

Organic Chemistry Cumulative Examination

16 January 2020

Total: **100 points**

(1) What is Fragment-Based Drug Discovery (FBDD)? What are some advantages over traditional high-throughput screening? (10 points)

(2) What are three techniques that are commonly used to detect fragment binding in FBDD? (9 points)

(3) What advantages does ^{19}F -NMR based screening provide over proton-based methods? (12 points)

(4) What is F_{sp^3} ? How does it relate to natural products and druglike small molecules? (10 points)

(5) What is a bioisostere? Why is fluorine commonly used as a bioisostere? (6 points)

(6) What information is obtained from a principal moment of inertia (PMI) plot? How did the newly created fragment library compare to commercial fragments? How did the newly created fragment library compare to the natural product collection? (10 points)

(7) When protein is added to the small molecule cocktail how does the signal change in the ^{19}F -NMR screen if a small molecule binds the protein? (5 points)

(8) Fill in the missing reagents or intermediates in the reaction schemes below that were used to create the new 3F small molecule library (38 points)



