Synthesis of the Glucocorticoid Agonist BI 653048 BS H$_3$PO$_4$

**Significance:** BI 653048 BS H$_3$PO$_4$ is a glucocorticoid agonist that is a candidate for the treatment of rheumatoid arthritis. In the synthesis depicted, the key step is the zinc-mediated asymmetric propargylation of trifluoromethyl ketone A using propargyl boronate C and proline-derived ligand B. The synthesis delivered 94 kg of the API in 17.6% overall yield.

**Comment:** A detailed exploration of the mechanism of the zinc-mediated propargylation of the trifluoromethyl ketone I is described in an accompanying paper (J. Org. Chem. 2013, 78, 3592) that includes a zinc-catalyzed variant. In the case of the zinc-catalyzed reaction, water is an essential component. The target molecule is isolated as a 1:1 complex (not a salt) with phosphoric acid.