**Significance:** Pyripyropene A is a fungal metabolite isolated from *Aspergillus fumigatus* FO-1289–2501. It is a potent inhibitor of Acyl-CoA:cholesterol-acyltransferase. Several semi-synthetic derivatives show even greater inhibition.

**Comment:** Key steps in this synthesis include the titanium-mediated epoxide opening–radical cyclization (A → D) and a Petersen-olefination/epoxide-opening sequence (F → J). A more scalable sequence from D to F involving Me₂NHB(OAc)₃ as an alternative reducing agent was also reported.