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Communication

A BN-Benzvalene

Tomoya Ozaki, Sierra K. Bentley, Nina Rybansky, Bo Li, and Shih-Yuan Liu*

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ABSTRACT: The synthesis and crystallographic characterization of BN-benzvalene, the first second-row heteroatom-containing benzvalene, is described. BN-benzvalenes are produced via photoexcitation of C5-aryl-substituted 1,2-azaborines under flow conditions. Mechanistic studies support a boron-specific, two-step photoisomerization pathway involving a BN-Dewar benzene intermediate, which is distinct from the photoisomerization pathway proposed in benzene and phospha- and silabenzenes for the formation of their respective benzvalene analogues.

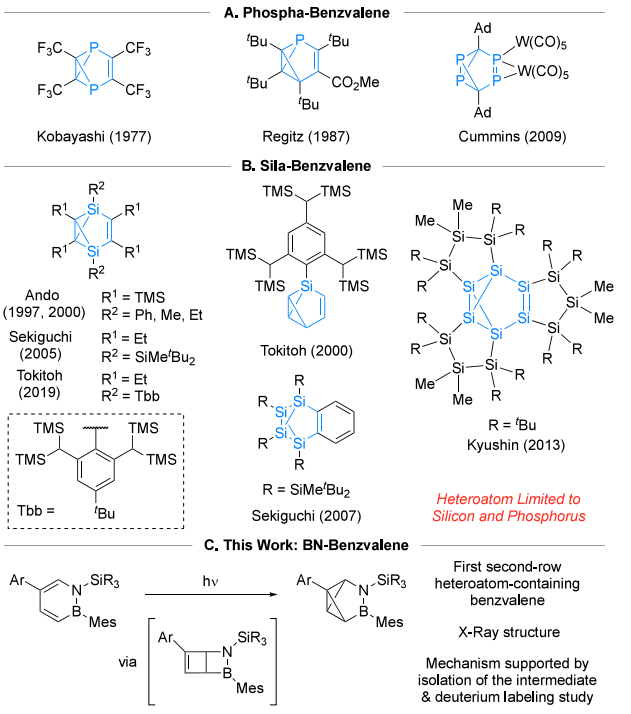
Benzene has four valence isomers:[1] benzvalene,[2] Dewar benzene,[3] prismane,[4] and bicyclopropenyl.[5] Among them, benzvalene has captured the attention of synthetic chemists due to its unique bonding and reactivity.[2] The development of a practical and facile synthesis of benzvalene by Katz[6] has led to the access to additional strained hydrocarbon scaffolds, including bicyclo[1.1.1]pentane[7,8] and bicyclo[2.1.1]hexane[9] derivatives that are of current interest as 3D bioisosteres of benzene in medicinal chemistry.[10]

In comparison to the carbonaceous benzvalene, main group heteroatom-containing benzvalene derivatives have been less developed. Kobayashi pioneered the first example in 1977 by synthesizing the 1,4-diphosphabenzvalene through the photoisomerization of 1,4-diphosphabenzene.[11] Subsequently, Regitz,[12] Ando,[13] Tokitoh,[14] Sekiguchi,[15] Cummins,[16] and Kyushin[17] et al. independently synthesized additional phosphorus- and silicon-containing benzvalenes (Schemes 1A and 1B).[18] Conspicuously, second-row element (B, N, O) heteroatom-containing benzvalenes have remained elusive to date.[19] Arguably, the involvement of heavier and larger third-row main group elements (P and Si) reduces the resonance stabilization (due to weak π-bonding) of the corresponding heteroarenes and attenuates the ring strain, resulting in some thermodynamic driving force for the formation of the heavier heteroatom-containing benzvalene structures.[17c,20]

In this Communication, we report the first example of a second-row heteroatom-containing benzvalene. Specifically, we describe the synthesis, characterization, and initial reactivity studies of the boron- and nitrogen-containing BN-benzvalene (Scheme 1C). Deuterium labeling analysis is consistent with a distinct mechanism that involves a corresponding Dewar valence isomer species (BN-Dewar benzene) as an intermediate that undergoes a photoinduced 1,2-boron shift to furnish the observed BN-benzvalene.

