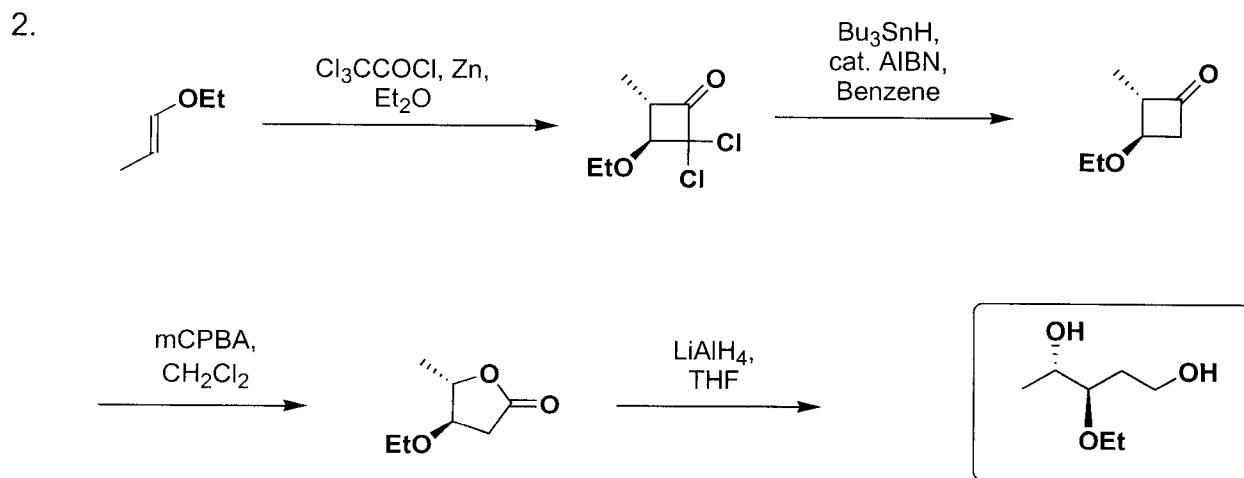
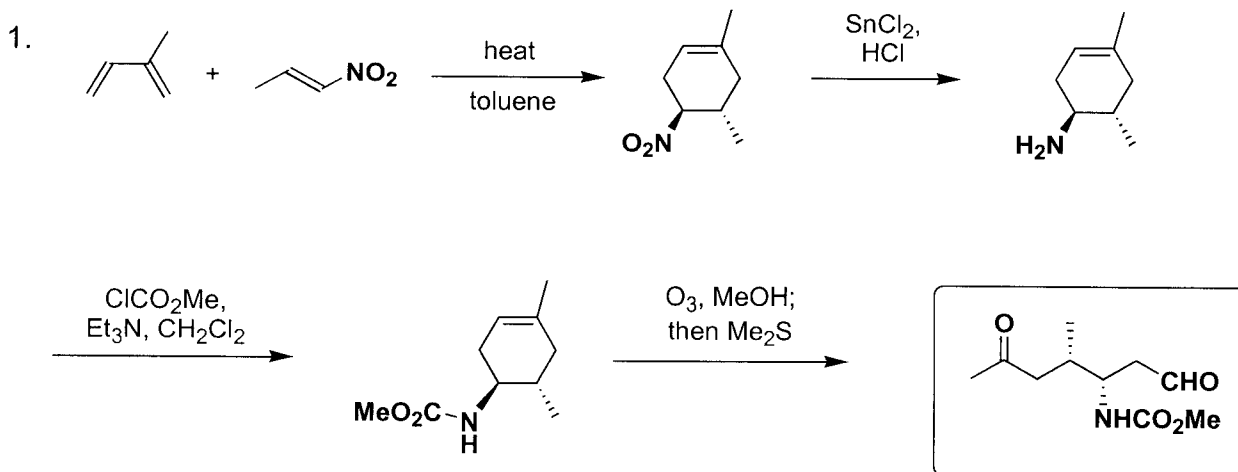
