Synthesis of Eravacycline

**Significance:** Eravacycline is a fully synthetic broad-spectrum antibiotic that has completed phase 2 clinical trials for the treatment of multidrug-resistant bacteria. The key step entails the construction of ring C by a tandem Michael addition of arene A to cyclohexenone B followed by a Dieckmann cyclization to afford pentacycle C in 94% yield on a mol scale.

**Comment:** The versatile Michael–Dieckmann route to tetracyclines was pioneered by Myers and co-workers (J. Am. Chem. Soc. 2008, 130, 17913). A seven-step multigram-scale synthesis of the crystalline cyclohexenone B has been described: J. D. Brubaker, A. G. Myers Org. Lett. 2007, 9, 3523. Several kilograms of eravacycline were synthesized by the route depicted.