Vibrational Spectroscopy of N-Methyliminodiacetic Acid (MIDA)-Protected Boronate Ester: Examination of the B-N Dative Bond

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Vibrational Spectroscopy of N-Methyliminodiacetic Acid (MIDA)-Protected Boronate Ester: Examination of the B-N Dative Bond

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Abstract

N-methyliminodiacetic acid (MIDA)-protected boronate esters are a new class of reagents that offer great promise in iterative Suzuki-Miyaura cross-coupling reactions. Compared to earlier reagents, MIDA esters are easily handled and are bench-top stable under air indefinitely. The success of this new species is tied to its unique molecular architecture. Compared to the simpler B-N containing molecules ammonia borane and trimethylamine borane, MIDA esters are much larger, and the sp\(^3\) hybridized boron atom is secured by two five membered rings, making this molecular class stable for spectroscopic study. Here, we present infrared, Raman, and surface enhanced Raman (SERS) spectra of methylboronic acid MIDA ester. Comparisons of the spectroscopic results to those from electronic structure calculations suggest that the B-N stretching mode in this molecule lies in the range 560-650 cm\(^{-1}\), making it among the lowest energy vibrations observed to date that can be primarily attributed to B-N stretching.

1 Introduction

The formation of many important biological polymers and macromolecules, as well as various synthetic materials, relies on iterative coupling of pre-assembled building blocks. The purpose of having these building blocks is to generalize and simplify the various methods of syntheses of large molecules.\(^1\) These processes are efficient and flexible, whereas the syntheses of smaller molecules are much more involved. A solution to the difficulty involved in synthesizing these smaller molecules is to employ boronic acids. Boronic acids are indeed very useful building blocks for organic syntheses.\(^2\) For example, the Suzuki-Miyaura reaction between an organohalide and a boronic acid is a powerful tool in generalizing the method for C-C bond formation in the synthesis of complex molecules. An underlying problem, however, involves reaction scheme incompatibilities between most synthetic reagents. An often employed solution to this incompatibility is to use boronic ester counterparts. These are more compatible with many synthetic schemes, although liberation of the boronic acid requires harsh conditions that interfere with the synthetic substrates.

Burke and co-workers recently developed a new class of molecules that allow for milder reac-
tion conditions. This was accomplished through complexation of the boronic acid with a trivalent ligand, N-methyliminodiacetic acid (MIDA).\textsuperscript{1–3} This rehybridizes the boron center to $sp^3$, dramatically increasing the stability of the boronic acid and allowing for the synthesis of complex molecules to take place. The MIDA esters are unreactive under anhydrous cross-coupling conditions, stable in air, and can be deprotected easily using mild aqueous basic conditions. This new molecular class serves as the first general solution where both benchtop stability and the capacity for in situ slow release of the boronic acids is included.\textsuperscript{1–3} The key to the success of these molecules as synthetic reagents is the B-N dative bond. The stability of the MIDA esters also makes them ideal candidates for studying B-N dative bonds spectroscopically. Here, we compare experimental infrared, Raman, and surface enhanced Raman spectroscopy (SERS) spectra of methylboronic acid (MBA) MIDA ester (structure shown in Figure 1) to theoretical predictions in an effort to describe the physical properties of the B-N dative bond contained in this molecule.

![Molecules that contain a B-N dative bond: ammonia borane (left), trimethylamine borane (middle), and methylboronic acid MIDA ester (right).](image)

