Acknowledgements:
The notes about the problems are prepared by Abraham Heifets, the designer of this benchmark. The attached images with the solutions to exams are downloaded from
http://ocw.mit.edu/courses/chemistry/5-13-organic-chemistry-ii-fall-2006/exams/

Problem 1
It is not related to exams. Synthesis as reported in (Brower et al. 1992) and (Roth 2002).
Brower, P. L. et al, and Roth, B. D. 1992. The synthesis of (4R-cis)-1,1-dimethylethyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate, a key intermediate for the preparation of CI-981, a highly potent, tissue selective inhibitor of HMG-CoA reductase. Tetrahedron Letters 33(17):2279-2282.
Roth, B. D. 2002. The discovery and development of atorvastatin, a potent novel hypolipidemic agent. In Progress in Medicinal Chemistry, vol 40. Elsevier. 1-22.

Problem 2
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Hour exam #4, Fall 2003, Question 8

Problem 3
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 5c

Problem 4
Massachusetts Institute of Technology 5.13: Organic Chemistry II
Practice exam #3, Fall 2006, Question 8

Problem 5
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #4 extra problems, Fall 2006, Question 12b

Problem 6
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Practice exam #3, Fall 2006, Question 9a

Problem 7
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 8c

We do oxidation of alcohol to carboxylic acid in two steps, via the aldehyde molecule (labeled "3" in solution 8c) treated with Cr2O7.

Problem 8
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 5a
Ozonolysis written to match precursors against the available starting materials.

Problem 9
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #4 extra problems, Fall 2006, Question 12a

Problem 10
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Hour exam #2, Fall 2006, Question 3

Problem 11
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 8e

Problem 12
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Hour exam #3, Spring 2001, Question 5
While the instructions require starting materials to contain fewer than 3 carbon atoms, the course solution uses pentadiene, which contains 5 carbons so we provide pentadiene as a starting material.

PhMgBr can be made from PhBr, which is made by electrophilic aromatic substitution on benzene (a permitted starting material). Our solution performs Grignard addition to an acid chloride rather than an ester.

Problem 13
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Practice exam #4, Fall 2006, Question 3
The Claisen condensation and decarboxylation reactions are written to specify ethyl reagents, as used in this problem. We could simplify this by adding OMe<->OEth interconversion reactions.

Problem 14
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Practice exam #4, Fall 2003, Question 10

Problem 15
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Practice exam #3, Fall 2006, Question 9b

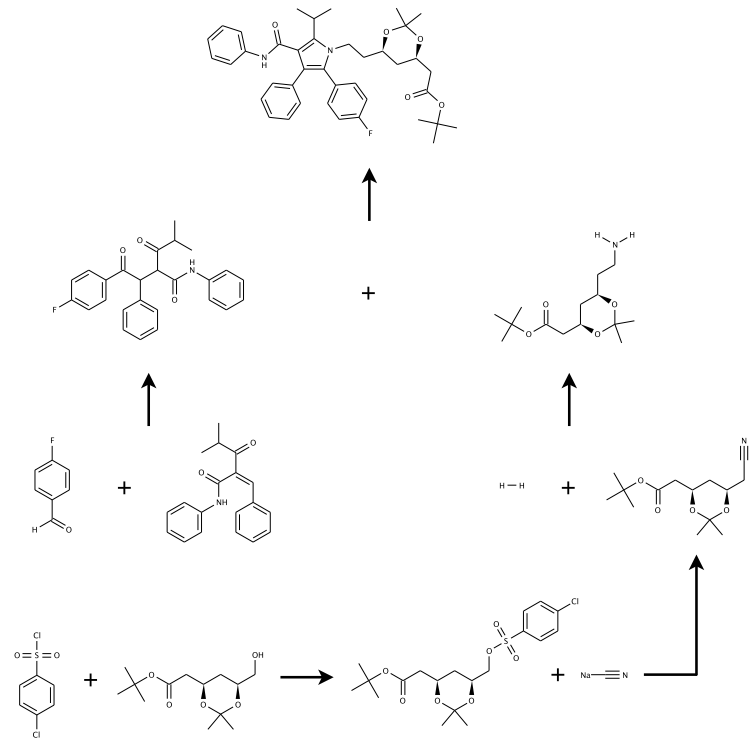
Problem 16
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Question 5, Generating lithium enolates, as in question 4.

Problem 17
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Question 4
The lithium enolate is misdrawn in the PDF solution: the double bond should go to one of the carbons. Our solution uses OH- to create the enolate rather than make lithium enolate as in the PDF solution.

