Asymmetric Fluorination Approach to an SYK Inhibitor

**Significance:** Spleen tyrosine kinase (SYK) is implicated in diverse cellular responses such as proliferation, differentiation, and phagocytosis. The target molecule is a SYK inhibitor that is of interest for the treatment of rheumatoid arthritis, B-cell lymphoma, and asthma. The highly telescoped, large-scale synthesis depicted delivered eight kilograms of API.

**Comment:** The asymmetric fluorination of β-keto ester A using (S)-BINAP as the chiral ligand gave a modest 44% ee but this improved to 72% ee with the bulkier DTBM-SEGPHOS ligand. The best results were obtained by the combined use of a chiral auxiliary (L-menthol) and an enantio- and diastereoselective fluorination (C + D → E) mediated by Pd[(S)-binap](OTf)₂.

**SYNFACTS Contributors:** Philip Kocienski

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