Our group has had a long-standing interest in the synthetic development and applications of 1,2-azaborines,[21] which are boron(B)−nitrogen(N) containing isosteres of benzene. In collaboration with the Bettinger group, we discovered that 1,2-azaborine undergoes a clean photoisomerization to BN-Dewar benzene upon UV light irradiation ($h\nu$ > 280 nm).[22]

Scheme 1. Main Group Heteroatom-Containing Benzvalenes



Subsequently, the BN-Dewar benzene species has been investigated as potential molecular solar thermal fuels,[23,24] new synthetic building blocks for 1,2-aminoborylated cyclobutane derivatives,[25] and as a monomer for ring-opening metathesis polymerization.[26] During our investigation of the

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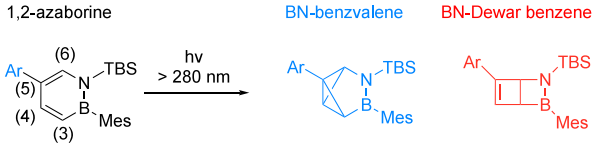
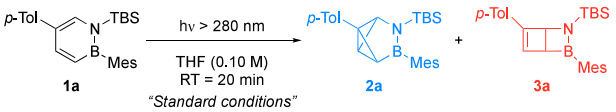
photochemistry of 1,2-azaborines, we discovered that a C5-aryl-functionalized 1,2-azaborine (with *N*-TBS and *B*-Mes substitution) produced the BN-benzvalene isomer in addition to the BN-Dewar isomer upon photolysis (Scheme 2).

Scheme 2. Initial Discovery



To optimize the formation of BN-benzvalene, we selected C5-*p*-Tol-*N*-TBS-*B*-Mes-1,2-azaborine **1a** as a model substrate using a Vapourtec UV-150 continuous-flow photochemical reactor with adjustable irradiation wavelength (by applying select filters to a mercury lamp). As can be seen from Table 1, we determined that 280 nm UV irradiation with a residence time (RT) of 20 min in THF (0.10 M) was optimal for the generation of BN-benzvalene.

Table 1. Optimization of the Photoisomerization



Entry	Variations from "standard conditions"	Conv. (%)[a]	2a	3a
1	None	>99	88	0
2	RT = 10 min	76	28	41
3	RT = 50 min	>99	81	0
4	hv > 300 nm	53	6	43
5	hv > 260 nm	>99	76	0
6	hexane, RT = 50 min	>99	77	0
7	CH_2Cl_2	93	56	21
8	0.50 mmol, RT = 50 min	>99	87 (80)	0
9	0.50 mmol, RT = 50 min, hv > 300 nm	62	7	53 (44)

[a]Yields were determined by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. Scale: 0.10 mmol, unless otherwise stated. Yields of isolated product are reported in parentheses. RT: residence time.

Under these conditions, we obtained BN-benzvalene **2a** in 88% yield without the formation of BN-Dewar benzene **3a** as a byproduct (Table 1, entry 1). Shortening the residence time (entry 2) or using a longer wavelength (entry 4) resulted in incomplete conversion, with BN-Dewar benzene **3a** being the major observed product. On the other hand, extending the residence time (entry 3) or using a shorter wavelength (entry 5) resulted in a slightly reduced yield of BN-benzvalene **2a**, likely due to product degradation. Hexane and CH_2Cl_2 are compatible reaction solvents; however, they produced lower yields compared to those obtained in THF (entries 6 and 7). The reaction is scalable to at least 0.50 mmol (200 mg) scale without a decrease in yield (entry 8).[27] Notably, both products **2a** and **3a** are stable toward silica gel column chromatography under an inert atmosphere.

We were able to isolate compounds **2a** and **3a** (Table1, entries 8 and 9, respectively), and Figure 1 shows their ^{1}H NMR spectra. In Dewar isomer **3a**, the two methyl groups on TBS (~0 ppm, orange arrow) are diastereotopic as evidenced by two distinct signals in the ^{1}H NMR spectrum. Similarly, the benzvalene isomer **2a** also exhibits two signals for the same methyl groups in its ^{1}H NMR spectrum, albeit with a smaller chemical shift difference. The mesityl *o*-methyl groups (~2.2 ppm, purple arrow) exhibit exchange dynamics (broadened signals) at room temperature for BN-Dewar benzene **3a**, whereas sharp diastereotopic mesityl *o*-methyl signals are observed for BN-benzvalene **2a**. These observations are consistent with a more restricted B−Mes bond rotation for **2a** relative to **3a**. The original 1,2-azaborine arene C−H proton signals H^a, H^b, H^c are upfield shifted in BN-benzvalene **2a** relative to the signals for BN-Dewar benzene **3a** and are consistent with previously reported similar tricyclic structures.[2a,19a]

