

Resonance Stabilization Energy of 1,2-Azaborines: A Quantitative Experimental Study by Reaction Calorimetry

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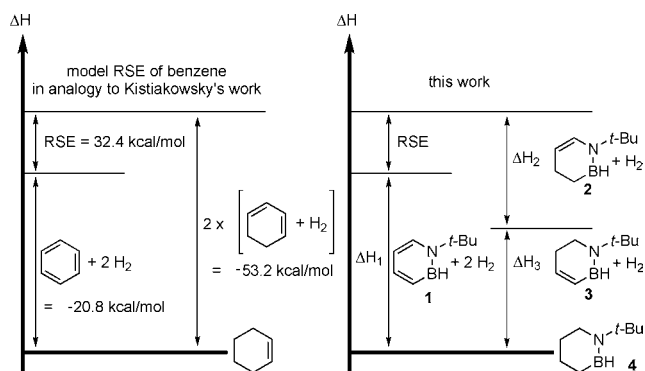
Abstract: Aromatic and single-olefin six-membered BN heterocycles were synthesized, and the heats of hydrogenation were measured calorimetrically. A comparison of the hydrogenation enthalpies of these compounds revealed that 1,2-azaborines have a resonance stabilization energy of 16.6 ± 1.3 kcal/mol, in good agreement with calculated values.

Since the isolation and structural description of benzene in the 19th century,¹ the concept of aromaticity has become one of the cornerstones of chemistry.² However, despite its relatively long history and the profusion of aromatic compounds in nature, the concept of aromaticity still lacks a single exact definition and has been a source of controversy.³ Several indices related to the energetic,^{4,5} geometric,⁶ and magnetic^{7–9} properties of aromatic compounds have been developed to quantitatively characterize aromaticity.¹⁰ One classic experimental method to quantitatively evaluate aromaticity is to determine the resonance stabilization energy (RSE) of a given aromatic compound.¹¹ This can be accomplished by comparing the heats of hydrogenation of the aromatic molecule in question against those of suitable nonaromatic reference compounds. The first reported use of this technique to measure the RSE of benzene was the work by Kistiakowsky and co-workers in 1936, who determined the RSE to be 36 kcal/mol.¹²

1,2-Azaborines are benzene mimics in which one CC bond unit has been replaced with an isoelectronic BN unit.¹³ These compounds are the focus of research in our group.^{14–20} Due to the ubiquity of the phenyl ring as a chemical building block, 1,2-azaborines show promise in potential biological²¹ and materials science^{22,23} applications. Because of the electronic and structural similarities between 1,2-azaborines and benzene, the characterization of aromaticity in 1,2-azaborines has received considerable attention.^{24,25} However, the extent of resonance stabilization in 1,2-azaborines has remained elusive from an experimental point of view. In this work, we provide the first experimental quantitative assessment of the RSE of a 1,2-azaborine using isothermal reaction calorimetry.

We undertook an approach similar to that of Kistiakowsky's classic work and compared the heat of hydrogenation of the aromatic species **1** to the sum of the heats of hydrogenation of the "N-vinyl" (**2**) and "B-vinyl" (**3**) reference BN heterocycles (Scheme 1, right diagram). Consequently, the RSE of a 1,2-azaborine can be determined using the equation $RSE = \Delta H_1 - (\Delta H_2 + \Delta H_3)$. The left diagram in Scheme 1 shows the hydrogenation enthalpies

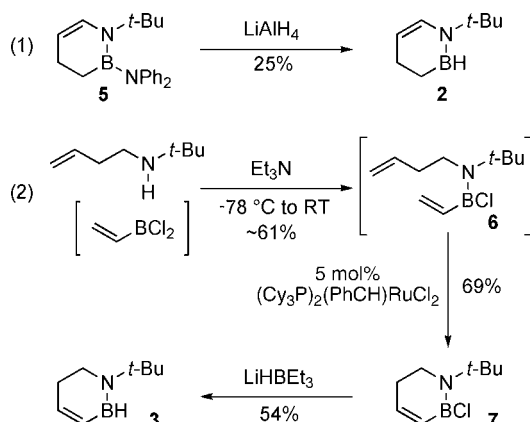
Scheme 1. RSE Derived from Hydrogenation Enthalpies



of the corresponding all-carbon system for direct comparison. On the basis of this model, in which the enthalpy of hydrogenation of the aromatic benzene to cyclohexene is compared with the hydrogenation of the nonaromatic cyclohexadiene to cyclohexene, an RSE of 32.4 kcal/mol for benzene can be derived;²⁶ this value is very similar to the one obtained by Kistiakowsky for conversion to cyclohexane.

