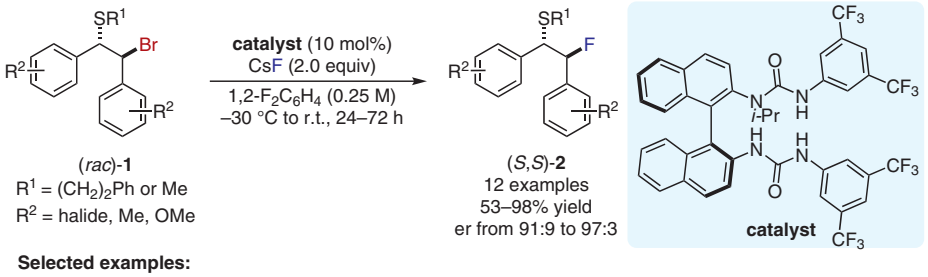
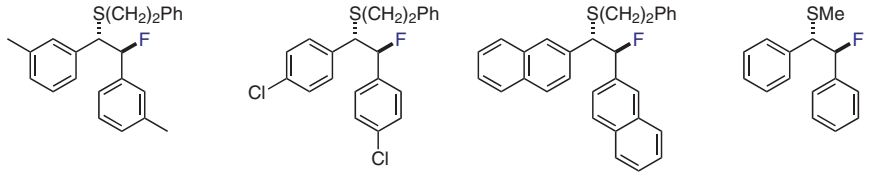
G. PUPO, F. IBBA, D. M. H. ASCOUGH, A. C. VICINI, P. RICCI, K. E. CHRISTENSEN, L. PFEIFER, J. R. MORPHY, J. M. BROWN, R. S. PATON, V. GOUVERNEUR* (UNIVERSITY OF OXFORD AND ELI LILLY AND CO. LTD., WINDLESHAM, UK)

Asymmetric Nucleophilic Fluorination under Hydrogen Bonding Phase-Transfer Catalysis
Science **2018**, *360*, 638–642.

Hydrogen-Bonding Phase-Transfer Catalyst Enabled Asymmetric Fluorination

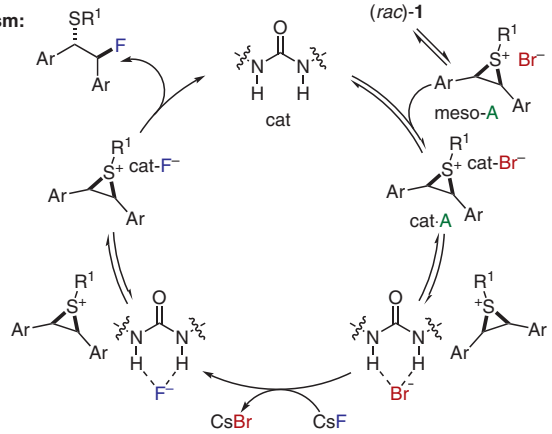


Selected examples:



62% yield, er = 94:6 (gram scale) | 53% yield, er = 93:7 | 72% yield, er = 95.5:4.5 | 87% yield, er = 91:9

Proposed mechanism:



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.

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Category
Organo- and Biocatalysis

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