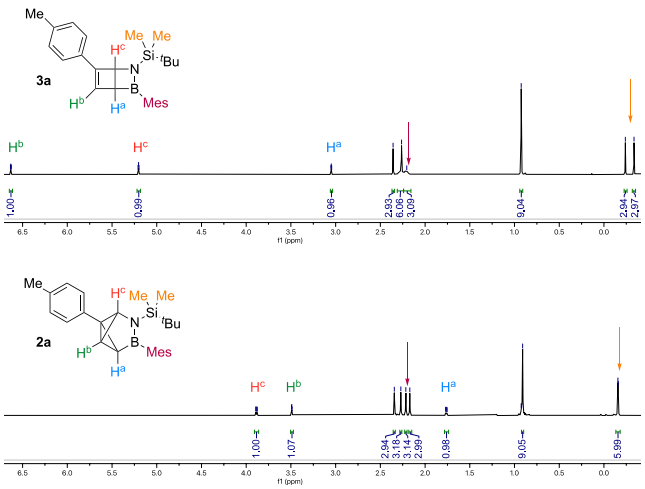


Figure 1. ^{1}H NMR spectra in $CDCl_3$ of C5-*p*-Tol-BN-Dewar benzene **3a** (top trace) and *p*-Tol-BN-benzvalene **2a** (bottom trace) in $CDCl_3$. Arene signals above 6.5 ppm are not shown.

We next evaluated the scope of the C5-aryl functional group under our optimized conditions (Table 2). A broad range of *p*-substituents are compatible, affording the corresponding products containing alkyl groups (entries **2a**−**2c**), trifluoromethoxy group (entry **2d**), and halogens (entries **2e**−**2g**) in good yields. The unsubstituted C5-Ph-1,2-azaborine substrate (entry **2h**), along with C5-3,5-dimethoxyphenyl- (entry **2i**), and C5-*o*-tolyl- (entry **2j**) derivatives, were also successfully converted to the BN-benzvalene products. Moreover, C5-1,2-azaborines containing electronically diverse heterocycles such as thiophene, pyridine, and thiazole (entries **2k**−**2m**) prove also to be suitable substrates.

We then turned our attention to determine the scope with respect to the nitrogen substituent (Table 3). The presence of silicon on nitrogen appears to be crucial for product formation. While silicon-based groups, such as TMS, TBS, and $SiPh_3$ (entries **2a**, **2n**, **2o**), generate the product cleanly, other groups on nitrogen, such as H, Me, Ph, and Ts (entries **2p**−**2s**), completely shut down the reaction, with unreacted starting material and/or decomposition being observed. The beneficial effect by an *N*-SiR_3 group can be presumably attributed to its kinetic stabilization of the BN-Dewar benzene and BN-benzvalene structures against thermal cycloreversion in addition to attenuating the resonance stabilization of the starting 1,2-azaborine.[28,29]

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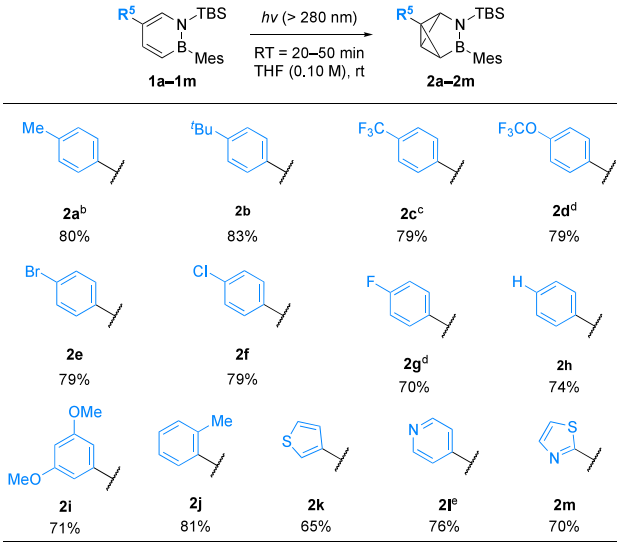
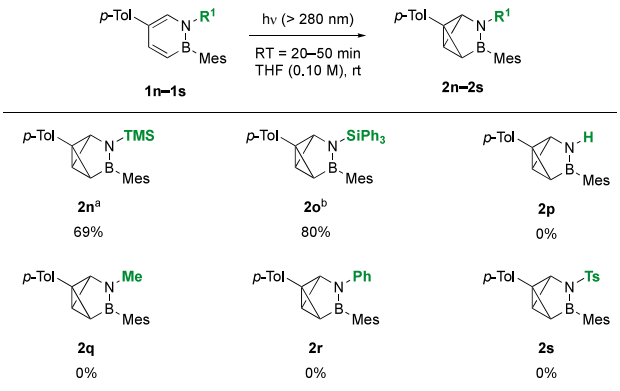
Table 2. Reaction Scope at the C5 Position[a]



