

## Comment on "Arresting an Unusual Amide Tautomer Using Divalent Cations"

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Herein, we comment on the interpretation of spectroscopic data in "Arresting an Unusual Amide Tautomer Using Divalent Cations", *J. Phys. Chem. B* **2019**, 123 (40), 8419–8424, by Bagchi and co-workers.<sup>1</sup> In their paper, the authors assign the appearance of a blue-shifted shoulder on the amide I vibration of *N*-methylacetamide (NMA), *N,N*-dimethylacetamide (DMA), and urea to the formation of a tautomer-like structure in the presence of divalent metal cations. In other words, the shoulder should originate from a  $C=N^+$  resonance that is stabilized by the presence of divalent metal cations. Moreover, Bagchi and co-workers argue that the  $C=N^+$  resonance is coincidentally located at a position just to the blue of the amide I band upon the introduction of divalent metal cation salts. This assignment represents an alternative to the idea that the blue-shifted shoulder on the amide I band arises from the dehydration of the amide oxygen upon interaction with metal cations.<sup>2,3</sup> Bagchi's putative new assignment can be directly tested by studying <sup>15</sup>N-isotope-labeled NMA. Such experiments were performed in our laboratory and are described below.

We synthesized NMA and <sup>15</sup>N-labeled NMA by reacting acetyl chloride with methylamine-HCl and <sup>15</sup>N-labeled methylamine-HCl, respectively (see Supporting Information for details). The resulting amide-containing molecules were introduced into D<sub>2</sub>O at a concentration of 100 mM (Figure 1A). In the absence of salt, there is a small isotope shift upon substitution with the <sup>15</sup>N-labeled molecule. This very modest red shift from 1620 to 1617 cm<sup>-1</sup> in the case of <sup>15</sup>N-labeled NMA is expected because the amide I resonance is not purely C=O in character. Upon adding 4 M CaCl<sub>2</sub>, a blue-shifted shoulder appears at 1645 cm<sup>-1</sup> with NMA as well as with <sup>15</sup>N-labeled NMA (Figure 1B). This is not what one would expect if the blue shoulder was from  $C=N^+$ . Indeed, if the  $C=N^+$  assignment was correct, then this mode should have been quite sensitive to the mass of the nitrogen atom. Moreover, one can look for an isotope shift upon the addition of acid to solution. As Bagchi and co-workers point out, one expects to observe the formation of a  $C=N^+$  resonance at low pH. As such, we added 1 M DCl to solution to directly examine this feature (Figure 1C). In the case of NMA, a new peak appears at 1680 cm<sup>-1</sup> (Figure 1C, black curve). Next, the same experiment was performed with a solution containing <sup>15</sup>N-labeled NMA

(Figure 1C, red curve). In this case, the new mode red-shifts down to 1663 cm<sup>-1</sup>. These observations confirm that the peak at 1680 cm<sup>-1</sup> arises from a CN bond while demonstrating that the one at 1645 cm<sup>-1</sup> does not.

The current results are consistent with previous assignments of the blue-shifted shoulder to the dehydration of the carbonyl oxygen atom when divalent metal cations are present.<sup>2,3</sup> Indeed, in the absence of CaCl<sub>2</sub>, there should be a small amount of charge transfer to the  $\sigma^*$  orbital of the water, which red-shifts the amide I resonance.<sup>4</sup> When the hydration shell is disrupted by metal ions, the peak is expected to blue-shift part way back toward its gas phase frequency. While the above results disprove the idea that the blue-shifted shoulder in the amide I spectra in Figure 1B comes from a  $C=N^+$  resonance, they do not mean that tautomerization cannot occur when salt is introduced. In fact, a recent study has shown that a trace amount of this structure can be formed, but only in the presence of 6 M CaCl<sub>2</sub>, and in that case the peak is also at 1680 cm<sup>-1</sup>.<sup>5</sup>

