Synthesis of Vaniprevir

**Significance:** The key step in this synthesis of vaniprevir is the construction of the macrocycle (91% yield) via ring-closing metathesis (RCM). By using simultaneous slow addition of the substrate and the catalyst \( \text{D} \) (0.2 mol%), the RCM reaction could be conducted at high concentration (0.13 M) on a 100 g scale.

**Comment:** 2,6-Dichloro-1,4-benzoquinone was added to suppress isomerization of the allyl alkene in the isoindoline unit in \( \text{C} \) and consequent competing formation of a 19-membered ring by-product. An important contributor to the success of the RCM reaction was the high purity of crystalline \( \text{B} \).