Massachusetts Institute of Technology
Organic Chemistry 5.512

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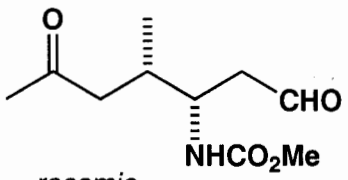
Problem Set 2
Strategies for Synthesis of Acyclic Molecules Based on Desymmetrization, Chirality Transfer, the "Chiron Approach", and "Ring Template" Strategies

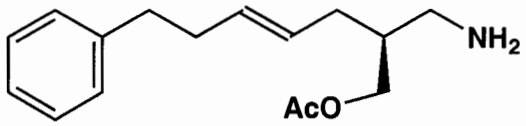
I. Design a highly stereoselective synthesis of the following target molecules beginning with commercially available materials and employing one of the strategies listed above. For the compounds indicated, a route to the target molecule in racemic form will be sufficient. Be sure to explicitly identify all reagents necessary for each transformation. Enantiomerically enriched reagents may be used if they are commercially available; however, each stereogenic center in the target molecule must be generated in your synthetic route. In other words, the stereogenic carbons in the chiral reagents you employ cannot be directly incorporated in the final product.

(1)

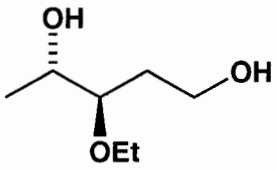


racemic

(3)

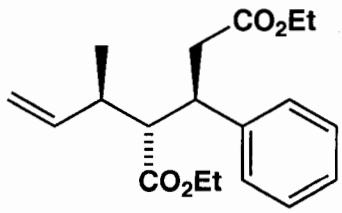


(2)



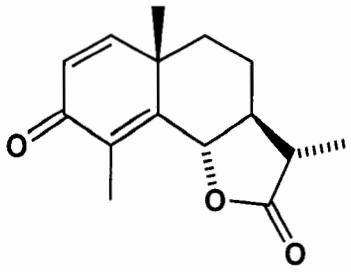
racemic

(4)



racemic

II. In 1944, Paranjape and coworkers in India announced a "total asymmetric synthesis" of the anthelmintic sesquiterpene santonin (see attached article). They reported that treatment of racemic 2-formylcyclohexanone with sodium ethoxide (to form the sodium enolate) followed by alkylation with methyl iodide (in either benzene, toluene, or ethanol as solvent) afforded 2-methyl-2-formylcyclohexanone as a liquid with an optical rotation of -26.2°! How do you account for these results?



Please Refer to

Paranjpe, K. D., N. L. Phalnikar, B. V. Bhide, and K. S. Nargund. “A Case of Total Asymmetric Synthesis.” *Nature*, no. 3874 (January 29, 1944): 141.