Ammonia borane and trimethylamine borane (structures shown in Figure 1) are simple prototypes that have been studied extensively to investigate dative B-N bonding interactions.\textsuperscript{4–51} Throughout the years, there have been many different attempts to assign the B-N dative bond stretching frequency in these and similar molecules. In 1957, Rice and co-workers experimentally recorded Raman and infrared spectra of liquid trimethylamine borane and assigned the B-N stretch-
ing motion to a peak at 1255 cm$^{-1}$. A year later, Taylor, et al. pointed out that the few already recorded spectra of amine boranes had an unexpectedly high value for the B-N stretch. For example, this motion in species such as BF$_3$NH$_3$, C$_5$H$_5$NBF$_3$, H$_3$NB(CH$_3$)$_3$, and (CH$_3$)$_3$NBH$_3$ had been previously assigned to between 980 and 1255 cm$^{-1}$. These authors asserted that the stretching frequency should be much lower in energy. As a result, they assigned the B-N stretch in trimethylamine borane to 667 and in ammonia borane to 785 cm$^{-1}$. In 1965, Sawodny, et al. measured the vibrational spectrum of ammonia borane (BH$_3$NH$_3$) in the solid state and assigned the B-N stretch at 776 cm$^{-1}$. Odom and co-workers realized in 1974 that the B-N stretch of trimethylamine borane should be in the same spectral window as C-N stretches. Together with the low intensity of this normal mode in infrared spectra, confusion with the assignment of this vibration in earlier studies is not surprising. Odom suggested that Raman spectroscopy is likely a better method than infrared to observe B-N stretching modes, and the authors re-assigned the B-N stretch in trimethylamine borane to 660 cm$^{-1}$.

In 1995, Vijay and co-workers performed a theoretical study on ammonia borane using various basis sets and levels of theory to ascertain which level of theory best agreed with the already available experimental spectra. The authors utilized Taylor’s assignment of the B-N stretch at 785 cm$^{-1}$ as the experimental value to which they compared. They suggested that the SCF method, which predicted a B-N stretch between 617 cm$^{-1}$ and 625 cm$^{-1}$, underestimated experimental observations and could not accurately describe the B-N bond in ammonia borane, even with extended basis sets. At the MP2 level, which predicted the B-N stretch between 678 cm$^{-1}$ and 690 cm$^{-1}$, the use of larger basis sets with more diffuse functions also did not improve the agreement between experiment and theory with regards to the location of the B-N stretching frequency. Calculations performed using the QCISD method lowered the energy of the B-N stretching motion by 13 cm$^{-1}$ compared to MP2, but the authors recommended the use of the CCSD(T) coupled cluster method with large basis sets, which they could not perform at the time due to disk space limitations.

Dillen, et al. in 2003 attempted to conclusively assign the B-N stretching frequency of solid ammonia borane and end the controversy observed in the previous decades. The authors assigned
the energy of the B-N stretching motion, that is effectively localized on a individual BH$_3$NH$_3$, to a gas phase calculated value 610 cm$^{-1}$. To model the crystalline environment of BH$_3$NH$_3$ in the solid state, the authors computed MP2/6-31G($d$) vibrational frequencies of a BH$_3$NH$_3$ molecule surrounded by its 8 nearest neighbors fixed at their positions from the crystal structure. HF/6-31G($d$) vibrational frequencies were also computed for models containing as many 30 neighboring ammonia borane molecules. The computed B-N stretching frequencies of these BH$_3$NH$_3$ clusters were compared to the previous experimental values, and the authors noted that Smith’s value of 968 cm$^{-1}$ seemed very unlikely. However, the molecular cluster computational results were consistent with Taylor’s earlier experimental assignment of 785 cm$^{-1}$ in the solid state. Ammonia borane is perhaps not the best dative bond containing candidate to study, however, due to intermolecular dihydrogen bonding between adjacent molecules in the solid state.$^{55,56}$ Dillen, et al. pointed out that these intermolecular interactions and the accompanying dramatic shortening of the B-N bond in the solid state produce a blue shift of over 100 cm$^{-1}$.\textsuperscript{31}

Computational studies of amine-boranes by Gilbert in 2004,$^{34}$ LeTourneau et al. in 2005,$^{39}$ and Plumley and Evanseck in 2007\textsuperscript{47} demonstrated that the B3LYP$^{57,58}$ hybrid density functional tends to overestimate the lengths and significantly underestimates the dissociation energies/enthalpies of coordinate covalent B-N bonds. Consequently, B3LYP cannot be expected to provide reasonable vibrational frequencies of the title compound, in the B-N stretching region. In contrast, the global hybrid density functional M06-2X\textsuperscript{59} has been shown to provide a far more reliable description of B-N dative bonds.$^{60,61}$ In fact, comparison to experimental data as well as results from CCSD(T) and QCISD(T) computations indicates that M06-2X even outperforms second-order Møller-Plesset perturbation theory (MP2)$^{62}$ for these systems.