Problem 18
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Final exam, Dec 19 2005, Question 6

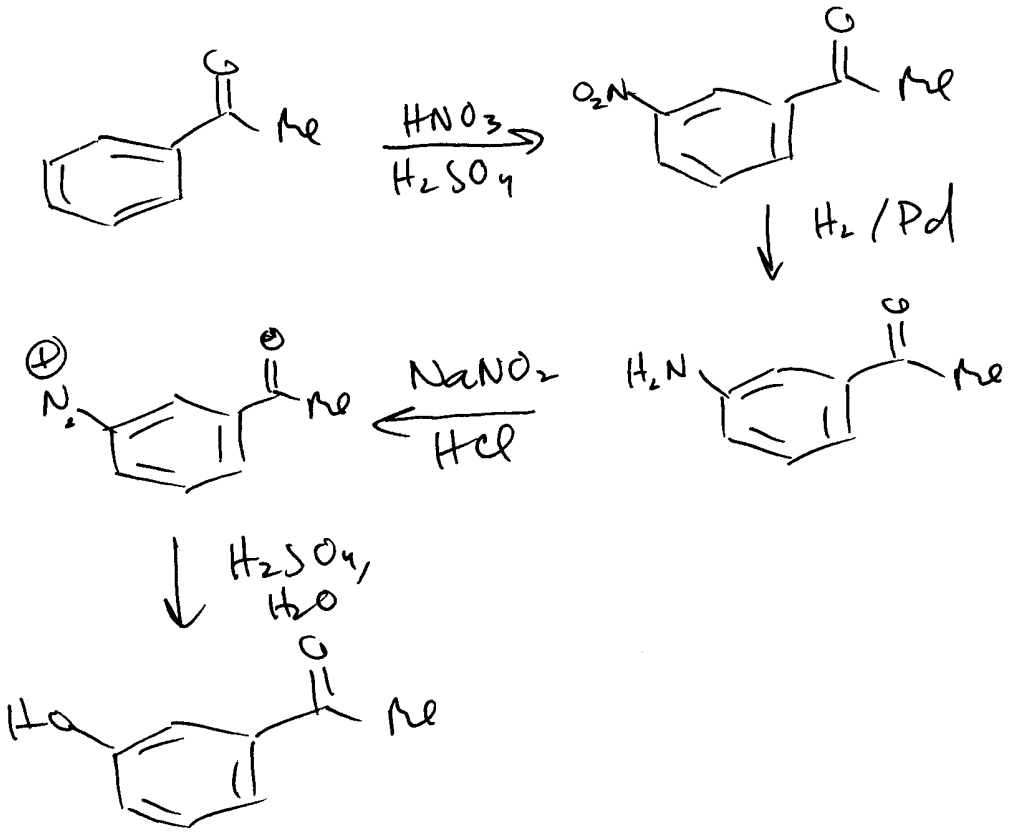
Problem 19
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 8d
We do oxidation of alcohol to carboxylic acid in two steps, via the aldehyde molecule (labeled "3" in solution 8c) treated with Cr2O7.

Problem 20
Massachusetts Institute of Technology, 5.13: Organic Chemistry II
Exam #3 extra problems, Fall 2006, Question 5b
The MeMgBr used in the final step of the solution can be created from MeOH starting material by PBr3 followed by Mg (analogous to the second conversion in the solution).
However, it is used without construction so, if you want to provide it to your solver, it described in SML/hidden/methyl-Grignard.smiles.



8. (11 points) Provide a synthesis that will *selectively* convert **A** to **B**. Show all of the key intermediates and furnish all of the important reagents. This is not a one-step process.

A **B**



Name Key

5. (Continued)