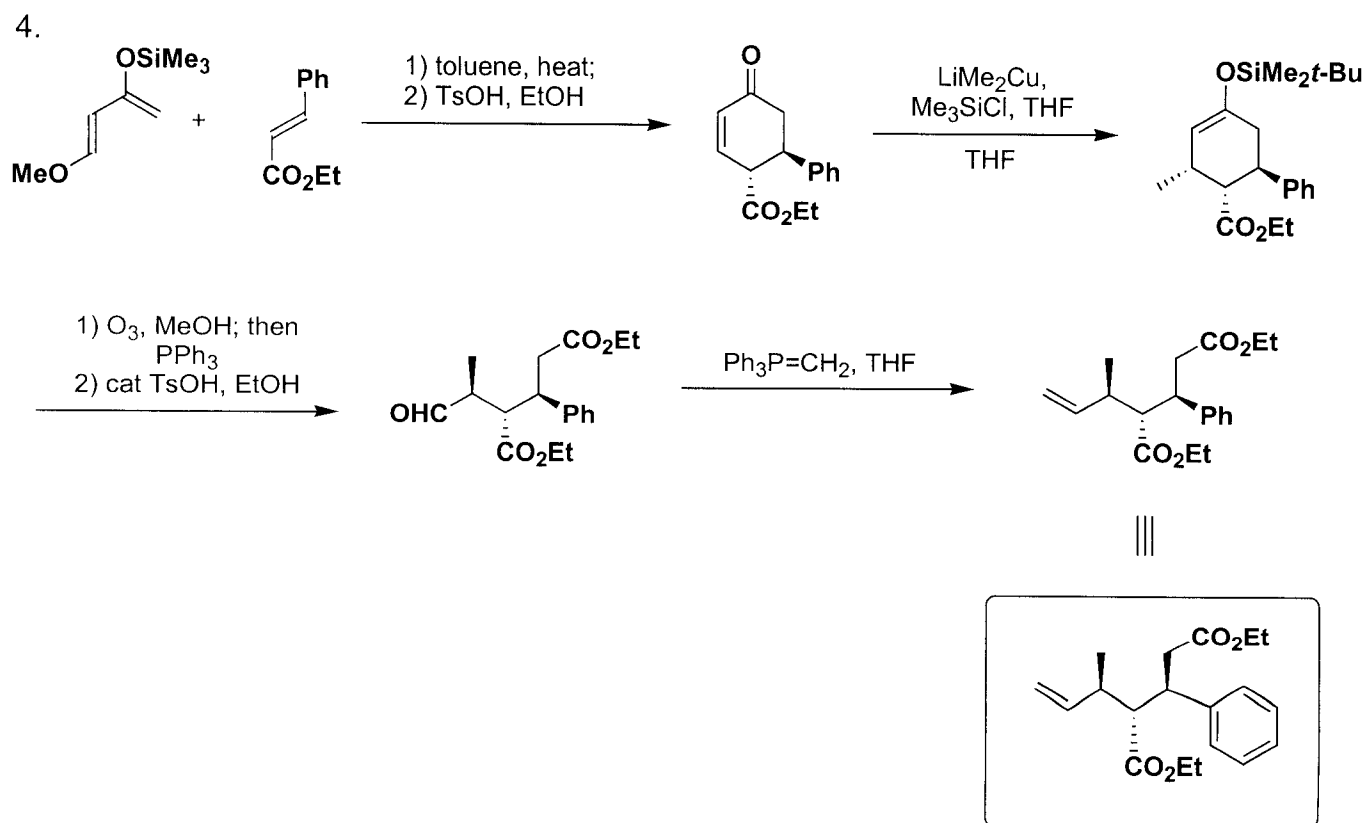
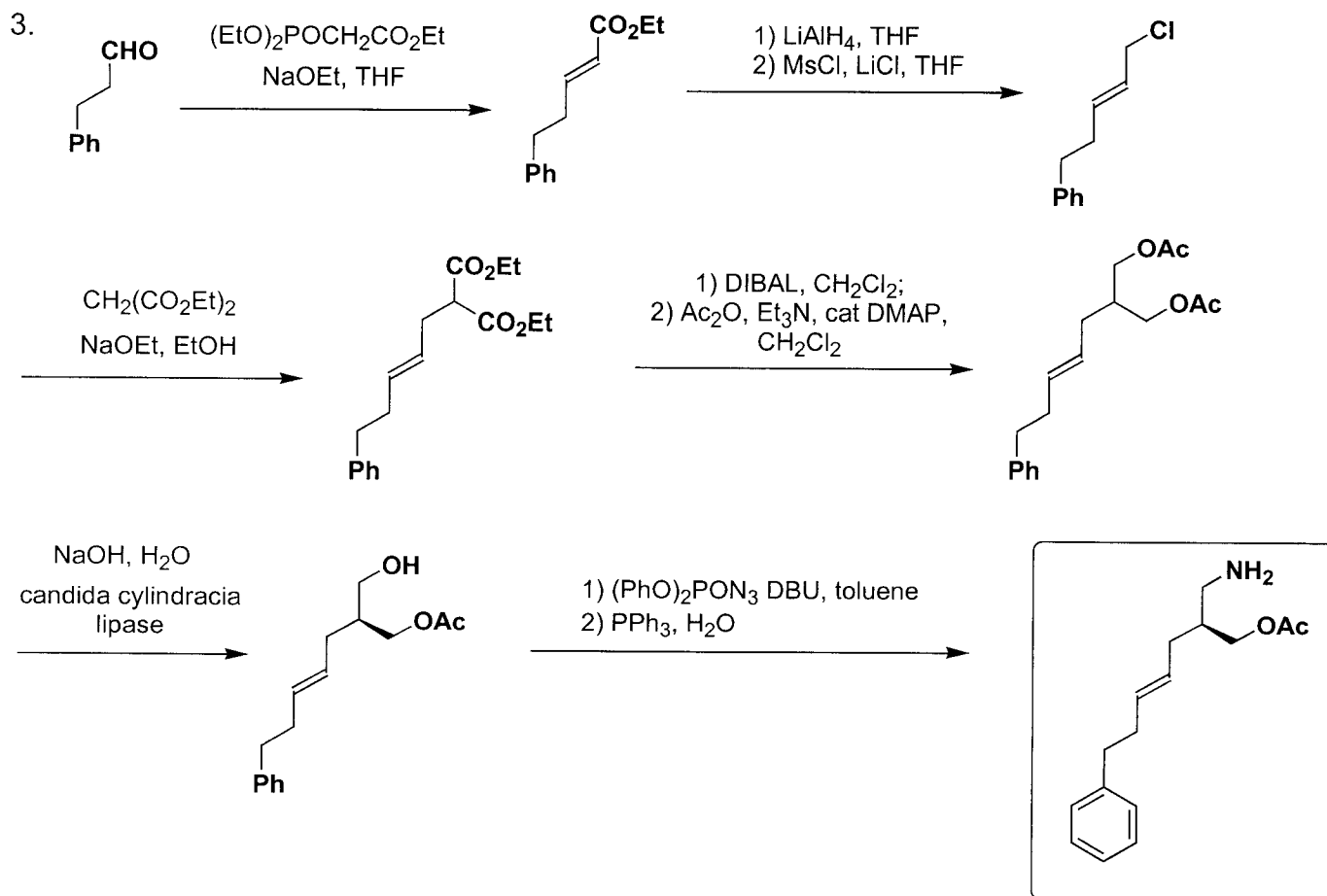


