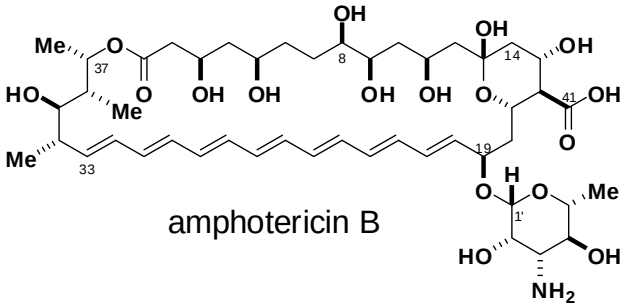
Synthesis-Enabled Investigation of the Amphotericin B-Based Ion Channel

Daniel S. Palacios and Martin D. Burke

The treatment of choice for systemic fungal infections over the past three decades has been and continues to be amphotericin B. Evidence suggests that amphotericin B inserts into sterol-rich lipid bilayers and self-assembles into a transmembrane ion channel that can disrupt transmembrane electrochemical gradients. In this way, amphotericin B represents a potential prototype for a small molecule with protein-like ion channel function. However, the nature of this channel remains elusive. To gain an atomistic understanding of this small molecule-based ion channel we employed synthetic organic chemistry to prepare derivatives lacking the functional groups thought to be essential for channel formation. A liposomal-based assay was then developed to quantify activity.



amphotericin B