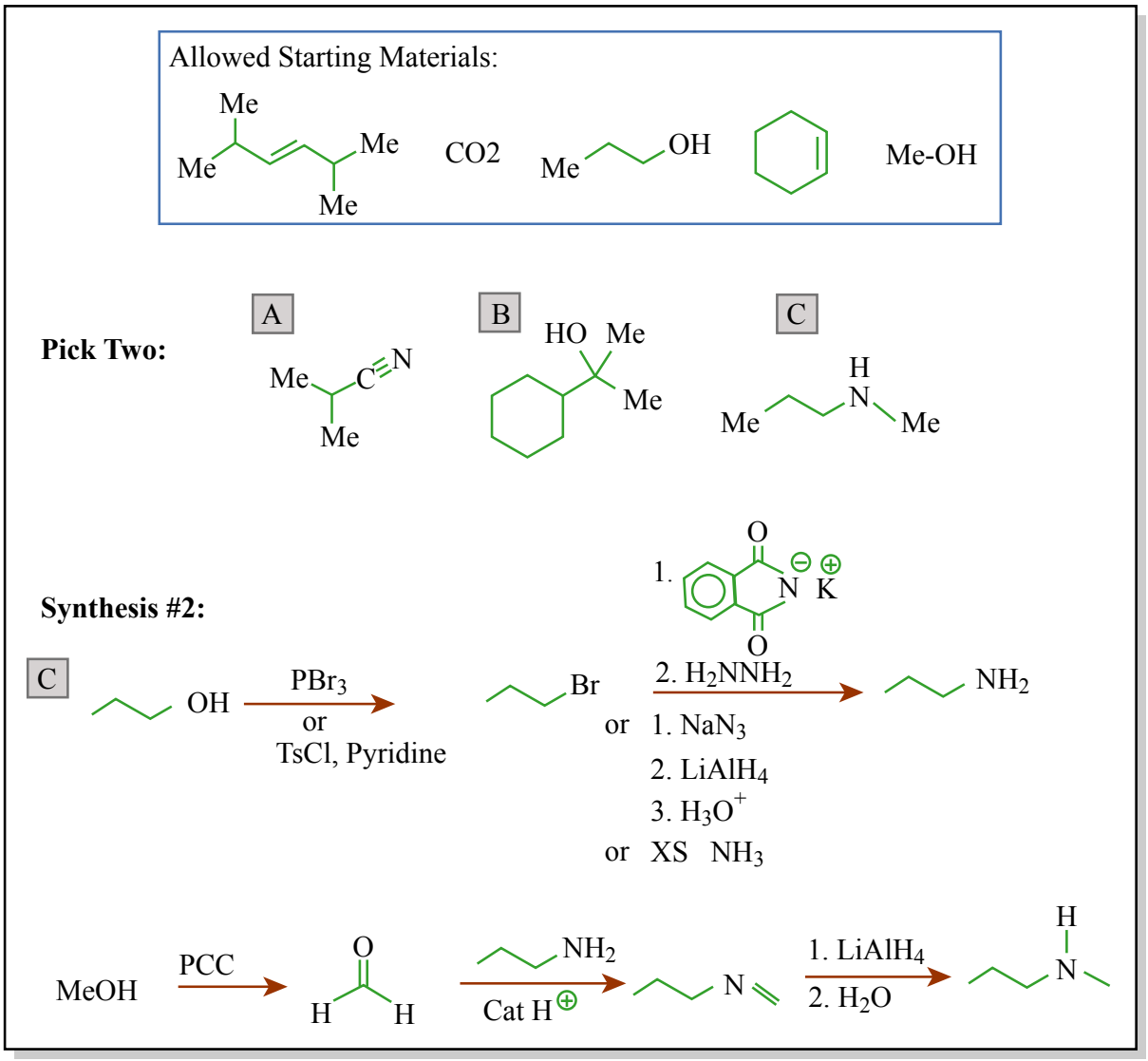


Figure by MIT OCW.

Name_____

8. Provide a synthesis that will *selectively* convert **A** to **B**. Show all the key intermediates, and furnish all of the important reagents.

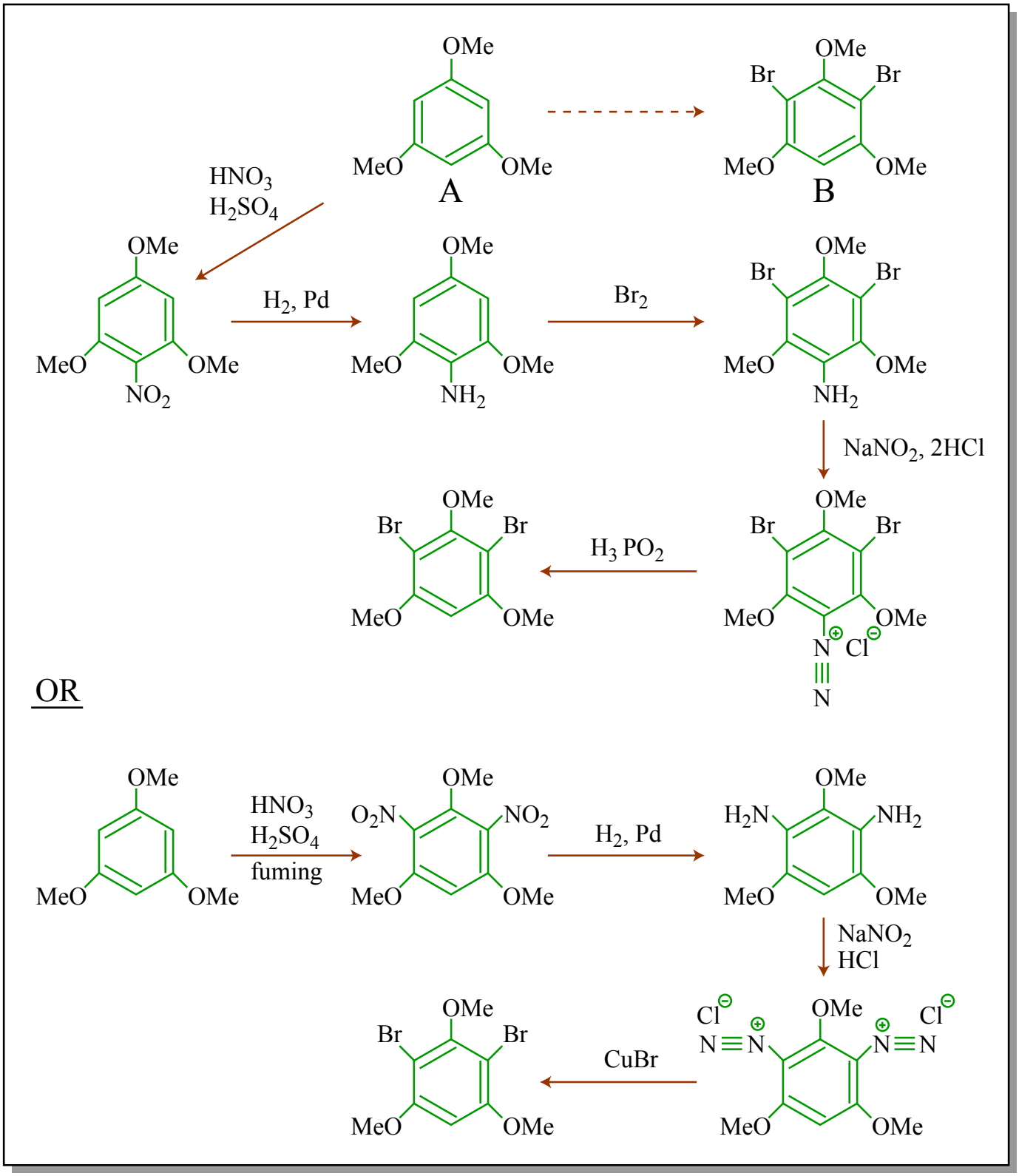
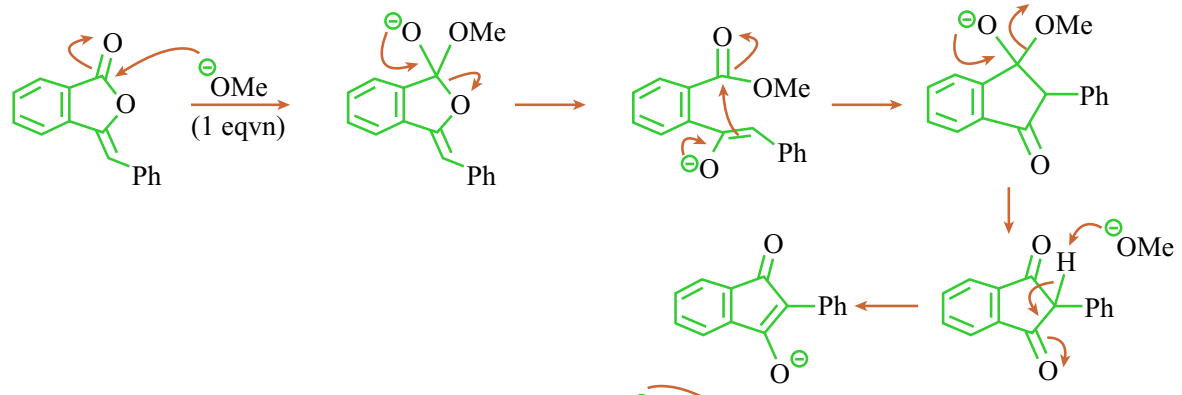