The synthesis of **1** has been recently published.²³ The preparation of *N*-vinyl heterocycle **2** was accomplished upon treatment of the previously reported precursor **5**^{24a} with LiAlH₄ (eq 1 in Scheme 2). We devised a new synthetic route for heterocycle **3** based on a modified version of our standard 1,2-azaborine synthesis. Condensation of the *in situ*-generated vinylboron dichloride with homoallyl-*tert*-butylamine in the presence of triethylamine generated bisolefin precursor **6** (eq 2 in Scheme 2). This material was carried through the subsequent ring-closing metathesis step with Grubbs first-

Scheme 2. Synthesis of *N*-Vinyl and *B*-Vinyl BN Heterocycles **2** and **3**



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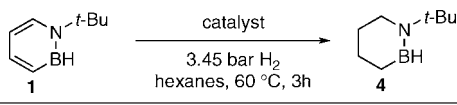
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generation catalyst to afford **7** in 69% isolated yield. Lastly, the addition of superhydride (LiHBEt_3) to **7** gave the desired *B*-vinyl product **3** in 54% yield.

With the required compounds in hand, we endeavored to find a hydrogenation catalyst amenable to the limitations imposed by our calorimeter cell (chiefly that mechanical stirring was not an option). Attempts using heterogeneous Pd/C gave erratic results for the hydrogenation of 1,2-azaborine **1**, which we attributed to the lack of effective mixing (Table 1, entry 1). We thus concluded that a homogeneous catalyst was required. After screening a series of homogeneous catalysts, we determined that Muetterties' allylcobalt catalyst ($\eta^3\text{-C}_3\text{H}_5\text{Co[P(OMe)}_3\text{]}_3$)²⁷ was uniquely suited for our purpose (Table 1, entry 2). As can be seen from Table 1, catalysts that have been reported to be active for olefin hydrogenations [e.g., Wilkinson's catalyst,²⁸ Crabtree's catalyst,²⁹ $\text{RuCl}_2(\text{PPh}_3)_3$,³⁰ $\text{Ru}(\text{H})(\text{Cl})(\text{CO})(\text{PPh}_3)_3$]³¹ did not hydrogenate 1,2-azaborine **1** under our screening conditions (Table 1, entries 3–6). In contrast, the optimized conditions of 10 mol % Muetterties catalyst and 3.45 bar H_2 pressure at 60 °C in hexanes completely hydrogenated each of the compounds of interest (**1–3**) in less than 3 h as determined by GC methods.³²

Table 1. Optimization Survey for Hydrogenation of **1**

|  | | yield of 4 (%) ^a | |
|---|--|------------------------------------|--------|
| entry | catalyst | run 1 | run 2 |
| 1 | Pd/C | 40 (49) | 3 (84) |
| 2 | η^3 -allylCo(P(OMe) ₃) ₃ | 98.5 (0) | 95 (0) |
| 3 | RhCl(PPh ₃) ₃ | 0 (82) | 0 (97) |
| 4 | [Ir(cod)(py)PCy ₃] ⁺ PF ₆ [−] | 0 (95) | 0 (99) |
| 5 | RuCl ₂ (PPh ₃) ₃ | 1 (80) | 1 (80) |
| 6 | Ru(H)(Cl)(CO)(PPh ₃) ₃ | 0 (99) | 0 (99) |

^a Determined by GC analysis versus a calibrated internal standard. Numbers in parentheses indicate percent of remaining starting material.

