



Organic synthesis and methodology inspired by artemisinin

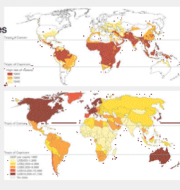
Gregory B. Dudley

Department of Chemistry and Biochemistry, Florida State University



Target: artemisinin

- Millions of deaths annually attributed to malaria among hundreds of millions of cases
- World Health Organization recommends artemisinin-combination therapy (ACT) for treatment of malaria
- Scarce and prohibitively costly
- Experimental cancer drug, likely for the same reasons it is effective against malaria
- Peroxo bridge challenges conventional wisdom in organic chemistry
- Arguably the most important unsolved problem in natural products research

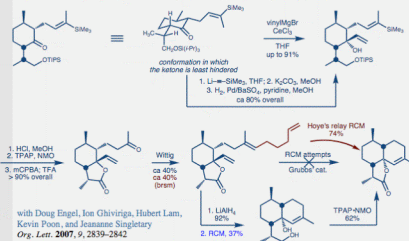


WHO World Malaria Report 2005: <http://rbm.who.int/wmr2005/index.html>



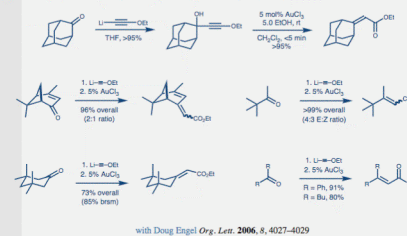
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Synthesis of (+)-dihydro-*epi*-deoxyartemisinin B



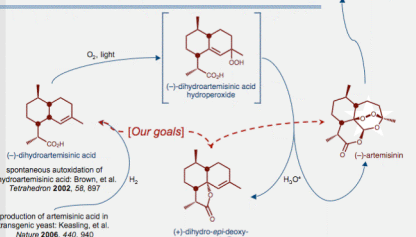
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Two-step olefination of hindered ketones



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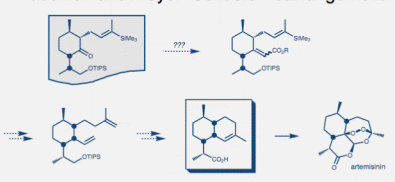
The endoperoxide pharmacophore



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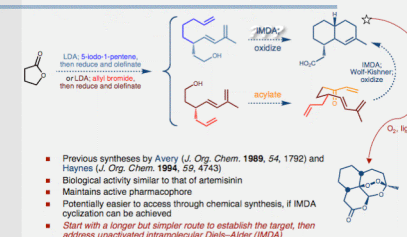
Towards Synthetic Dihydroartemisinic Acid

- Olefination of the hindered ketone via acetylide addition and Meyer-Schuster rearrangement?



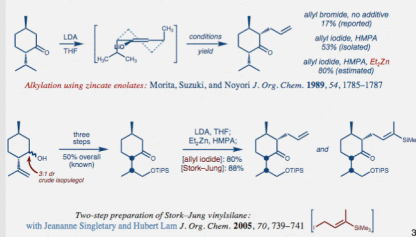
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Aim: Six-step synthesis of 6,9-didesmethyl-artemisinin



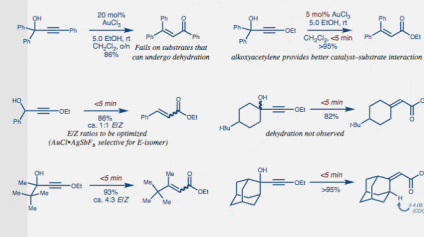
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Alkylation of enolates derived from menthone



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The Gold(III)-Catalyzed Meyer-Schuster Rearrangement

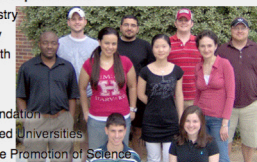
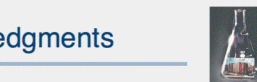


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Acknowledgments

Dudley Research Group Members

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