Synthesis of Natural Products and

Potential Drugs

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.

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tetracycline antibiotics

Michael-Dieckmann annulation