Massachusetts Institute of Technology
Organic Chemistry 5.512

March 15, 2005
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Problem Set 2 Solutions
 Strategies for Synthesis of Acyclic Molecules Based on
 Desymmetrization, Chirality Transfer, the "Chiron Approach",
 and Ring Template Strategies





- II. The creation of a mixture of products favoring one enantiomer over another from a racemic mixture in the absence of chiral reactants is impossible. In the case of the "asymmetric synthesis" of santonin from 2-methyl-2-formylcyclohexanone, the optical rotation is likely due to the presence of impurities in the sample.

Nature, 1944 (153) ~~317~~ 317

Reported Asymmetric Synthesis of Santonin

SOME time ago¹ Paranjape, Phalnikar, Bhide and Nargund reported a synthesis of santonin from optically inactive materials: they now² claim that their product was active, being almost entirely the natural (*l*-) isomer. They state that the activity originated in the methylation of a 2-formylcyclohexanone derivative, and that the crude methylation product from 2-formylcyclohexanone (I) itself had the large specific rotation of -26.2° in chloroform. Although they did not isolate 2-methyl-2-formylcyclohexanone (II), they claim that an optically active derivative was prepared in a state of purity.

Such an asymmetric synthesis from inactive materials violates no fundamental law and might theoretically be expected to occur once in about $(10^{10})^{20}$ trials.

Nevertheless, Paranjape *et al.* claim to have achieved the asymmetric synthesis repeatedly. As we were interested in the products for another reason, it seemed worth while to repeat one of these experiments.

Sen and Mondal³ prepared (II), though not in a pure condition, and established its structure by hydrolysis to 2-methylcyclohexanone. We find that (II) may readily be purified by fractionation at low pressure, forming a colourless oil of camphoraceous odour, b.p. $47^\circ/0.05$ mm., n_D^{18} 1.4683 (Found: C, 68.2, 68.4; H, 8.6, 8.4. $C_8H_{12}O_2$ requires C, 68.6; H, 8.6 per cent); the hydrolysis to methylcyclohexanone was confirmed. Neither the crude methylation product from (I) nor pure (II) showed any optical activity whatsoever.

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¹ *Current Science*, 12, 150 (1943).

² *NATURE*, 153, 141 (1944).

³ *J. Ind. Chem. Soc.*, 5, 609 (1928).