Synthesis of a Phosphoinositide 3-Kinase (PI3K) β Inhibitor

**Significance:** The target molecule \( K \) is a phosphoinositide 3-kinase (PI3K) β inhibitor that is of interest for the treatment of various cancers. The restricted axis of rotation around a carbon–nitrogen bond of rac-\( K \) generated atropisomeric compounds (P)-\( K \) and (M)-\( K \) with significantly different pharmacological and pharmacokinetic profiles.

**Comment:** The metabolism of the inactive atropisomer (M)-\( K \) is the result of the action of the enzyme aldehyde oxidase (AO) whereas the active atropisomer (P)-\( K \) has lower affinity for AO resulting in better metabolic stability. The atropisomers (\( \Delta E_R = 35 \text{ kcal/mol} \)) were separated by preparative chiral SFC chromatography.