Generality in Organic Chemistry

Abstract: The most useful reactions in organic chemistry are “general” in that they should work well for any substrate. However, we typically screen on a single model system, which leads to narrow substrate scope. In my first story, I’ll explain how advances in high-throughput experimentation (HTE) now allow multi-substrate screening and can lead to improved generality. Of course, some reactivity is so new that it is not ready for HTE, and we’d just like to understand how it works. In my second story, I’ll explain how the photochemical system recently developed by the Wendlandt group for the isomerization of sugars can be so stereoselective. I’ll show that there are analogs of kinetic and thermodynamic control in photochemical reaction networks. Remarkably, even though ~50 selectivity-determining steps involved, stereoselectivity can emerge naturally through mechanistically-correlated rate constants. Finally, I’ll demonstrate that machine learning (ML) can dramatically improve the prediction of nuclear magnetic resonance (NMR) chemical shifts. Typically, chemical shifts are predicted using density functional theory (DFT), and then linearly corrected with regression parameters. I’ll explain how explicitly modeling solute-solvent interactions using classical molecular dynamics (MD), followed by ML-accelerated NMR shielding computation, leads to significant reductions in errors vs. experiment across a broad range of solutes and solvents.