S. M. BANIK, J. W. MEDLEY, E. N. JACOBSEN* (HARVARD UNIVERSITY, CAMBRIDGE, USA) Catalytic, Asymmetric Difluorination of Alkenes to Generate Difluoromethylated Stereocenters *Science* **2016**, *353*, 51–54.

Catalytic Asymmetric Geminal Difluorination of β-Substituted Styrenes

$$R^{4} \stackrel{\text{II}}{ \text{II}} \qquad R^{3} \qquad Py.9HF \ (100 \ \text{equiv}) \qquad R^{4} \stackrel{\text{II}}{ \text{II}} \qquad R^{2} \qquad R^{3} = \text{Alk, } (CH_{2})_{2}CI \qquad 32 \ \text{examples} \qquad R^{2} = \text{ester, amide,} \qquad R^{4} = \text{halogen, OAc,} \qquad 28-93\% \ \text{yield} \qquad R^{2} = \text{Alk, Ar} \qquad NPhth, NO_{2}, Me \qquad \text{er from } 82:18 \ \text{to } 98.5:1.5$$

Proposed reaction mechanism:

Significance: Jacobsen and co-workers report a direct, catalytic, and highly enantioselective transformation of β-substituted styrenes to form difluoromethylated tertiary or quaternary stereocenters. The reaction starts with the oxidation of the aryl iodide catalyst to give iodoso arene I, which reacts with HF to give hypervalent iodine intermediate II. The catalytic cycle proceeds with an enantioselective 1,2-fluoroiodination to give IV, followed by the stereospecific formation of phenonium ion V. The final regioselective fluoride addition leads to product 2 in high yield and high enantioselectivity.

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a diastereoselective 1,2-difluorination of alkenes (*J. Am. Chem. Soc.* **2016**, 138, 5000), which occurs through anchimeric assistance by a carbonyl group, whereas here the 1,1-difluorination is achieved through skeletal rearrangement via phenonium ion intermediate **V**.

Comment: Geminal difluoro groups are important

inert isosteres of polar functional groups such as

alcohols and thiols. The authors recently reported

Category

Organo- and Biocatalysis

Key words

fluorination

asymmetric catalysis

hypervalent iodine

phenonium ion intermediates

styrenes