Figure by MIT OCW.

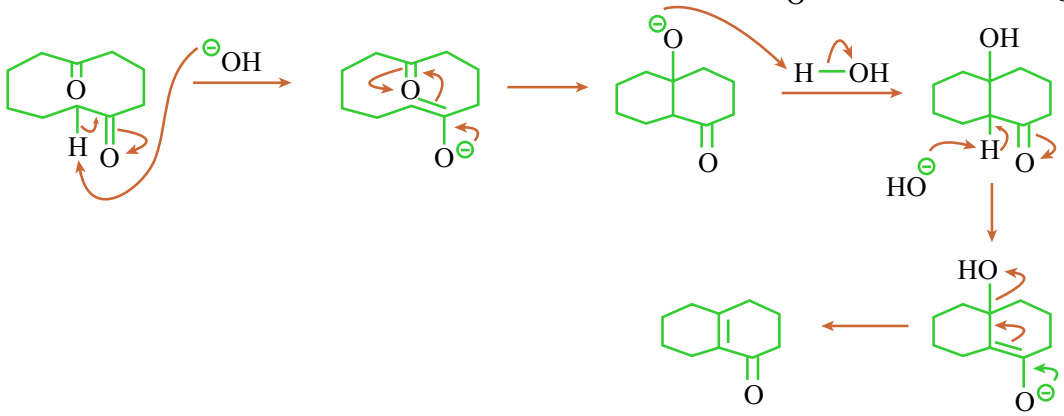
5.13: Organic Chemistry II

11.

(a)

