Discovery and in Vivo Evaluation of Macrocyclic Mcl-1 Inhibitors Featuring an \(\alpha\)-Hydroxy Phenylacetic Acid Pharmacophore or Bioisostere

**J. Med. Chem. 2019, 63, 10258–10271.**

**Synthesis of a Macrocyclic Mcl-1 Inhibitor**

**Significance:** Overexpression of the antiapoptotic protein Mcl-1 benefits survival of some cancer cells. The target molecule **R** is an inhibitor of Mcl-1. A key step in the synthesis depicted is the macrocyclization of diene **J** by ring-closing metathesis.

**Comment:** The addition of Reformatsky reagent **F** to the keto group in **E** generated a mixture of diastereoisomers **G** (dr = 2:1) that was later separated by column chromatography to give the desired diastereoisomer **K**.

**Key words**
- Mcl-1 inhibitor
- ring-closing metathesis
- macrocyclization
- Reformatsky reaction
- \(\alpha\)-hydroxy phenylacetic acids