[a]Yields of isolated products are reported as an average of two trials. Scale: 0.10 mmol, unless otherwise stated. [b]0.50 mmol scale. [c]Hexane was used as a solvent. [d]Yields were determined by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard; reported yields are the average of two trials. [e]0.05 M Substrate concentration. RT: residence time.

Table 3. Reaction Scope at the N Position



[a]Yields were determined by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. Scale: 0.10 mmol. Reported yields are the average of two runs. [b]Yields of isolated products are reported as an average of two trials. Scale: 0.10 mmol. RT: residence time.

BN-benzvalenes (**2a**–**2n**) are generally noncrystalline oily substances, with the exception being the *N*-$SiPh_3$-substituted **2o**, which is a white solid. We successfully grew crystals of **2o** (CCDC 2359775) suitable for single crystal X-ray diffraction analysis by slow evaporation from a CH_2Cl_2 solution at −40 °C. We also obtained the structure of the corresponding 1,2-azaborine starting material **1o** (CCDC 2359773) for comparative bonding analysis. Two structural features of **2o** are noteworthy (Figure 2): (1) The N−B bond distance (1.419(3)Å) in **2o** is shorter than that for **1o** (1.446(3) Å), which is consistent with loss of electron delocalization/aromaticity[30] after the photoisomerization. 2) In **2o**, the C−C bond distances associated with C6 (C6−C5 = 1.497(3) Å, C6−C3 = 1.494(3) Å) are shorter than the C−C bond

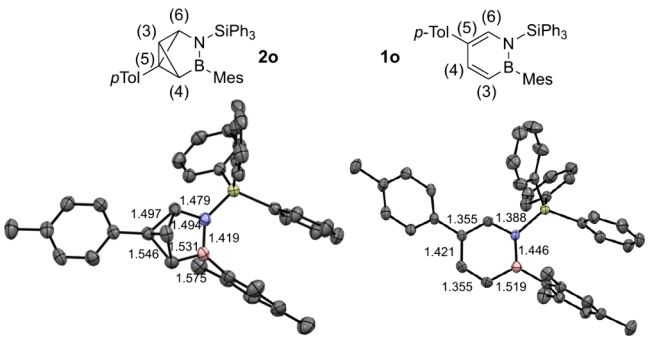
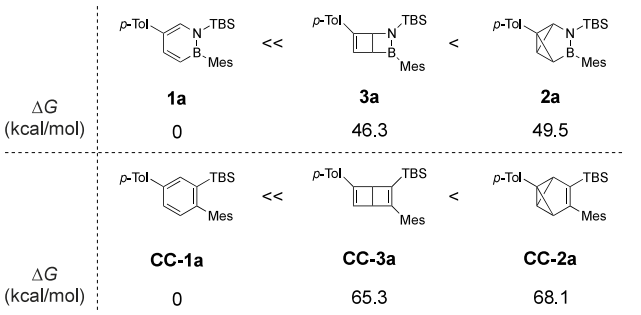


Figure 2. Crystal structures of **2o** and **1o** (hydrogen atoms have been omitted for the sake of clarity). Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths in Å for **2o** are N−B = 1.419(3), N−C6 = 1.479(3), B−C4 = 1.575(3), C4−C3 = 1.531(3), C4−C5 = 1.546(3), C6−C3 = 1.494(3), C6−C5 = 1.497(3); Selected bond lengths in Å for **1o** are N−B = 1.446(3), N−C6 = 1.388(2), B−C3 = 1.519(3), C3−C4 = 1.355(3), C4−C5 = 1.421(3), C6−C5 = 1.355(3).

distances associated with C4 (C4−C3 = 1.531(3) Å, C4−C5 = 1.546(3) Å). The bond distance differences are consistent with reported crystallographically characterized aminoborylated cyclopropanes.[31] Notably, density functional theory (DFT) calculations nicely reproduce the experimentally observed structural asymmetry in **2o** whereas the direct carbonaceous benzvalene analogue exhibits symmetrical *σ*-bonding according to DFT predictions (see Supporting Information for details).

