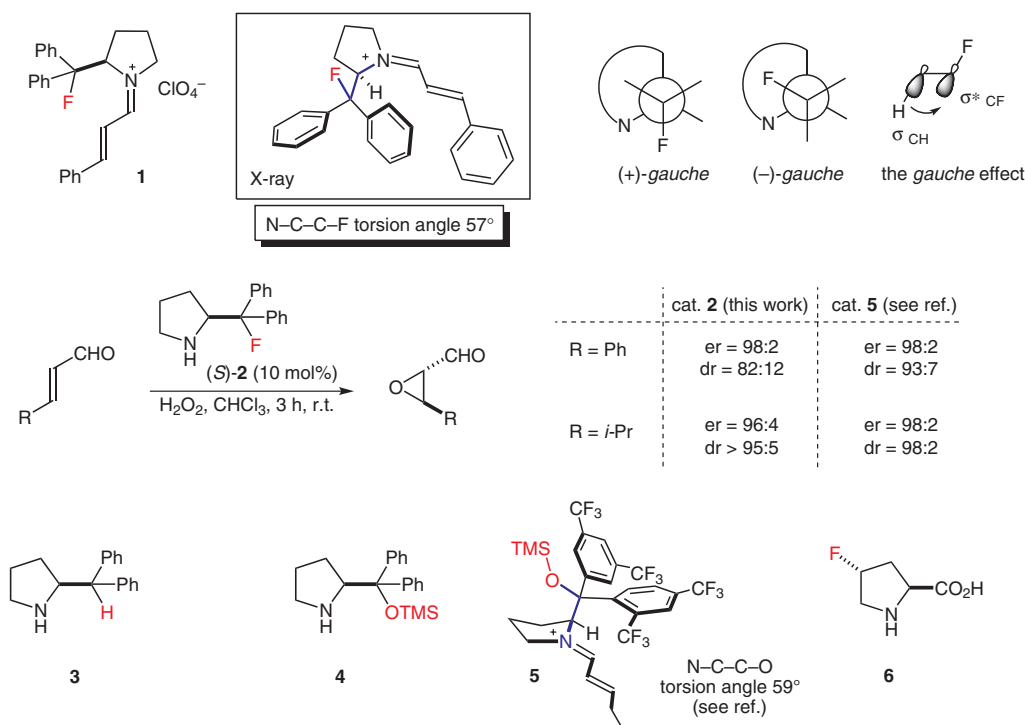


A Fluorinated “Designer” Organocatalyst



Significance: Gilmour and colleagues report the study and application of commercially available 2-(fluorodiphenylmethyl)pyrrolidine **2** as a secondary amine organocatalyst. The authors hypothesized that a fluorine atom beta to the pyrrolidine nitrogen would lead to a pronounced preference for a *gauche* conformation of the iminium intermediate of type **1**, possibly resulting in enhanced asymmetric induction. Crystallographic and computational studies were used to support this hypothesis. As proof of principle, catalyst (S)-**2** was applied to a Weitz–Scheffer epoxidation. The observed enantioselectivity of catalyst (S)-**2** proved to be comparable to the original Jørgensen catalyst **4** (*J. Am. Chem. Soc.* **2005**, *127*, 6964) and superior to the non-fluorinated analogue **3**.

Comment: The fluorine-iminium ion *gauche* effect may become a stimulating concept for catalyst design and find use in solving problems in organocatalysis. Remarkably, computational and X-ray studies of analogous iminium ions derived of the Hayashi–Jørgensen prolinol silyl ethers by Seebach et al. (*Helv. Chim. Acta* **2008**, *91*, 1999) revealed a very similar *gauche* N–C–O torsion angle of 59° (structure **5**), suggesting the possibility that the OTMS group exerts the same effect. Furthermore, it is interesting to speculate on the role of the fluorine atom in the transannular aldol reactions catalyzed by fluoroproline derivative **6**, recently disclosed by Chandler and List (*J. Am. Chem. Soc.* **2008**, *130*, 6737).