Here, we present experimental vibrational spectra of MBA MIDA ester using a variety of vibrational spectroscopic methods. Compared to the simpler B-N containing molecules ammonia borane and trimethylamine borane, MBA MIDA ester is much larger, and the sp$^3$ hybridized boron atom is secured by two five membered rings, making it stable for spectroscopic study. We compare our experimental spectra with the results of ab initio calculations using both the MP2 and
M06-2X methods and different sized basis sets in order to assign the location of the B-N stretching frequency of the dative bond in MBA MIDA ester.

2 Experimental and Theoretical Methods

2.1 Spectroscopic Methods

Methylboronic acid MIDA ester was obtained from Sigma-Aldrich and was used for the Raman, SERS, and infrared experiments presented here without any further purification. Raman spectra of MBA MIDA ester were obtained using 514.5 nm and 676.4 nm laser lines from Argon or Krypton ion lasers. A Ramanor HG2-S Raman scanning spectrometer was employed to acquire Raman spectra using the 514.5 nm line from an Ar ion laser. A Nachet NS 400 microRaman setup was used to analyze the sample with an incident laser power of 300 mW at the sample, and a 0.5 cm$^{-1}$/s scan speed was employed over the range of 0-4000 cm$^{-1}$. Spectra were acquired and interpreted using a custom computer program written using National Instruments LabView. A Jobin-Yvon T64000 Raman spectrometer with CCD detection was used to acquire Raman spectra using the 676.4 nm line from a Kr ion laser. Infrared spectra were acquired in a salt pellet using a Bruker IFS 66 spectrometer with 1024 scans with 1 cm$^{-1}$ resolution.

The SERS substrates created to study MBA MIDA ester were fabricated using a vacuum deposition chamber. Pressures in the deposition chamber were approximately 1 x 10$^{-6}$ torr throughout the deposition process. Glass slides were cleaned and then coated with silver island films to 7 nm at a deposition rate of 0.02 nm/s. MBA MIDA ester was deposited on the SERS active substrates from solutions in various solvents via the drop method. SERS spectra were acquired using the 514.5 nm line from a Coherent Innova Ar ion laser providing approximately 300 mW of power at the sample. The microRaman setup described above was used to collect and analyze the scattered light.
2.2 Theoretical Methods

The Gaussian 09 software package was employed to optimize the structure and to calculate the unscaled harmonic vibrational frequencies as well as the corresponding Raman and infrared intensities of MBA MIDA ester. The M06-2X global hybrid density functional and second-order Møller-Plesset perturbation theory (MP2) were used in conjunction with two split-valence basis sets, 6-31G(d,p) and 6-311G(2df,2pd). Harmonic vibrational frequencies confirmed that the optimized geometry corresponds to a true minimum on the potential energy surface associated with each combination of method and basis set. Default convergence criteria and frozen core conventions were employed in each calculation. Simulated spectra were created by combining Lorentzians for each normal mode using a custom program developed with National Instruments LabView. The INTDER2005 program was employed to determine the total energy distributions (TEDs) characterizing the normal modes. The B-N stretch is defined as the simple internal coordinate \( S_1 = r(B-N) \). The complete set of \( 3N - 6 = 60 \) simple internal coordinates and TEDs at each level of theory are provided in the electronic Supporting Information.

