Asymmetric Nucleophilic Fluorination under Hydrogen Bonding Phase-Transfer Catalysis


Hydrogen-Bonding Phase-Transfer Catalyst Enabled Asymmetric Fluorination

**Significance:** Gouverneur and co-workers merge two fundamental strategies of modern catalyst design, hydrogen-bonding interactions and phase-transfer catalysis, to report a chiral bis-urea catalyzed asymmetric nucleophilic fluorination of episulfonium salts formed in situ. The fluorinated products are formed in good to excellent yields and moderate to good enantioselectivities by using CsF.

**Comment:** Hydrogen-bonding phase-transfer catalysis (HB PTC) has been previously reported in highly enantioselective nitro-Mannich reactions (B. Wang, Y. Liu, C. Sun, Z. Wei, J. Cao, D. Liang, Y. Lin, H. Duan Org. Lett. 2014, 16, 6432). Gouverneur and co-workers develop such catalysts to solve a synthetic challenge; namely, to enable an asymmetric fluorination reaction using a safe and readily accessible inorganic fluorine source. Henceforth, the expansion of HB PTC to other systems is expected.

**Selected examples:**

- **R1 = (CH2)2Ph or Me, R2 = halide, Me, OMe**
  - (S,S)-2: 12 examples, 53–98% yield, er from 91.9 to 97.3

  **Proposed mechanism:**

  

  ![Proposed mechanism](image)

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**SYNFACTS 2018, 14(08), 0861 Published online: 18.07.2018 DOI: 10.1055/s-0037-1609893; Reg-No.: B05418SF

**Category**

Organo- and Biocatalysis

**Key words**

- phase-transfer catalysis
- nucleophilic fluorination
- hydrogen bonding
- bis-urea catalysis