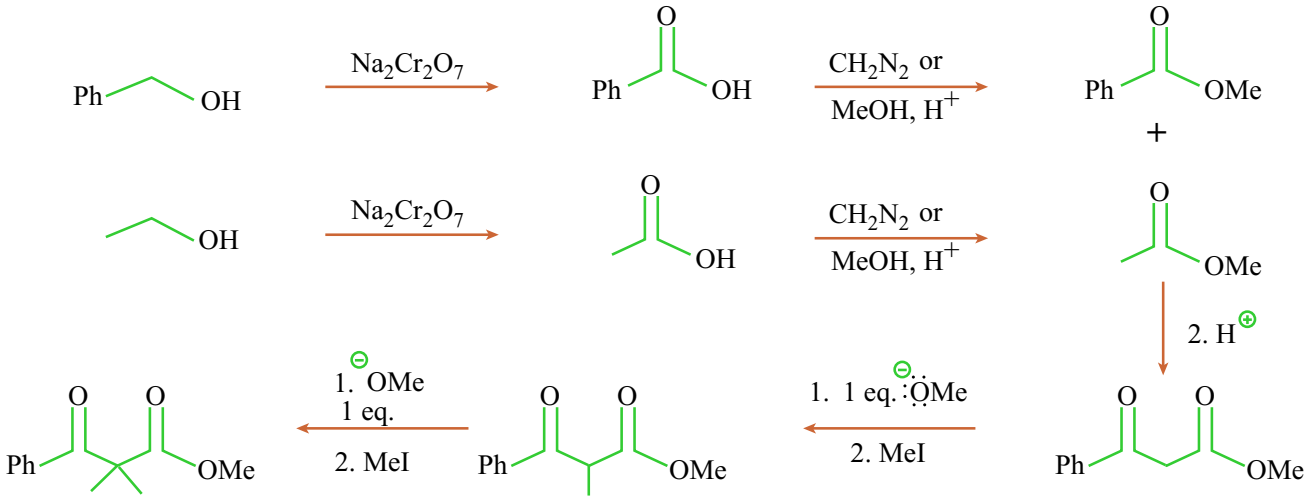


(b)

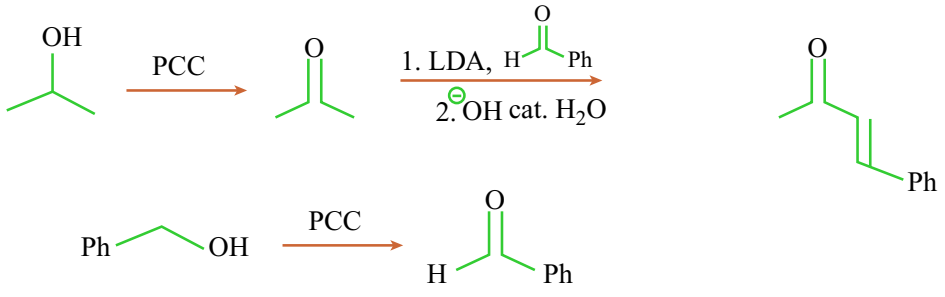


12.

(a)



(b)



Figures by MIT OCW.

9. Provide synthesis for the following compounds. All of the carbons in the target molecules should be derived from the allowed starting materials. You may use any common reagents.