The calorimetric experiments were performed in a Setaram C-80 Calvet calorimeter. The sample cell was loaded with the catalyst and substrate solutions in a glovebox, and the reference cell was left empty under N_2 . The two cells were then inserted into the calorimeter and allowed to equilibrate at 60 °C for ~30 min. Data collection was started, and hydrogen gas was introduced to both cells, initiating the reaction. Data collection continued until the reaction was complete (3 h). Post-run data processing was limited to subtraction of the baseline run (to eliminate the thermal effects of introducing cold H_2 gas) and integration of the resulting curve to give the corresponding internal energy of hydrogenation, ΔE . The corresponding enthalpy value could then be determined via the equation $\Delta H = \Delta E + \Delta n_g RT$, where Δn_g is the number of moles of gas consumed or generated by the reaction. Figure 1 illustrates representative heat flow traces for the hydrogenation reactions. Under identical reaction conditions, the hydrogenation of compound **1** (Figure 1a) was slower than the hydrogenations of **2** and **3** (Figure 1b,c, respectively). The distinctive shape of Figure 1a may be indicative of two sequential hydrogenation steps for compound **1**. The heat flow traces for **1–3** are also consistent with non-zeroth-order reaction kinetics with respect to the substrate, suggesting that mass transfer is not rate-limiting under the reaction conditions.³³

A summary of the experimentally determined hydrogenation enthalpies (averages of three runs) is shown in Table 2 together with computational predictions at the G3(MP2) level^{34,35} obtained

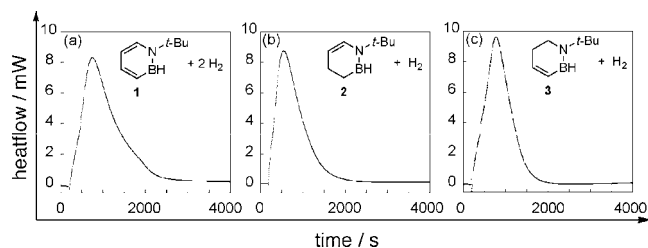
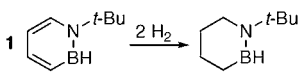
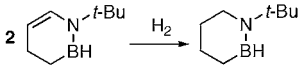
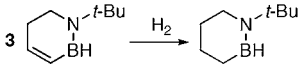


Figure 1. Heat flow traces for the hydrogenation reactions of **1**, **2**, and **3**.

by using the Gaussian 09 program.³⁶ The experimental heats of hydrogenation are -30 ± 1 , -22.7 ± 0.5 , and -23.9 ± 0.7 kcal/mol for **1**, **2**, and **3**, respectively. These values are within 1.1 kcal/mol of the computationally derived (gas-phase) results and follow the same general energetic trend (i.e., the hydrogenation of **3** is slightly more exothermic than that of **2**). The experimentally derived RSE for 1,2-azaborine **1** is 16.6 ± 1.3 kcal/mol, as calculated from the equation $\text{RSE} = \Delta H_1 - (\Delta H_2 + \Delta H_3)$. The G3MP2 value for the RSE is 18.4 kcal/mol, in good agreement with the experimental value. The effect of the *tert*-butyl substituent on the RSE is small (1.2 kcal/mol), as use of our previously reported G3MP2 results¹⁸ for the RSE of the parent 1,2-dihydro-1,2-azaborine gives 19.6 kcal/mol. This is significantly less than the RSE of benzene (32.4 kcal/mol according to the model in Scheme 1) and is consistent with nucleus-independent chemical shift (NICS) calculations indicating that 1,2-azaborines are less aromatic than benzene.^{15,25b}

Table 2. Experimental versus Calculated Heats of Hydrogenation

| reaction | ΔH experimental (kcal/mol) | $\Delta H(298\text{ K})$ calculated G3(MP2) (kcal/mol) |
|--|------------------------------------|--|
|  | $\Delta H_1 = -30 \pm 1$ | -30.1 |
|  | $\Delta H_2 = -22.7 \pm 0.5$ | -23.8 |
|  | $\Delta H_3 = -23.9 \pm 0.7$ | -24.7 |

In summary, we have provided the first experimental determination of the resonance stabilization energy of 1,2-azaborines through hydrogenation enthalpy measurements. Muetterties' allylcobalt catalyst served as a uniquely capable "homogeneous" catalyst for hydrogenation of 1,2-azaborine **1**. We found the RSE of 1,2-azaborine **1** to be 16.6 kcal/mol, indicating that significant additional stability is imparted by six- π -electron delocalization in six-membered BN heterocyclic ring systems. This result is consistent with previous findings that 1,2-azaborines are less aromatic than their all-carbon counterparts and aids in completing the "aromatic picture" of 1,2-azaborines by making available a quantitative experimental assessment.

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Supporting Information Available: Experimental procedures, compound characterization data, G3MP2 energies, optimized Cartesian coordinates, and complete ref 36. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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