3 Results

3.1 Spectroscopic Results

Infrared and Raman spectra of MBA MIDA ester are presented in Figure 2. Raman spectra acquired using the 514.5 nm Ar ion laser line exhibited a very large, polynomial-shaped background. In 2007, Zhao, et al. proposed a solution for eliminating the fluorescence background common in Raman spectra by implementing an automated background subtraction algorithm employed while Raman spectra were being collected. Following that suggestion, we fitted a polynomial to the baseline of the raw spectra and subtracted it. The resulting spectrum for the 514.5 nm excitation (shown in Figure 2) represents the sum of on average 20 individual scans, displays a relatively flat baseline, and agrees well with the spectra obtained using the Kr ion 676.4 nm laser line. Inter-
Interestingly, spectra acquired using the Kr ion 647.1 nm laser line (not shown) also exhibited a large polynomial-shaped background.

![Infrared spectrum (bottom) and Raman spectra of methylboronic acid MIDA ester using 676.4 nm (middle) and 514.5 nm (top) laser excitation.](image)

Figure 2: Infrared spectrum (bottom) and Raman spectra of methylboronic acid MIDA ester using 676.4 nm (middle) and 514.5 nm (top) laser excitation.

It is observed that the positions of the peaks in the Raman and infrared experimental spectra agree closely with one another. However, at the lower energy end of the spectrum, the vibrational modes in the Raman spectra are relatively more pronounced than they are in the infrared spectrum. This is consistent with the earlier observations by Odom and co-workers in the case of trimethylamine borane. The opposite is true in the central part of the spectra where peaks in the infrared spectrum are more prominent than in the Raman. The carbonyl stretches at 1700 cm\(^{-1}\) correlate well with one another in both Raman and infrared, appearing as a doublet, as do the location of the C-H stretches. The carbonyl stretching region represents the most intense features in the infrared spectrum. The C-H stretches at 2900 – 3050 cm\(^{-1}\) have a greater intensity in the 514.5 nm excited Raman spectrum than in the 676.4 nm Raman or infrared spectra. Also, there are additional peaks evident in the Raman spectrum using 514.5 nm excitation that are not observed when employing 676.4 nm.
3.2 SERS Results

Surface-Enhanced Raman Spectroscopy (SERS) was employed for enhancing the Raman peaks in the spectrum of MBA MIDA ester and to explore possible interactions with a silver substrate. It was observed that the choice of solvent had a great effect on the resulting SERS spectrum. For example, SERS spectra acquired using varying concentrations of MBA MIDA ester in methanol showed no significant peaks. Results using acetone were much more pronounced and are shown in Figure 3. The prominent peaks in the SERS spectrum indicate that the apparent fluorescence background has been quenched to some extent. However, the SERS continuum, the sloping baseline present in many SERS spectra, is evident in the spectrum presented here. Recent studies suggest that this continuum may be of physical importance, arising from surface-enhanced fluorescence. The peaks in Figure 3, using the 676.4 nm laser line, correlate well with the peaks in the SERS spectrum, suggesting that MBA MIDA ester was likely physisorbed to the SERS substrate. Visible exceptions include the broad feature observed at 1000 cm$^{-1}$ and a prominent peak at 1126 cm$^{-1}$, which is marked with an asterisk. The prominence of these features suggest an intimate interaction between MBA MIDA ester and the silver substrate. By comparison with theoretical predictions, most peaks in this region of the vibrational spectrum correlate to motion of the nitrogen atom and its three neighboring CH$_n$ groups. The intensity of this peak may point to an interaction between the nitrogen atom and silver atoms in the substrate in some of the MBA MIDA ester molecules.

3.3 Theoretical Results

To aid in the characterization of normal modes in the experimental spectra and to help characterize the structure of MBA MIDA ester, quantum chemistry computations were performed using a variety of method and basis set combinations. The B-N bond lengths are listed in Table 1 for each level of theory. For a given basis set, the MP2 and M06-2X bond lengths differ by only 0.02 Å.

