Effects of Solvent and Protonation on the Stereodynamics of Tri-Substituted Triazine Compounds

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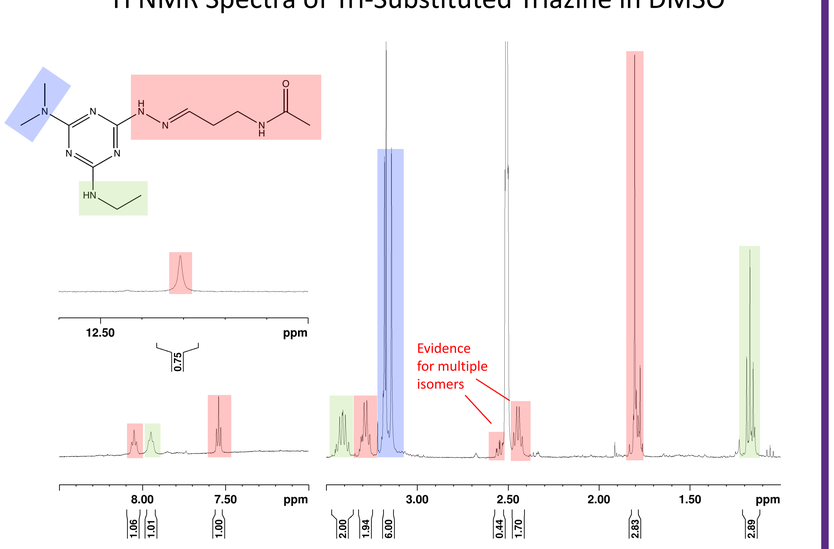
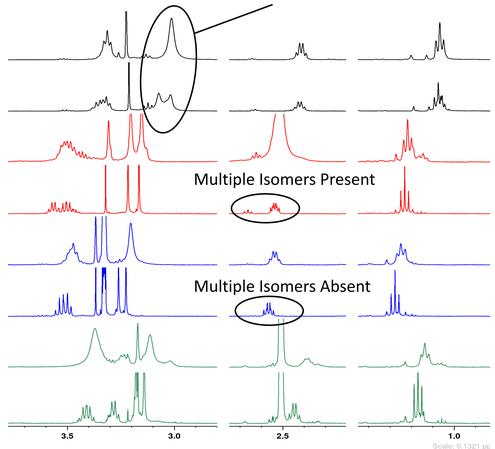
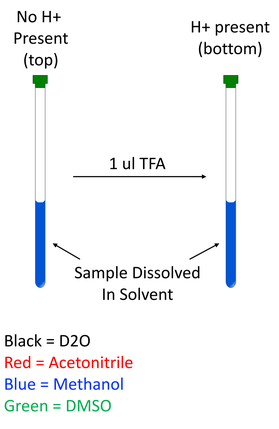
^{1}H NMR Spectra of Tri-Substituted Triazine in DMSO



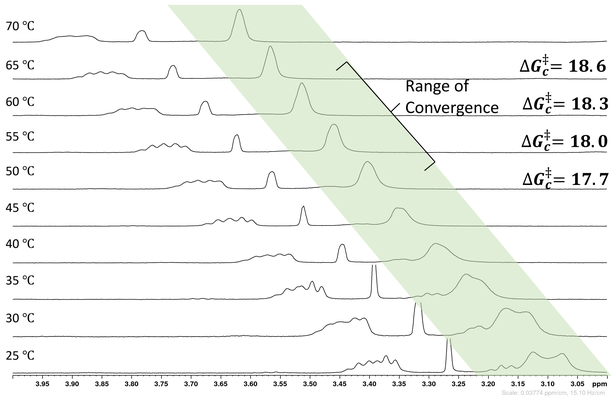
Distribution of Rotamers Depends on Solvent and Protonation State





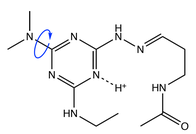
Black = D2O
Red = Acetonitrile
Blue = Methanol
Green = DMSO

Protonation Increases Barrier to Rotation of N-Ar Bond



$$\Delta G_c^{\ddagger}= RT_c Ln\frac{hk_{ex}}{kT_c}$$

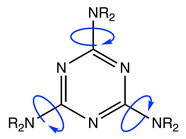
$$\Delta G_c^{\ddagger}= 18.2 \pm 0.5$$



Abstract

Barriers to rotation within triazine compounds have been previously explored by Katritzky and Birkett [1-2], but these studies have been limited to differences in the substituent groups on the triazine as well as the degree of substitution (mono, di, tri). This study explores how the barriers to rotation within triazine containing compounds are affected by solvent and protonation state. Overall, these molecules are of interest due to their wide range of applications in dendrimer and macrocycle synthesis as well as pharmaceutical drug development [3-4]. The results of this study illustrate how solvent selection can significantly impact the distribution of rotational isomers (rotamers) and how barriers to rotation can be increased by protonation of the triazine ring.

