A Regio- and Stereo-Selective Annulation to Form the “Inside-Out” *trans*-Bicyclo[9.2.1]Tetradecane Ring System

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Revisions are highlighted in blue

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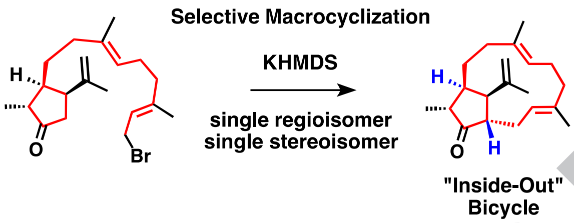
Graphic Abstract:



Highlights

- The macrocyclization proceeds with complete stereocontrol
- The shape of the precursor controls the alkylation's regioselectivity
- The overall synthesis averages 85% yield per step

Abstract:

trans-Bicycles (commonly known "inside-out" bicycles) are structurally interesting synthetic challenges and include various biologically active natural products. The current results describe a synthetic strategy to access the *trans*-bicyclo[9.2.1]tetradecane ring system, which has been relatively unexplored until now. This method utilizes the inherent reactivity of trisubstituted cyclopentanones to control an intramolecular macrocyclization and establish the bicyclic structure as a single isomer. The cyclopentanone precursor is readily accessible as a single enantiomer, and the full synthetic sequence provides a 9% overall yield (85% average yield per step) of the bicycle.