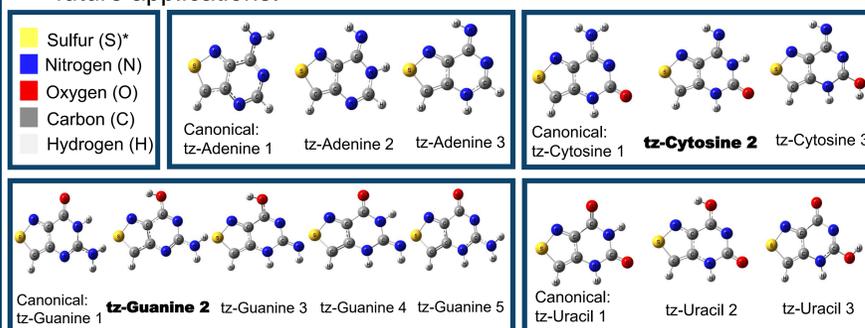


The Thermochemical and Structural Analysis of Tautomers of Sulfur and Selenium Modified RNA Nucleobases

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Introduction

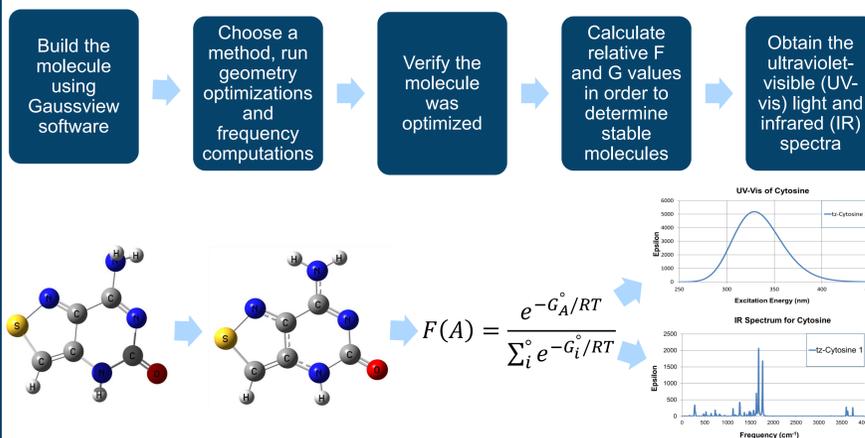
- Nucleobases are found in all living species and are the building blocks of RNA and DNA.¹
- The emissive properties of modified nucleobases have been discovered to be useful for probing in comparison to their non-emissive canonical structures.^{2,3}
- The purpose of this research is to analyze the previously studied nucleobases containing sulfur (tz- molecules) and nucleobases containing selenium (ts- molecules).² In doing so, the tautomers with the most stable and beneficial properties can be used in future applications.



*Sulfur atoms were replaced with selenium atoms for the ts- set of molecules that were analyzed

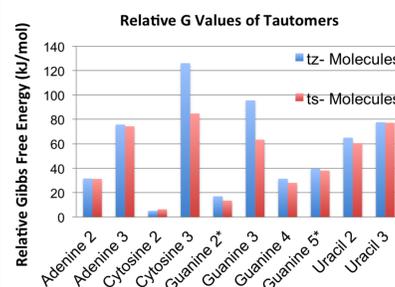
Methods

- The analysis of these molecules was done using Gaussian 09 computational chemistry software.⁴
- Geometry optimizations and frequency computations were performed using the semi-empirical PM6 method and was followed by the density functional theory (DFT) method with B3LYP/6-31++G(d,p) level of theory.⁵ Time-dependent density functional theory (TD-DFT) computations were done with B3LYP/6-31+G(d,p) level of theory.⁶
- The methodology followed for this research:



Results and Discussion

Which Molecules Are The Most Stable?



* The molecule did not fully converge while undergoing computations

Figure 1. The relative G values of nucleobase tautomers. The relative G value is the difference of Gibbs Free Energy between the original molecule and the tautomer.

Table 1. The equilibrium fractions of tautomers found by using the relative G values. Each number represents their stability and presence in an equilibrium with other forms of the nucleobase (the larger the value, the more stable).

Tautomer	Equilibrium Fraction for tz- Molecules	Equilibrium Fraction for ts- Molecules
Adenine 2	3.11×10^{-6}	3.54×10^{-6}
Adenine 3	5.42×10^{-14}	9.71×10^{-14}
Cytosine 2	0.121	0.0753
Cytosine 3	7.09×10^{-23}	1.29×10^{-19}
Guanine 2	1.12×10^{-3}	4.55×10^{-3}
Guanine 3	1.78×10^{-17}	8.01×10^{-12}
Guanine 4	3.33×10^{-6}	1.27×10^{-6}
Guanine 5	1.18×10^{-7}	2.20×10^{-7}
Uracil 2	4.18×10^{-12}	2.51×10^{-11}
Uracil 3	2.47×10^{-14}	2.98×10^{-14}

How Can These Molecules Be Detected Experimentally?