Harmonic vibrational frequencies were also computed, and analysis of the corresponding TEDs reveals that only one mode has significant B-N stretching character (simple internal coordinate $S_1$).
Figure 3: Comparison of a SERS spectra of methylboronic acid MIDA ester in acetone (top), nascent Raman spectrum using 514.5 nm (middle), and 676.4 nm (bottom) excitation, respectively.

These vibrational frequencies are also provided in Table 1 along with the percent B-N stretching character. At the MP2/6-31G(2df,2pd) level of theory, for example, the mode at 601 cm$^{-1}$ is 62% B-N stretch, while no other mode has more than 14% B-N stretching character. Similar results are obtained for the MP2/6-31G(d,p) and M06-2X/6-31G(2df,2pd) vibrational frequencies. Only with the small basis set and the M06-2X functional does another vibrational mode have more than 16% B-N stretching character. The complete list of simple internal coordinates and TEDs for each level of theory are reported in the Supporting Information.

**Table 1:** B-N bond length (in Å) and vibrational frequencies (in cm$^{-1}$) of the mode with the largest percentage of B-N stretching character (simple internal coordinate $S_1$).

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<th>Method</th>
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<th>$r$(B-N)</th>
<th>$\omega$</th>
<th>$% S_1$</th>
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<td>MP2</td>
<td>6-31G(d,p)</td>
<td>1.67</td>
<td>602</td>
<td>(65 %)</td>
</tr>
<tr>
<td>MP2</td>
<td>6-311G(2df,2pd)</td>
<td>1.66</td>
<td>601</td>
<td>(62 %)</td>
</tr>
<tr>
<td>M06-2X</td>
<td>6-31G(d,p)</td>
<td>1.69</td>
<td>577</td>
<td>(42 %)</td>
</tr>
<tr>
<td>M06-2X</td>
<td>6-311G(2df,2pd)</td>
<td>1.68</td>
<td>579</td>
<td>(71 %)</td>
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4 Discussion

There has been great controversy over the assignment of B-N stretching frequencies in the past. Reasons for this disagreement include the instability of the molecules studied and the poor correlation between theoretical methods and earlier experiments. Shown in Figure 4 is a comparison of the Raman spectrum of MBA MIDA ester in the range 50 – 1900 cm\(^{-1}\) with unscaled results at the MP2/6-311G\((2df,2pd)\) and M06-2X/6-311G\((2df,2pd)\) levels of theory. Frequencies were calculated using both isotopes of boron and weighted using the appropriate natural abundances. With two isotopes having significant natural abundances (80.1% \(^{11}\)B and 19.9% \(^{10}\)B), peaks involving motion of the central boron atom are broadened, yielding a slight shoulder.

![Raman spectra comparison](image)

Figure 4: Comparison of experimental (676.4 nm excitation) and theoretical Raman spectra.

Figures 5 and 6 show a detailed comparison between experiment and theory in the region associated with B-N stretching. Agreement between experiment and theory is quite good for most peaks, as is the agreement between the MP2 and M06-2X results. Significant coupling of simple internal coordinates is to be expected in a molecule of this size, particularly in a system with
fused rings and C\textsubscript{1} symmetry. On average, the maximum contribution to the TED of a vibrational mode from a single simple internal coordinate is 40%. The B-N stretch, however, is predominantly associated with one normal vibrational mode. With the larger basis set, M06-2X predicts this mode to occur at 579 cm\textsuperscript{-1}, whereas MP2 predicts a higher energy of 601 cm\textsuperscript{-1}, and the corresponding TEDs indicate they are 71\% and 62\% B-N stretch (simple internal coordinate \textit{S}_1), respectively.

To further put this in perspective, at the MP2/6-311G(2\textit{df},2\textit{pd}) level of theory, only seven of the sixty normal modes have a larger contribution from one simple motion. Thus, the B-N stretch in MBA MIDA ester is predicted by both methods to be quite “pure.” No other vibrational mode has more than 14\% and 11\% B-N stretching character at the MP2/6-311G(2\textit{df},2\textit{pd}) and M06-2X/6-311G(2\textit{df},2\textit{pd}) levels of theory, respectively.