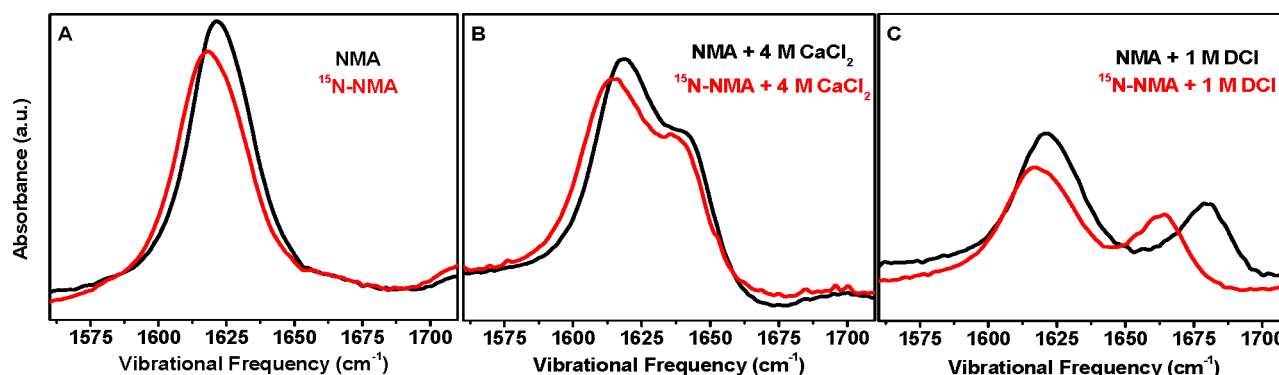
Finally, we have measured the vibrational spectrum of 40 mM acetone in the presence and absence of 4 M CaCl<sub>2</sub> (Figure 2). As can be seen, a shoulder similar to the one in Figure 1B appears, albeit somewhat less pronounced. As such, a CN resonance is not required for this observation. This is significant, because acetone cannot tautomerize. Curiously, Bagchi and co-workers provide spectra for acetone in the presence of CaCl<sub>2</sub> in Figure S2 of their paper.<sup>1</sup> The authors claim that these spectra serve as controls to demonstrate that the blue-shifted shoulder is specific to amide-containing molecules. Nevertheless, it is straightforward to demonstrate that such shoulders can also occur with simple ketones such as acetone.

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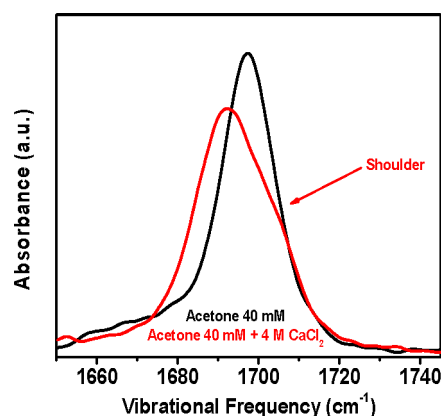
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**Figure 1.** ATR-FTIR absorption spectra of the amide I resonance for solutions containing 0.1 M NMA and 0.1 M  $^{15}\text{N}$ -labeled NMA. All solutions were prepared in  $\text{D}_2\text{O}$ . (A) The amide I resonances of NMA and  $^{15}\text{N}$ -labeled NMA, respectively, in  $\text{D}_2\text{O}$ , respectively. (B) The same molecules in the presence of 4 M  $\text{CaCl}_2$  and (C) upon the addition of 1 M  $\text{DCl}$ .



**Figure 2.** Absorption spectra of the  $\text{C}=\text{O}$  stretch resonance of acetone in the presence and absence of 4 M  $\text{CaCl}_2$ . Both solutions were prepared in  $\text{D}_2\text{O}$ . The acetone concentration was 40 mM. The blue-shifted shoulder is denoted by an arrow.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcb.0c04272>.

Synthesis information and spectra (PDF)

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### Notes

The authors declare no competing financial interest.

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