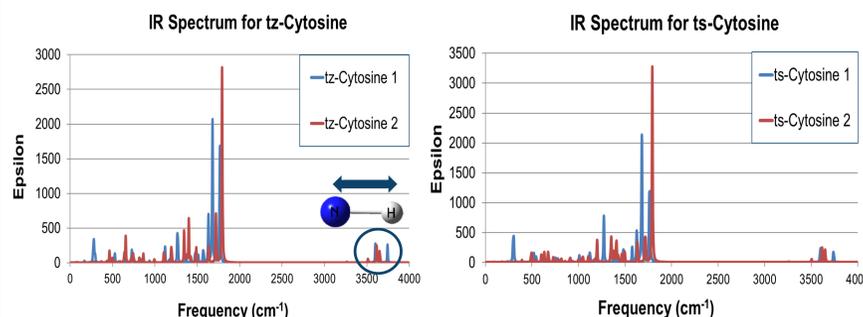


Figure 2. The IR spectra for Cytosine 1 and its tautomer Cytosine 2 with sulfur and selenium, respectively. Each peak represents the vibration of a specific bond in the molecule, for example, the peak found in the N-H bond range between 3500-4000cm⁻¹. For both graphs, tautomer peaks have a greater intensity and peaks are shifted to the right compared to the canonical molecules.

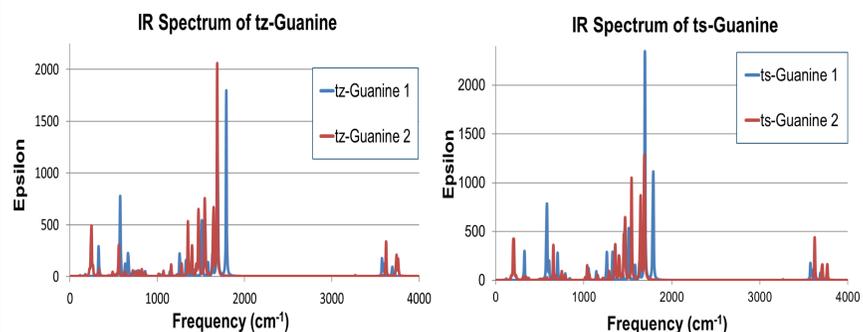


Figure 3. The IR spectra for Guanine 1 and 2 with sulfur and selenium. Tz-Guanine 2 has a greater intensity compared to the ts-Guanine 2 molecule; however, the results are similar in that the peaks for the ts- and tz- molecules are occurring at roughly the same frequencies.

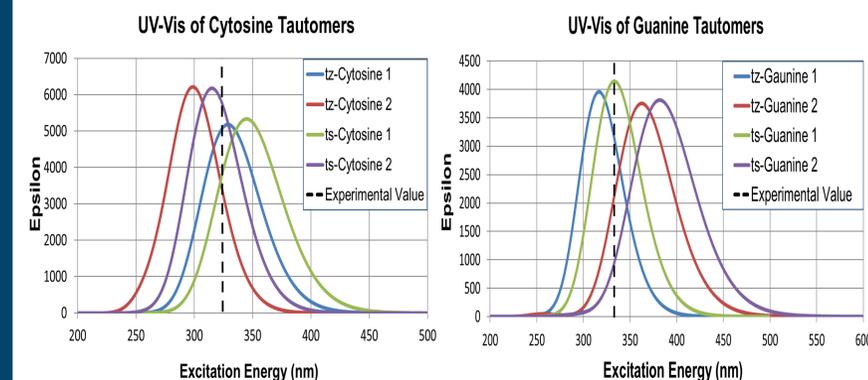


Figure 4. The UV-vis spectrum for Cytosine 1 and 2 with sulfur and selenium, and Guanine 1 and 2 with sulfur and selenium. Peaks represent the molecule's electronic excitation after absorbing light in the UV-vis region. The vertical dotted lines represent the experimental λ max values for tz-Cytosine 1 and tz-Guanine 1 molecules for comparison.²

Conclusions

- The four most stable tautomers are tz-Cytosine 2, ts-Cytosine 2, tz-Guanine 2 and ts-Guanine 2, which can be seen through the relatively high equilibrium fractions and low relative G values.
- The cytosine tautomer's stability can be attributed to the double bonded oxygen atom, but the oxygen atom has the opposite effect on the guanine tautomers.
- The adenine and uracil tautomers were not looked at due to the high relative G values and low equilibrium fractions, suggesting instability at equilibrium.
- Based on the UV-vis and IR spectra, these four tautomers should be detected separately experimentally from their canonical forms due to their shifted peak positions. This difference can guide experimentalists performing experiments with these molecules.

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