilic aromatic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

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 (Figure 7a). In contrast, the N-Bn protected compound **7b** did not undergo nucleophilic aromatic substitution (Figure 7b); a non-aromatic quaternary borane was identified by ^{11}B NMR spectroscopy (δ –3.9). Interestingly, nucleophilic aromatic substitution of **7a** also proceeded with alkoxide nucleophiles (e.g. NaO*t*-Bu), which are insufficiently basic to deprotonate the NH (1,2-dihydro-1,2-azaborine, pKa ca. 26 vs. *t*-BuOH pKa ca. 29 in DMSO). For alkyllithiums, Liu and Dixon suggested a mechanism involving first NH-deprotonation then an associative substitution mechanism proceeding through a stepwise addition-elimination sequence (Figure 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 (Figure 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 vinyllithium → ethylene process; in the case of **3**, vinyllithium protonation could occur during work-up. The substitution reaction with B-*i*Pr **4** showed that elimination is not limited to C(sp^2) carbanions, as 2-lithiopropane would be formed.[28,29]

We suggest that the outcomes herein may reflect kinetic phenomena. As the pKa of BN2VN is likely similar to 1,2-dihydro-1,2azaborine **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 alkyllithium 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 cationic

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.

Acknowledgements

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