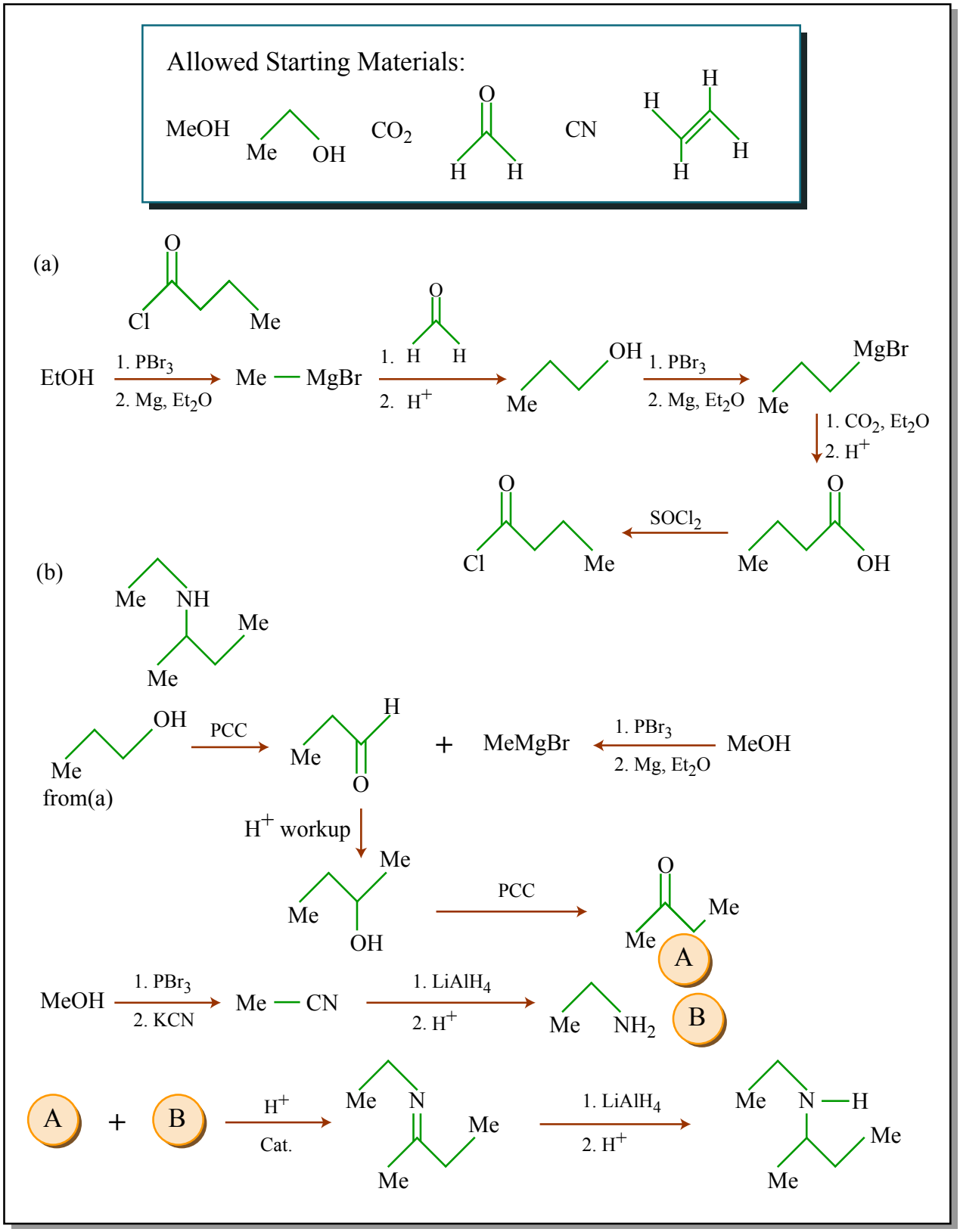


Figure by MIT OCW.

Massachusetts Institute of Technology

5.13: Organic Chemistry II

8. Synthesize the indicated compounds from the allowed starting materials shown below. All of the carbons of the target compounds should be derived from the allowed starting materials.

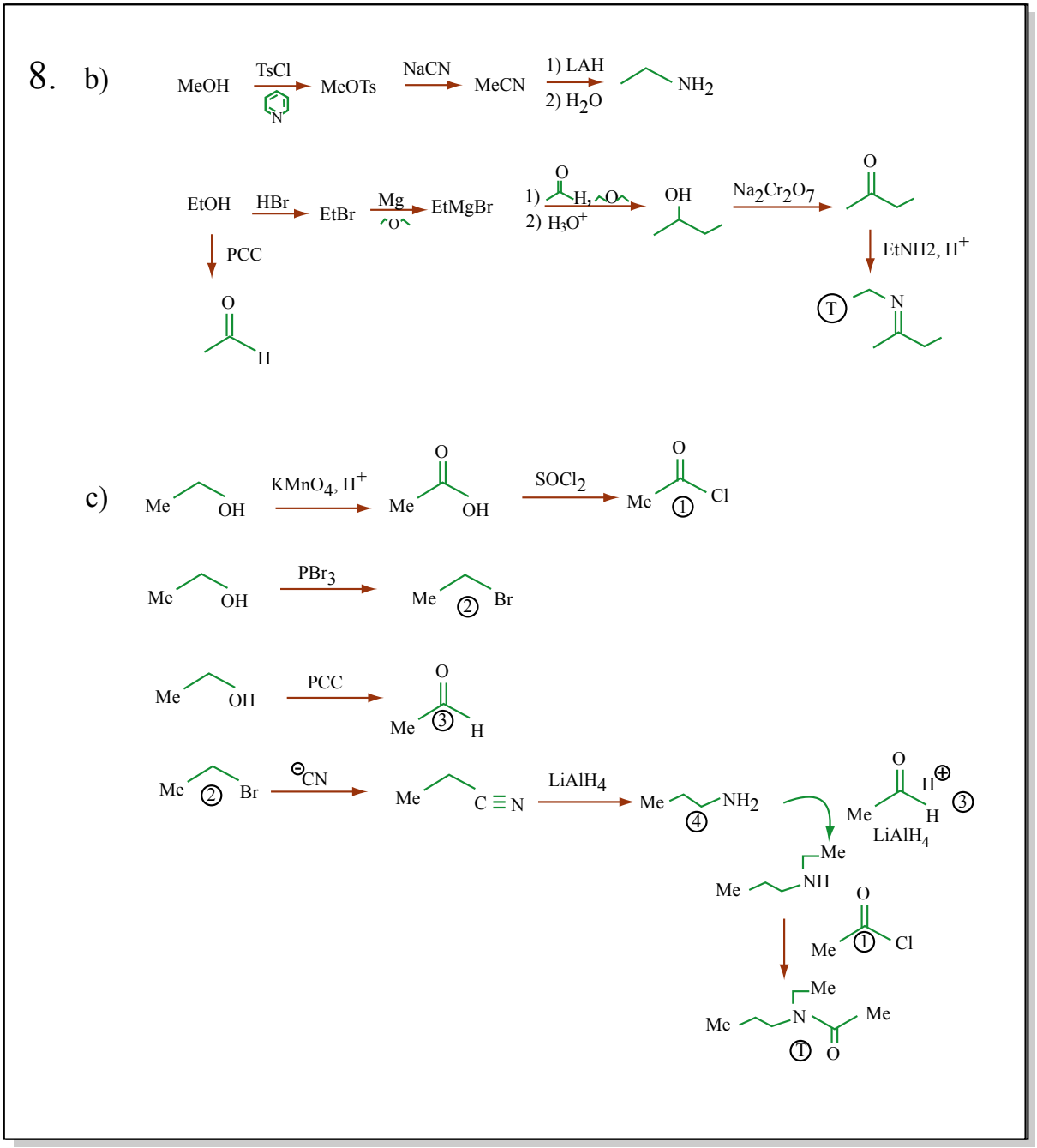


Figure by MIT OCW.

