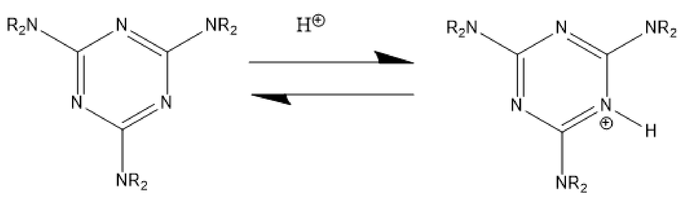
DFT Simulations of pKa Values of Triazines

Nicholas Henderson, Eric Simanek, Benjamin Janesko
Texas Christian University, Fort Worth, TX 76129

Abstract

Triazines appear in pharmaceuticals, agrochemicals, and as building blocks for polymers used in materials science and medicine. Predicting the structure and dynamics in water as a function of pH requires reliable simulations of the pKa values for different sites for protonation. We present the initial DFT methods and continuum solvent for pKa of amines, ring nitrogens, and 2,4,6-triamino-1,3,5-triazine (melamine) derivatives. These M06-2X/6-311++G(2d,2p) calculations in SMD continuum solvent provide consistent accuracy for tested systems, use for future studies of more complex structures.

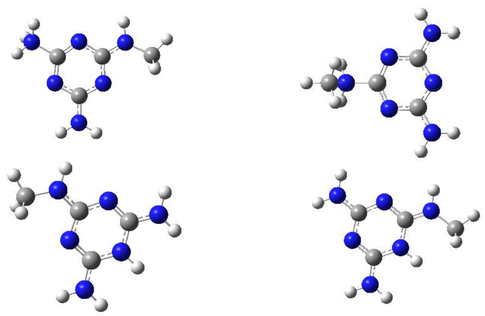


Experimental Details

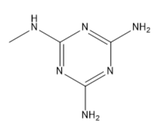
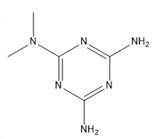
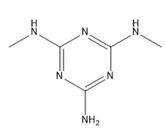
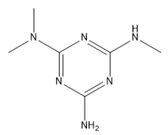
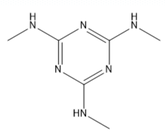
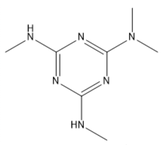
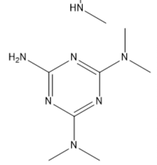
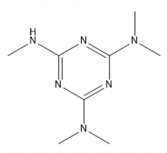
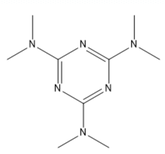
Computed stabilities for every potential protonation site were compared for a test set of triazines. The most negative computed free energy indicated the most stable species which is the most likely protonation site. Geometry optimization plus frequency calculations were performed using the Gaussian 16 electronic structure passage to compute pKa of each structure. Reported pKas were calculated by using the formula computed pKa-11.07 for error compensation.

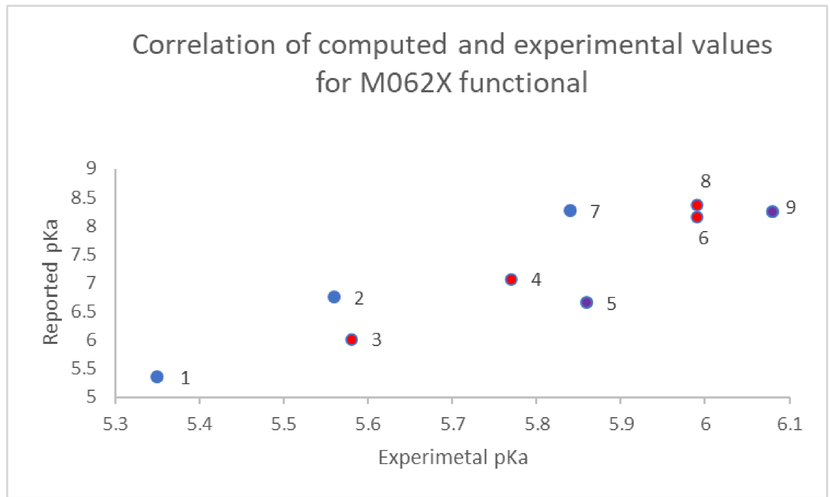
Geometry Optimized Structures

2,4-diamino-6-methylamino-1,3,5-triazine has four unique protonation sites. The stability and pKa was calculated for each unique site. This practice was employed for all structures in the data table.



Results

	Structure	Experimental pKa	Reported pKa
1		5.35	5.35
2		5.56	6.75
3		5.58	6.02
4		5.77	7.07
5		5.86	6.66
6		5.99	8.16
7		5.84	8.26
8		5.99	8.36
9		6.08	8.25



Conclusions

- The preferred protonation site is a ring nitrogen
- Apart from number 9, computed pKa values increase as number of methyl groups attached to the acyclic nitrogens increase, suggesting that addition of methyl groups results in a more basic
- A clear linear trend in the increase of computed pKa is observed for structure 1,2, and 7, as well as structure 3,4, and 8. Further work should be done to determine why this trend occurs.

Computational details

M062X/6-311++G(2d,2p) in SMD solvent water were calculated using Gaussian 16 software

References

Gabriel, H.; List, M.; Monkowius, U.; Puchinger, H.; Schwarzinger, C. *J. Org. Chem.* **2016**, 81, 4066−4075

Acknowledgements

The authors acknowledge the TCU High-Performance Computing Center for providing HPC resources