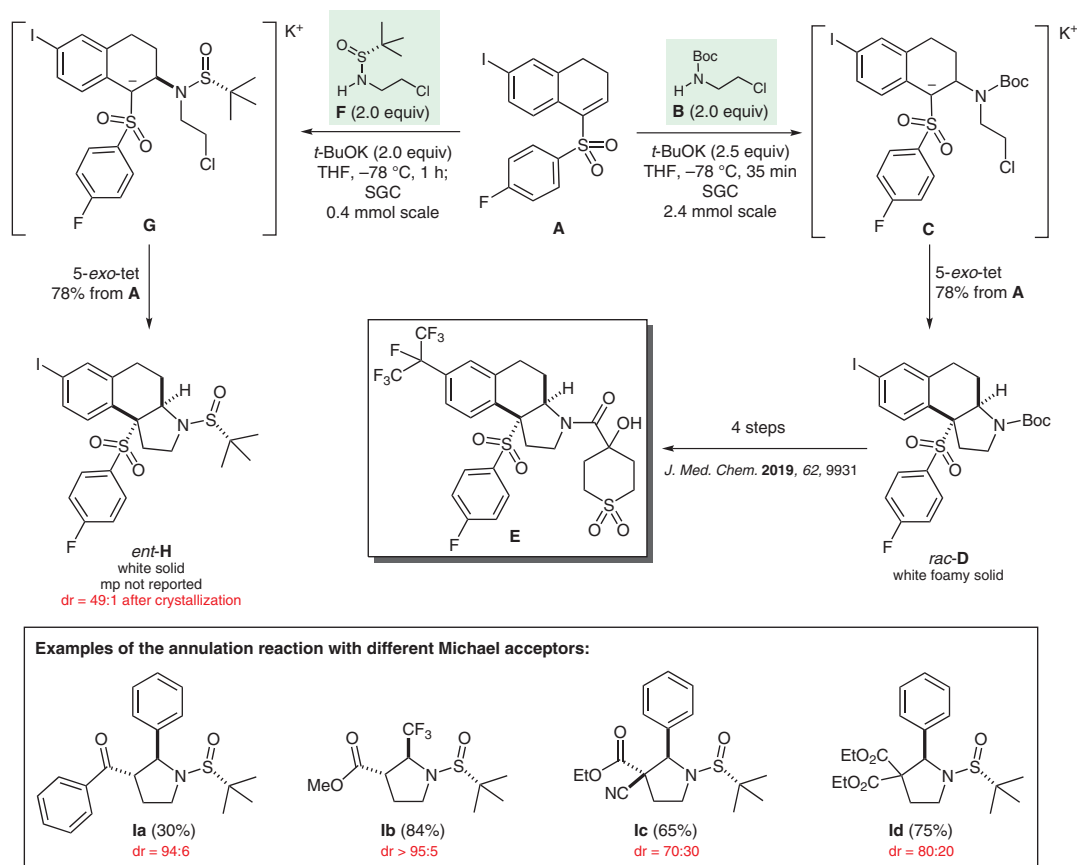


Diastereoselective Pyrrolidine Synthesis Using a Sulfonamide Annulating Agent



Significance: A recent synthesis of the ROR γ t inverse agonist **E** (*J. Med. Chem.* **2019**, 63, 9931) featured an aza-Michael addition of metallated carbamate **B** to Michael acceptor **A** followed by cyclization of adduct **C** to give pyrrolidine *rac*-**D** as a single diastereoisomer in 75% yield. The conversion of *rac*-**D** into the target molecule **E** then required four steps including an SFC separation of enantiomers. An asymmetric variant of the pyrrolidine annulation has now been developed that obviates the need for chromatographic resolution. Thus, the diastereoselective aza-Michael addition of chiral sulfonamide **F** to sulfone **A** afforded adduct **G** which then cyclized to give pyrrolidine *ent*-**H** in 75% yield and dr = 49:1.

Comment: The novel and versatile annulating reagent **F** is crystalline and stable at room temperature for more than one year. Moreover, the sulfonamide group renders the corresponding products crystalline. The annulation reaction possesses a wide scope, as a variety of singly and doubly activated Michael acceptors provide the corresponding pyrrolidines in moderate to high yields with excellent diastereoselectivities (24 examples).