Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

KEVIN VOS

BSc (University of Victoria, 2015)


Department of Chemistry

Monday, June 1, 2020
1:30 P.M.
Remote Defence

Supervisory Committee:
Dr. Cornelia Bohne, Department of Chemistry, University of Victoria (Supervisor)
Dr. Fraser Hof, Department of Chemistry, UVic (Member)
Dr. David Berg, Department of Chemistry, UVic (Member)
Dr. Perry Howard, Department of Biochemistry and Microbiology, UVic (Outside Member)

External Examiner:
Dr. Vance Williams, Department of Chemistry, Simon Fraser University

Chair of Oral Examination:
Dr. Anastasi Mallidou, School of Nursing, UVic
Abstract

Systems chemistry is an emerging field of chemistry that studies complex mixtures of molecules that give rise to emergent properties that are not always predictable when studying the components of the mixtures in isolation. A systems chemistry approach has been adopted in fields such as self-assembly and self-sorting, where the dynamic recognition of complementary binding motifs to organize molecules is the central focus. Supramolecular systems are assembled through reversible, non-covalent interactions. The reversibility of supramolecular systems makes them dynamic. Understanding the dynamic nature of complex systems will allow for a bottom-up approach to the rational design of complex mixtures, such as kinetically trapped self-sorting systems.

The first objective of this work was to understand the effects the identity and concentration of biologically relevant metal cations have on the mechanism of binding and rate of kinetics of a cucurbit[7]uril (CB[7])-guest complex. Metal cations are frequently added to cucurbit[n]uril (CB[n]) systems. While metal cations are known to decrease the overall equilibrium constant of a CB[n]-guest complex, there has not been much consideration about how different metal cations can affect the CB[n]-guest binding mechanism beyond introducing competitive equilibria. Kinetic studies of the interactions between CB[7] and 1-(2-naphthyl)ethylammonium (NpH+) in the presence of Ca^{2+} and Na^{+} were investigated. It was found that the binding mechanism between NpH+ and CB[7] was the formation of an exclusion complex and an inclusion complex. An exclusion complex is the formation of a complex where the cationic ammonium group of the guest associates to the carbonyl lined portals of CB[7], while the aromatic group remains exposed to the surrounding; while an inclusion complex is formed when the aromatic group of the guest enters the hydrophobic cavity of CB[7]. By increasing the metal cation concentrations, the exclusion complex was seen to disappear from the overall kinetics. When Ca^{2+} cations were used instead of Na^{+} cations, a Ca^{2+} cation capped inclusion complex was formed. The Ca^{2+} cation capped inclusion complex was found to have a lower dissociation rate constant than the uncapped complex between NpH+ and CB[7].

The second objective of this work was to understand how the structure of guest molecules effected the kinetic time scale of reaction with CB[7]. The kinetics between CB[7] and three
different aromatic dications were measured to understand the structural features that influence the change in kinetic time scales: methyl viologen (MV$^{2+}$), benzidine (Bn$^{2+}$) and 2,7’-dimethyl-diazapyrenium (MDAP$^{2+}$). It was found that moving the cationic charges further apart slowed down the kinetics from the sub millisecond time scale (MV$^{2+}$) to the millisecond time scale (Bn$^{2+}$); further, it was found that adding rigidity and width to the molecule (MDAP$^{2+}$) slowed down the kinetics onto the minute time scale.

The final objective of this work was to use the understanding of complexity gained in the metal cation project and the guest design for kinetic time scales project to rationally design a kinetically-trapped self-sorting system. The equilibrium constants and time scale of kinetics between a ditopic guest molecule and three host molecules (CB[6], CB[7] and β-CD) were determined to investigate the feasibility of the kinetically-trapped self-sorting system. Due to the complexity introduced by metal cations discovered earlier, β-cyclodextrin (β-CD) was used to modulate the concentration of guest that could be bound by CB[n]s. As a concentration modulator the requirements of β-CD were that the kinetics must be faster than the millisecond time scale and the equilibrium constant with the guest must be much lower than the equilibrium constants between the guest and CB[n]s. CB[6] was proposed as a thermodynamic sink due to its slow kinetics for complex formation with benzyl ammonium. The requirements for the guest complexation with CB[6] were that the kinetics had to be on the minute to hour time scale and the equilibrium constant with the guest had to be the highest of the three host molecules. CB[7] was chosen as the kinetic trap of the self-sorting system. The requirements for the CB[7] complex were that the kinetics had to be on the millisecond to second time scale and the equilibrium constant needed to be lower than the equilibrium constant of the guest@CB[6] complex, but higher than the guest@β-CD complex. The kinetic and thermodynamic requirements between the guest molecule and CB[7], and between the guest molecule and β-CD were met. The kinetics between CB[6] and the guest molecule were on the hour time scale, meaning the kinetic requirement was met, however, the equilibrium constant was found to be lower than the equilibrium constant between the guest molecule and CB[7]. The results in this work showed that the rational design of kinetically-trapping self-sorting systems is possible, but some modifications to the structure of the guest molecule is required to make this self-sorting system work.