![Figure 5: Detailed comparison of experimental (676.4 nm excitation) and theoretical Raman spectra.](image)

All of the experimentally observed peaks in Figures 5 and 6 are accounted for by both levels of theory. Both MP2 and M06-2X predict large Raman and infrared intensities for the B-N stretch, suggesting that it should be readily visible in both spectra. In the range 560 – 650 cm\textsuperscript{-1},...
Figure 6: Detailed comparison of experimental and theoretical infrared spectra.

Experimentally there are four peaks, one of which appears as a shoulder at 617 cm$^{-1}$ in the Raman spectrum but is clearly visible in the infrared. Both MP2 and M06-2X predict four peaks in this spectral window, which accounts for all of the experimentally observed peaks. A direct comparison of the MP2/6-311G(2df,2pd) and experimental spectra suggests that the mode with the greatest B-N stretching character is likely the experimentally observed peak at 608 cm$^{-1}$, while M06-2X/6-311G(2df,2pd) frequencies suggest that it is the experimental peak at 568 cm$^{-1}$. The close proximity of experimental peaks in this region makes it difficult to assign this mode to a specific experimental peak, but our computational results indicate that the mode with the greatest amount of B-N stretching character appears in this spectral window. Assignment to the experimental peak at 608 cm$^{-1}$, using the MP2 results as a guide, would yield an experimental wavenumber value that is actually higher than that for the calculated harmonic vibrational frequency. The M06-2X/6-311G(2df,2pd) results suggest the B-N stretching mode is most likely associated with the peak at 568 cm$^{-1}$, slightly below the computed harmonic value of 579 cm$^{-1}$. Although these
results preclude a definitive assignment of the B-N stretching mode, the correlation between the
computed spectra and experimentally observed peaks strongly suggest that the vibrational mode
dominated by the B-N stretch is one of the four peaks in the range 560 – 650 cm\(^{-1}\). This observ-
ervation makes it one of the lowest, if not the lowest, energy vibrations observed to date that can be
primarily attributed to B-N stretching.

5 Conclusions

Comparison of experimental infrared, Raman, and SERS spectra of methylboronic acid MIDA
ester with theoretical predictions suggests that the vibrational mode with the most significant B-N
dative bond stretching character in this molecule occurs in the range of 560 – 650 cm\(^{-1}\). In MBA
MIDA ester, this mode is very localized and predominantly due to one motion, a surprising result
for such a large and constrained molecule. This spectral assignment makes it one of the lowest,
if not the lowest, experimentally observed B-N stretching modes. SERS spectra also exhibit an
enhanced peak at 1126 cm\(^{-1}\), indicating a possible interaction of the nitrogen atom with the silver
surface.

5.0.1 Acknowledgment

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Allen and Jowa Wu at the University of Georgia for their assistance with the INTDER2005 pro-
gram and interpretation of the TEDs.
5.0.2 Supporting Information Available:

Cartesian coordinates of optimized structures, set of $3N - 6 = 60$ simple internal coordinates, and total energy distributions (TEDs). This material is available free of charge via the Internet at http://pubs.acs.org.
The B-N stretching mode in methylboronic acid MIDA ester is predicted to occur in the vicinity of 600 cm$^{-1}$, making it one of the lowest, if not the lowest, experimentally observed.
References


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(56) Klooster, W. T.; Koetzle, T. F.; Siegbahn, P. E. M.; Richardson, T. B.; Crabtree, R. H. 


(64) INTDER2005 is a general program developed by Wesley D. Allen and co-workers which 
    performs various vibrational analyses and higher-order nonlinear transformations among 
    force field representations.


The B-N stretching mode in methylboronic acid MIDA ester is shown to occur in the vicinity of 600 cm\(^{-1}\), making it one of the lowest, if not the lowest, experimentally observed.