Highly Enantioselective Fluorination of Unprotected 3-Substituted Oxindoles: One-Step Synthesis of BMS 204352 (Maxipost)


**Synthesis of Maxipost**

**Significance:** Maxipost is a post-stroke neuroprotective agent that acts by opening large conductance Ca$^{2+}$-activated (maxi-K) potassium channels. Previous syntheses of maxipost by asymmetric fluorination of oxindoles required protection of the oxindole nitrogen as the N-Boc derivative. The route depicted features the direct asymmetric catalytic fluorination of the oxindole A using N-fluorobenzenesulfonimide (B) in the presence of 10 mol% of a chiral complex derived from scandium triflate and the amine oxide ligand C.

**Comment:** Attempts to perform the maxipost synthesis on a 3.5 mmol scale resulted in decreased yield and enantioslectivity (53% yield, 86% ee) due to the low solubility of the substrate. By contrast, the asymmetric fluorination of oxindole D on a 4.0 mmol scale gave E in 93% yield and 97% ee. The small selection of the 29 examples described, showed that yields and enantioselectivities are generally high.

**Asymmetric fluorination of oxindole D on a gram scale:**

**Further examples of the asymmetric fluorination of oxindoles:**

- 81% (er > 97:3)
- 85% (er > 96:4)
- 90% (er > 98:2)
- 84% (er > 95:5)

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