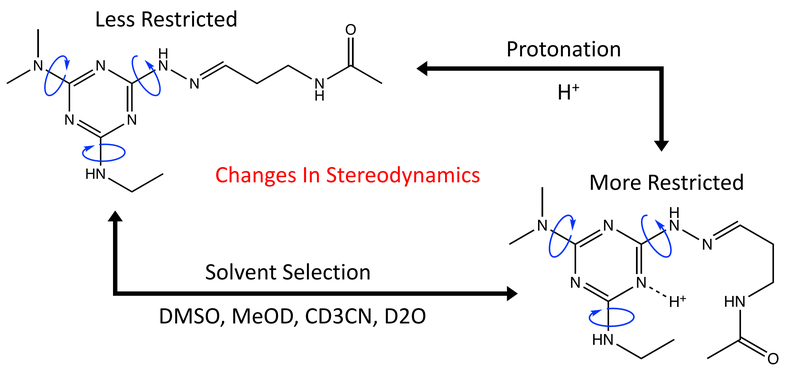
Previous Work Completed by Katritzky



R = Et
R = Pr
R = Pr^i
R = Bu
R = Bu^i
R = C_5H_{11}
R = C_8H_{17}

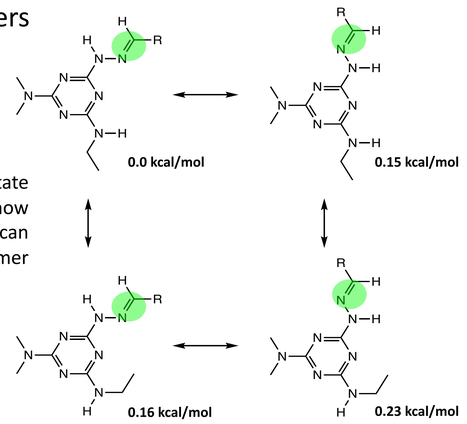
$$\Delta G_c^{\ddagger}= \sim 15.6\ kcal\ mol^{-1}$$

Current Strategy

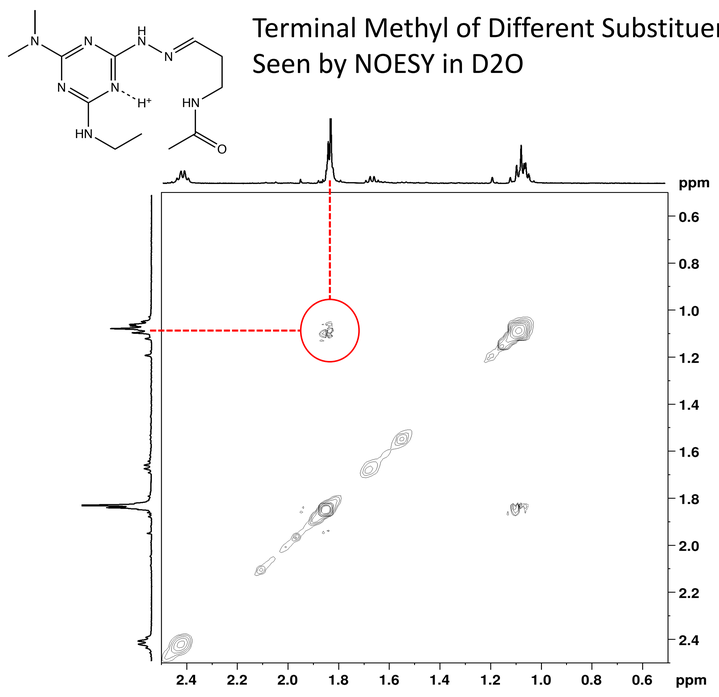


Energies of Different Rotamers

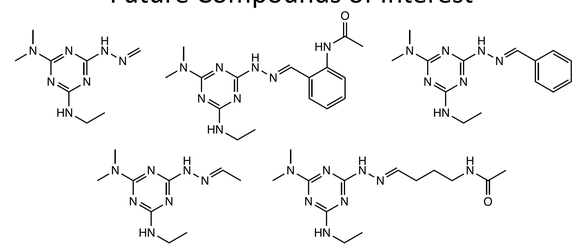
Small differences in relative ground state energies of rotamers illustrates how solvent selection or protonation state can cause bias towards one rotational isomer via non-covalent interactions.



Terminal Methyl of Different Substituents Seen by NOESY in D2O



Future Compounds of Interest



Conclusions

Solvent selection and protonation state play a large role in controlling the dynamic stereochemistry of tri-substituted triazine compounds. The results of this study provide foundational information for future design and synthesis of triazine containing compounds.

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References:

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