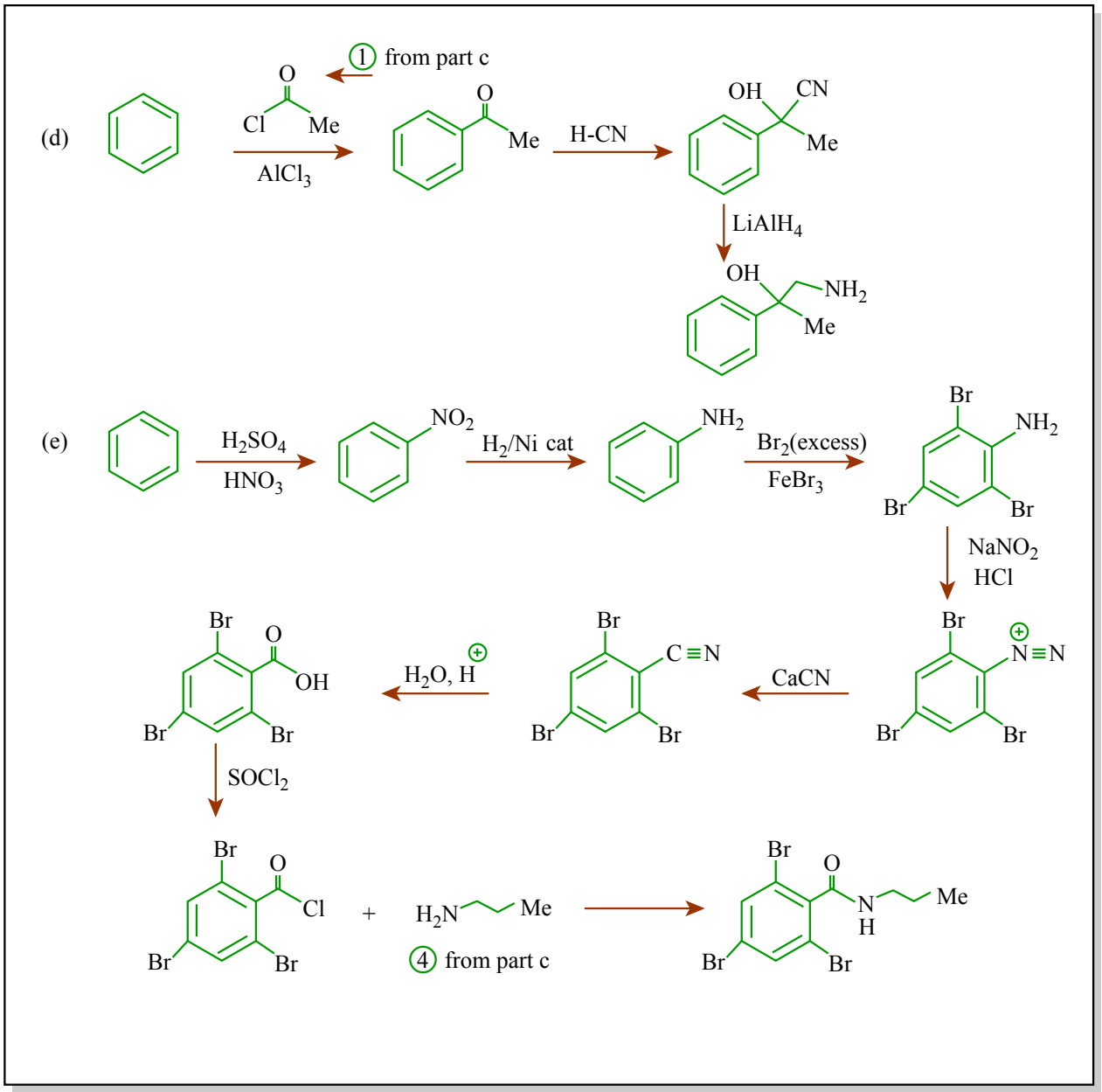


Figure by MIT OCW.

5. (11 points each, 22 points total) Please provide syntheses for **only two of the three** indicated compounds. All the carbon atoms should be derived from the allowed starting materials. You may use any common reagents.

