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 (\(\Delta E_{rot} = 35\) kcal/mol) were separated by preparative chiral SFC chromatography.