Hydrogen-Bonding Phase-Transfer Catalysis toward \(\beta\)-Fluoroamines

**Significance:** Gouverneur and co-workers report a nucleophilic fluorination of \(\beta\)-chloroamines by using a chiral bisurea catalyst and KF or CsF as a solid source of fluoride in hydrogen-bonding phase-transfer catalysis (HB-PTC). Both fluoride sources are easy to handle, nontoxic, and cheap in comparison with other fluorination reagents. The \(\beta\)-fluoroamines were obtained in high yields and high enantioselectivities, and, for some examples, on a large scale.

**Comment:** The concept of HB-PTC was recently applied to nucleophilic fluorination reactions by the authors (Science 2018, 360, 638). On the basis of this work, they were able to further decrease the cost of the fluoride source, without loss of enantioselectivity, by using KF. Furthermore, the authors approached a broader scope by using aziridinium ion precursors, which led to the synthesis of several fluoro derivatives of approved drugs (e.g., diphenidine).

**Selected examples:**
- Conditions A: 69% yield, \(er = 85.5:14.5\)
- Conditions B: 60% yield, \(er = 85.15\)
- Conditions A: 89% yield, \(er = 95.5:4.5\)
- Conditions B: 72% yield, \(er = 95.5:4.5\)
- Conditions A: 56% yield, \(er = 96.4\)
- Conditions B: 90% yield, \(er = 95.5\)
- Conditions A: 71% yield, \(er = 95.5\)
- Conditions B: 95% yield, \(er = 95.5\)

On 50 g scale (fluorinated diphenidine)

**Proposed mechanism:**

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\begin{align*}
\text{catalyst} & \quad \text{KF (5 equiv), CHCl}_3 (0.5 \text{ M}) \\
\text{conditions A: catalyst} (5-10 \text{ mol%}) & \quad \text{KF} (5 \text{ equiv}), \text{CHCl}_3 (0.5 \text{ M}) \\
\text{conditions B: catalyst} (5-10 \text{ mol%}) & \quad \text{CsF} (3 \text{ equiv}), \text{CHCl}_3 (0.25 \text{ M})
\end{align*}
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