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PS #4 - Robinson Annulation Mechanism and Synthetic Planning

Part A) When a conjugate addition (Michael addition) is followed by an intramolecular aldol condensation, a new ring is formed. This sequential process is called the Robinson annulation (or annelation). Annulation is a term that describes the formation of a ring. As a group, work out the detailed mechanism for the Robinson annulation reaction between 2-methylcyclohexanone and methyl vinyl ketone (3-buten-2-one).

Part B) Platensimycin is a novel lead compound recently discovered by researchers at Merck Research Laboratories. It was isolated from a strain of *Streptomyces platensis* and is the first new chemical class of antibiotic to be found in more than two decades! Platensimycin kills several of the major drugresistant bacteria that plague hospitals (MRSA and bacteria resistant to vancomycin). Platensimycin works differently from other commercially available antibiotics. It disrupts a

bacterial enzyme responsible for the production of fatty acids, thus preventing bacteria from making the fatty cell membranes they need to grow. Since the structure of Platensimycin was elucidated, several research groups have been working to synthesize the antibiotic. It has been proposed the complex tetracyclic core structure of Platensimycin (B) could be synthesized using an intramolecular Robinson annulation. Working as a group, propose a reasonable synthetic route to synthesize the Platensimycin precursor (B) from the starting material (A) below.