We also used DFT calculations at the B3LYP/6-311G**//B3LYP/6-31G** level of theory to evaluate the relative energies of Dewar benzene and benzvalene isomers vs their (hetero)arene structures for both the BN and CC series (Table 4). We determined that benzvalenes **2a** and **CC-2a** are slightly

Table 4. Relative Energies of 1,2-Azaborine's Valence Isomers at 298.15 K (Calculated at the B3LYP/6-311G//B3LYP/6-31G** Level of Theory)**



less stable than Dewar benzene isomers **3a** and **CC-3a** by 3.2 and 2.8 kcal/mol, respectively. BN-benzvalene **2a** is higher in energy by 49.5 kcal/mol compared to 1,2-azaborine **1a** whereas benzvalene **CC-2a** is higher in energy by 68.1 kcal/mol relative to its benzene isomer **CC-1a**. The difference in the relative stability between the **BN** and **CC** congeners (**BN**: 49.5 kcal/mol vs **CC**: 68.1 kcal/mol) can be ascribed to the stronger resonance stabilization energy present in **CC-1a** vs **1a**.[28]

We have also conducted preliminary reactivity studies of BN-benzvalene **2a** and determined that **2a** reacts with thiophenol to cleanly furnish the ring-opened adduct **4a** (Scheme 3).[9b,32] Notably, the reaction is sluggish under dark

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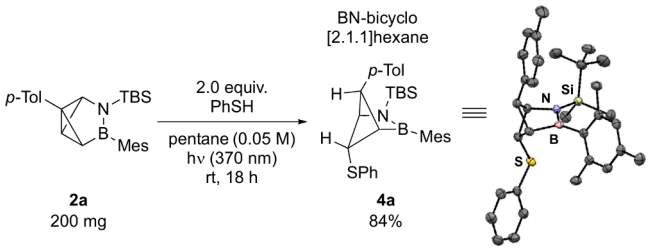
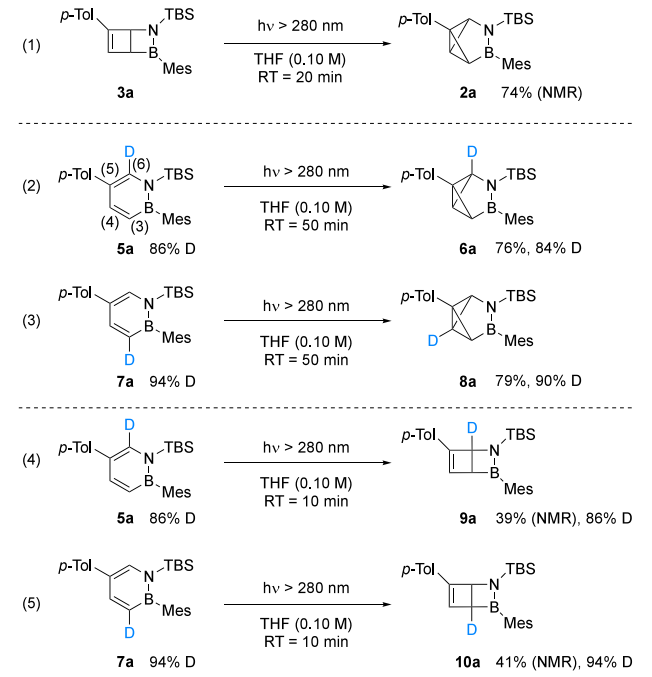
Scheme 3. Synthesis of BN-Bicyclo[2.1.1]hexane



conditions, and irradiation with purple light accelerates the reaction.[33] Compound **4a** (CCDC 2359774), the first example of a BN-bicyclo[2.1.1]hexane, is stable toward air and moisture and can be isolated by silica gel column chromatography under ambient conditions.

