

ACS-PRF Annual Report October 2019

Asphaltenes are the insoluble component of crude oils, and are responsible for clogging of oil pipelines. Asphaltenes are large, polymorphous compounds composed of aromatic groups, aliphatic chains, and heteroatoms such as oxygen, nitrogen and sulfur. Research supported by this ACS-PRF award is aimed at understanding the factors involved in aggregation of model asphaltenes, in order to understand aggregation of asphaltenes so that it may be prevented. The use of small polycyclic aromatic hydrocarbons and similar small molecules as model asphaltenes ensures that our project remains fundamental.

In the first year of the grant, we examined the aggregation behavior of 5-fluorouracil (5FU) in both D₂O and DMSO. 5FU has three NMR handles that can be used to judge the performance of various theoretical methods and models. Figure 1(a) shows the chemical structure of 5FU with carbons numbered. Since this molecule has only one protonated carbon, we had to use the heteronuclear multiple-bond coherence (HMBC) technique to observe carbon chemical shifts at low concentrations. Typical one-dimensional ¹³C NMR experiments for this molecule would have required prohibitively long acquisition times. A representative HMBC spectrum of 5FU is shown with carbon peak assignments in Figure 1(b).

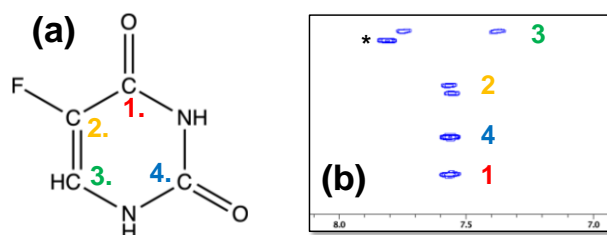


Figure 1. (a) Chemical structure of 5-fluorouracil (5FU) with carbons indicated. (b) Heteronuclear multiple-bond coherence (HMBC) spectrum used to observe carbon chemical shifts at low concentrations with carbons indicated. * indicates the peak for benzene, which was added within a coaxial insert for chemical shift referencing.

In order to examine aggregation in the two different solvents, we monitored the ¹H, ¹³C, and ¹⁹F NMR chemical shifts as a function of concentration. Proton and carbon chemical shifts are shown in Figures 2 and 3, respectively. Proton chemical shifts indicate aggregation in DMSO but not in D₂O. Carbon chemical shifts are less sensitive to changes in concentration. Last, in Figure 3 (c) and (d) we show that chemical shift calculations (B3LYP/6-311G//B3LYP/6-31G* using the polarizable continuum model for water) are able to reproduce the trends in carbon chemical shifts with a change of pH. These

preliminary studies set the stage for future studies with other molecules, including aromatic molecules with two or more fused rings. The next steps in these studies are to examine experimental and calculated ¹⁹F chemical shifts at various levels of theory to determine how well calculations can predict ¹⁹F chemical shifts. Since the ¹⁹F nucleus has a large chemical shift dispersion and is located on the outside of the molecule, we expect this nucleus to be a sensitive reporter of the environment. Chemical shifts will also be calculated for various proposed dimer structures, and will be compared to dimer chemical shifts that have been extrapolated from experiment. We are also in the process of exploring other NMR methods in order to deduce the dimer structure of these small aromatic molecules, and hope to report the results of these experiments in the next annual report.

This grant has thus far had an enormous impact on my career and that of my students. My graduate student Hui Xu won a Mandel fellowship from the chemistry department while being funded by the ACS-PRF grant. Three undergraduate students have been involved on the project so far, and have learned both experimental and theoretical NMR techniques. NMR chemical shift

calculations related to aggregation of asphaltenes were also incorporated into an undergraduate/graduate course: CH 4360/6360 Computational Quantum Chemistry and Electronic Structure Methods. Haley Yetter, a Clemson undergraduate, worked on the ACS-PRF project in summer 2019, and presented her results at the Clemson undergraduate poster session. She is currently working in the lab during the academic year, extending her summer studies and writing them up as an honors thesis. One publication has been published from the first year of the grant, and several more are in preparation. I was invited to contribute an invited special features review article on the topic of chemical shift calculations in solvated systems to the journal *Magnetic Resonance in Chemistry*, largely due to my work on this ACS-PRF project. The manuscript has been submitted and is currently under review.

