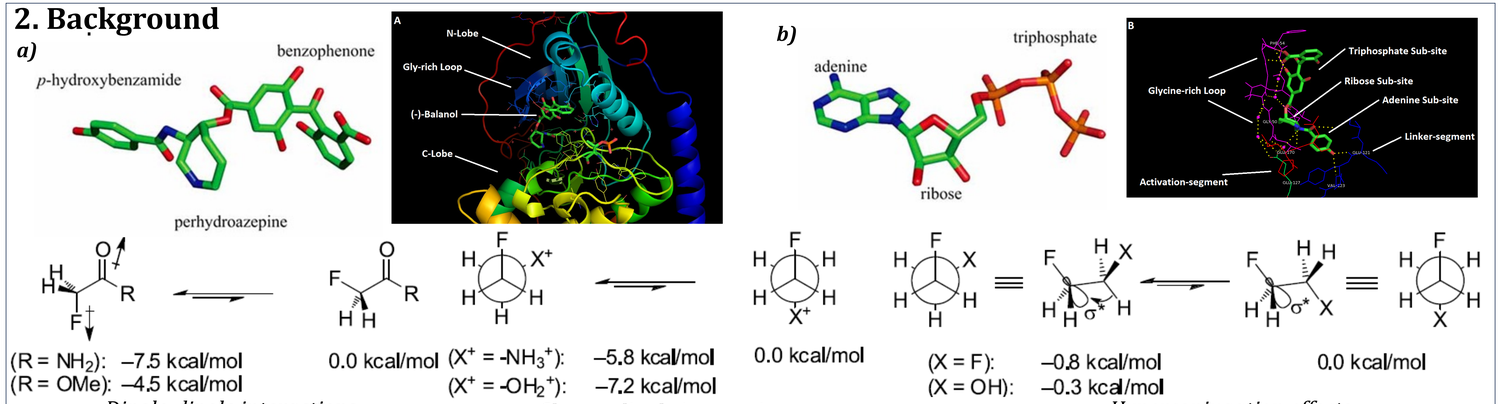
Total Synthesis of Fluorinated (–)-Balanol Analogues for Probing Selectivity Towards AGC Kinases in Cancer

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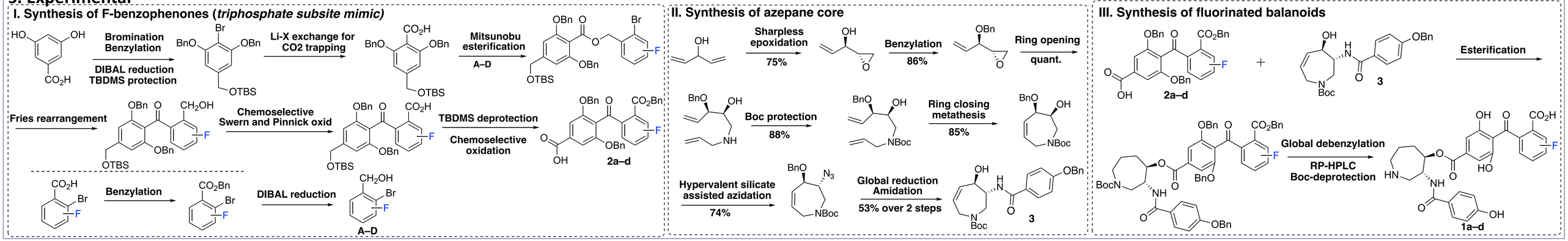
1. Abstract

With the recent recognition of conformation entropy following the discovery of Imatinib, there has been a growing interest in taking the approach of congruent conformation induction between a protein and its ligand for developing specific drug leads. We investigated this conformational induction using C–F bond as a tuning handle on (–)-balanol as a model system for enhanced selectivity toward AGC protein kinases. (–)-Balanol **1**, a fungal metabolite, is a potent protein kinase A (PKA) and PKC competitive ATP mimic. However, the inhibitor displays limited selectivity across the AGC superfamily. In this work, four fluorinated balanoids were synthesised in 26 steps each and binding affinity profile of the balanoids showed that fluorination in benzophenone (triphosphate subsite mimic) retains affinity for prototype PKA with enhanced selectivity (>600-fold) in balanoid **1b.**

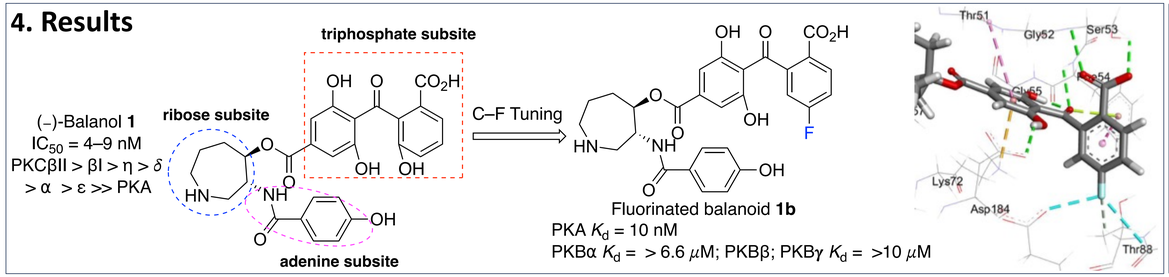
2. Background



3. Experimental



4. Results



5. References

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