

## Synthesis of a Phosphoinositide 3-Kinase (PI3K) $\beta$ Inhibitor

Category

Synthesis of Natural Products and Potential Drugs

Key words

phosphoinositide 3-kinase  $\beta$  inhibitor

aldehyde oxidase

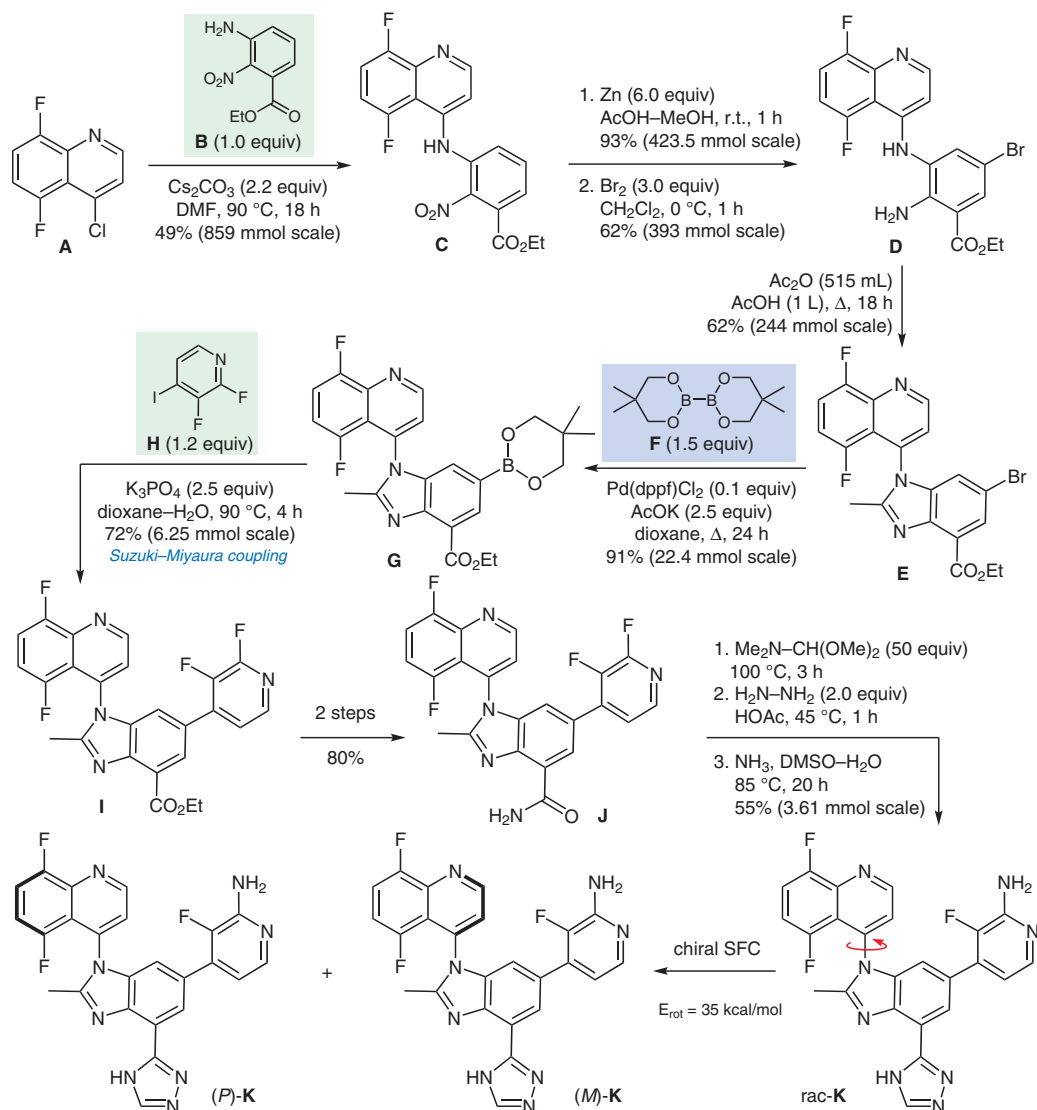
atropisomers

benzimidazole ring formation

1,2,4-triazole ring formation

Suzuki–Miyaura coupling

Synfact  
of the month



**Significance:** The target molecule **K** is a phosphoinositide 3-kinase (PI3K)  $\beta$  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 ( $\Delta E_{\text{rot}} = 35$  kcal/mol) were separated by preparative chiral SFC chromatography.

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