Catalytic Asymmetric Geminal Difluorination of β-Substituted Styrenes

**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.

**Comment:** Geminal difluoro groups are important inert isosteres of polar functional groups such as alcohols and thiols. The authors recently reported 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.

**Selected examples:**

- 67% yield, er = 96:4
- 49% yield, er = 92:8
- 29% yield, er = 98.2
- 57% yield, er = 96.5:3.5
- 74% yield, er = 85.5:14.5
- 93% yield, er = 88:12

**Proposed reaction mechanism:**

1. **Iodination:** Oxidation of the aryl iodide catalyst to give iodoso arene I.
2. **Fluoroiodination:** Enantioselective 1,2-fluoroiodination to give IV.
3. **Phenonium ion formation:** Stereospecific formation of phenonium ion V.
4. **Fluoride addition:** Regioselective fluoride addition to give product 2.