To elucidate the reaction mechanism for the formation of BN-benzvalene, we conducted experiments as outlined in Scheme 4. The observations during our reaction optimization

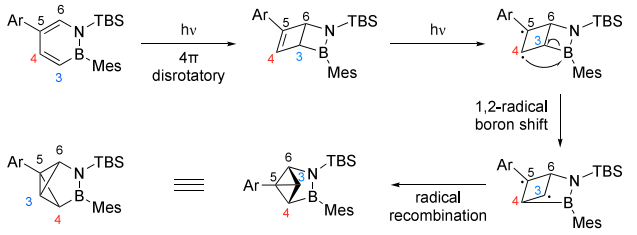
Scheme 4. Mechanistic Studies



work (Table 1, entries 2 and 4 vs entry 1) hinted at BN-Dewar benzene **3a** serving as an intermediate toward the formation of BN-benzvalene **2a**. We were able to isolate pure BN-Dewar benzene **3a** and determine that **3a** cleanly converts to **2a** under the standard reaction conditions (Scheme 4, eq 1). Thus, BN-Dewar benzene **3a** is a chemically and likely kinetically competent intermediate for the BN-benzvalene formation. Next, we conducted a deuterium labeling study to identify the bond connectivity over the course of the reaction. We synthesized C6- and C3-deuterated 1,2-azaborine analogues **5a** and **7a**, respectively. These substrates, when subjected to the standard photoisomerization conditions, furnish labeled BN-benzvalene products **6a** and **8a**. Formation of **6a** (eq 2) is consistent with the N−C6 bond remaining connected throughout the reaction. To our surprise, the deuterium in **8a** switched its location to the bridgehead C−H position, indicating that the B−C3 bond is cleaved during the formation of the BN-benzvalene product (eq 3). By shortening the residence time, we were able to monitor the formation of deuterium-labeled BN-Dewar benzenes **9a** and **10a**. Consistent with the previously reported mechanism for BN-Dewar benzene formation,[29,34] no N−C6 and B−C3 bond cleavage was observed (eqs 4 and 5). The findings illustrated in Scheme 4 indicate that the B−C3 bond must be cleaved during the transformation from BN-Dewar benzene to BN-benzvalene.

Scheme 5 illustrates our proposed mechanism, which is consistent with our deuterium labeling and reaction

Scheme 5. Proposed Mechanism for Formation of BN-Benzvalene



intermediate analysis. First, the starting 1,2-azaborine undergoes a photoinduced formal 4π disrotatory electrocyclization to generate the BN-Dewar benzene intermediate.[29,34] Then, the styrene chromophore in BN-Dewar benzene is excited by UV-light to generate a biradical species. The radical at the C4 position subsequently undergoes a 1,2-boron shift,[35] producing a C3 radical via a C3−B bond cleavage. Finally, radical−radical recombination of C3 and C5 radicals creates the central C−C bond of BN-benzvalene. The proposed reaction mechanism is consistent with the C5-aryl functional group facilitating the generation of BN-benzvalene by providing extra conjugation in the BN-Dewar benzene intermediate for the photoinitiated formation of the biradical. The proposed 1,2-boron shift for BN-benzvalene formation is distinct from mechanisms proposed in benzene[36,37] and phospha-[12] and sila-benzene[14,15a] analogues to yield their respective benzvalenes.

In conclusion, we presented the synthesis and crystallographic characterization of the first second-row heteroatom-containing benzvalene exemplified as the boron−nitrogen containing BN-benzvalene. Photoexcitation of C5-aryl-substituted 1,2-azaborines under flow conditions furnishes BN-benzvalenes with a broad substrate scope, including halogen functional groups and heteroaromatic rings. Mechanistic studies support a distinct stepwise photoisomerization pathway from 1,2-azaborine via a BN-Dewar benzene intermediate involving a radical-induced 1,2-boron shift. BN-benzvalene reacts with thiophenol in the presence of light to generate a BN-bicyclo[2.1.1]hexane. Current efforts are directed toward exploring novel modes of reactivity of BN-benzvalene derivatives.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c08088.

Experimental procedures, compound characterization data (NMR, Hi-res MS and IR data, NMR spectra for all new compounds), computational (Cartesian coordinates of all computed structures) and crystallographic information (PDF)

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Accession Codes

CCDC 2359773−2359775 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Author

Shih-Yuan Liu − *Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States;* orcid.org/0000-0003-3148-9147; Email: shihyuan.liu@bc.edu

Authors

Tomoya Ozaki − *Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States*

Sierra K. Bentley − *Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States;* orcid.org/0000-0001-6017-1432

Nina Rybansky − *Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States*

Bo Li − *Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.4c08088

Notes

The authors declare no competing financial interest.

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