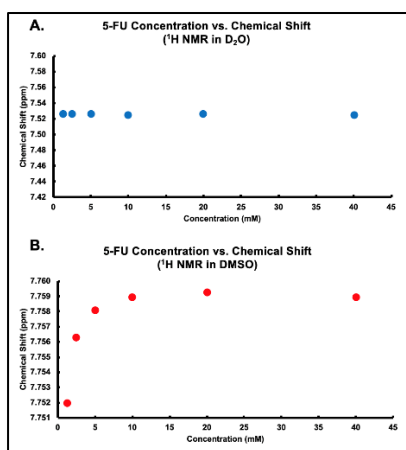


Figure 2. Change in ¹H chemical shift with concentration for 5FU in different solvents. The nearly constant chemical shift in D₂O indicates lack of aggregation in this solvent, while the change in chemical shift with concentration in DMSO indicates that 5FU aggregates in this solvent.

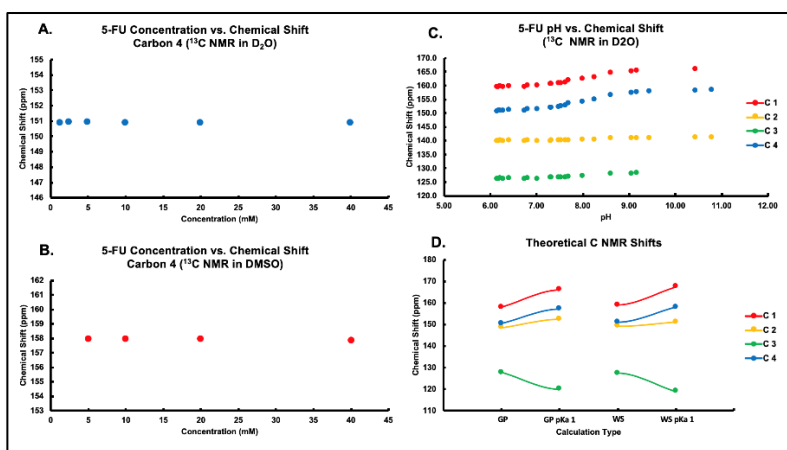


Figure 3. Carbon chemical shifts of 5FU under different conditions. The carbon chemical shift remains relatively constant with a change in concentration in both D₂O (a) and DMSO (b) solvents. (c) With increasing pH, chemical shifts of carbons 1, 3, and 4 increase while that of carbon 2 increases only slightly. (d) Chemical shift calculations in both gas phase and using implicit solvent reproduce the trend that the chemical shift of carbons 1 and 4 increases more than that of carbon 2 with an increase in pH.



Figure 4. Undergraduate Haley Yetter presenting her poster at the undergraduate poster session.

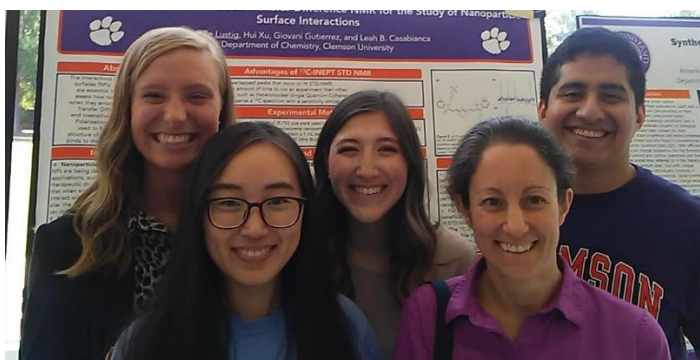


Figure 5. The Casabianca group at the undergraduate poster session.