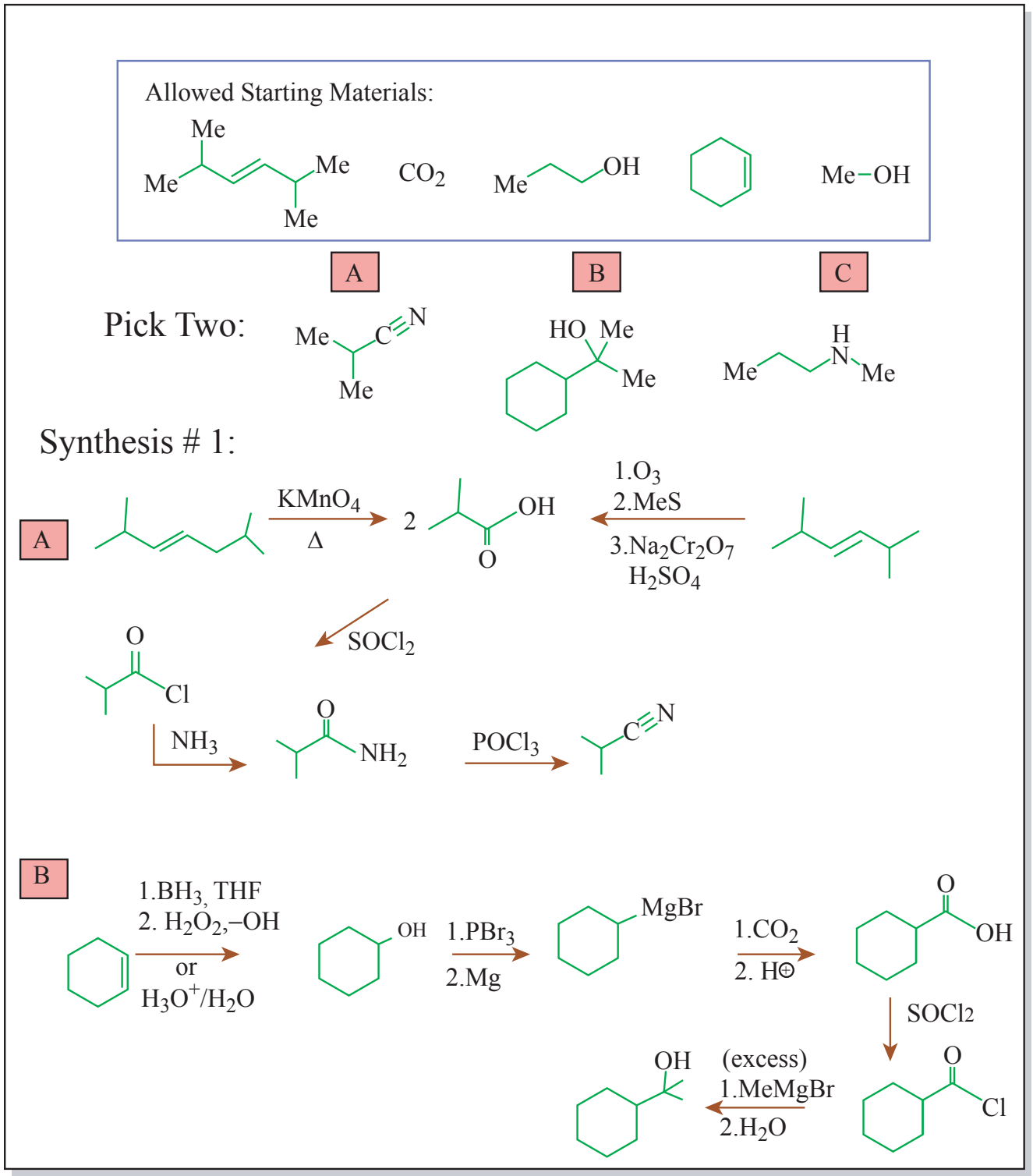


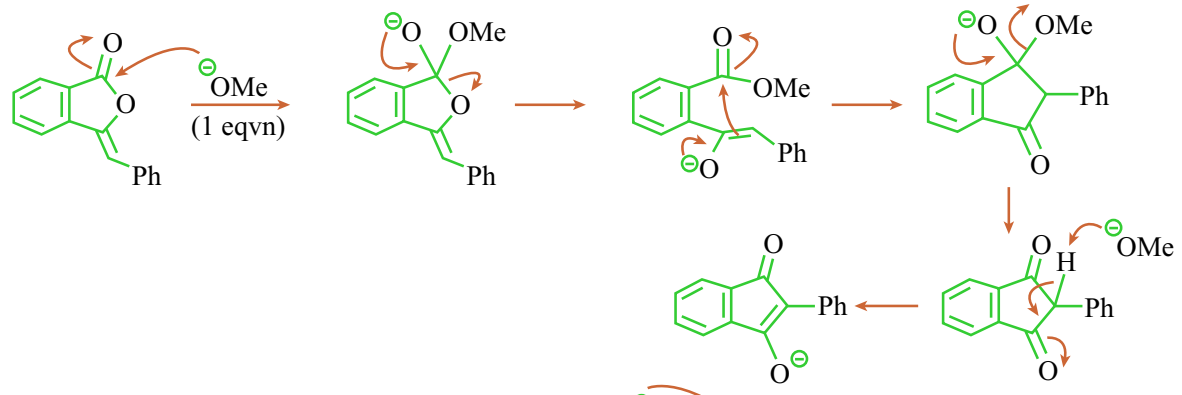
Figure by MIT OCW.

Name_____

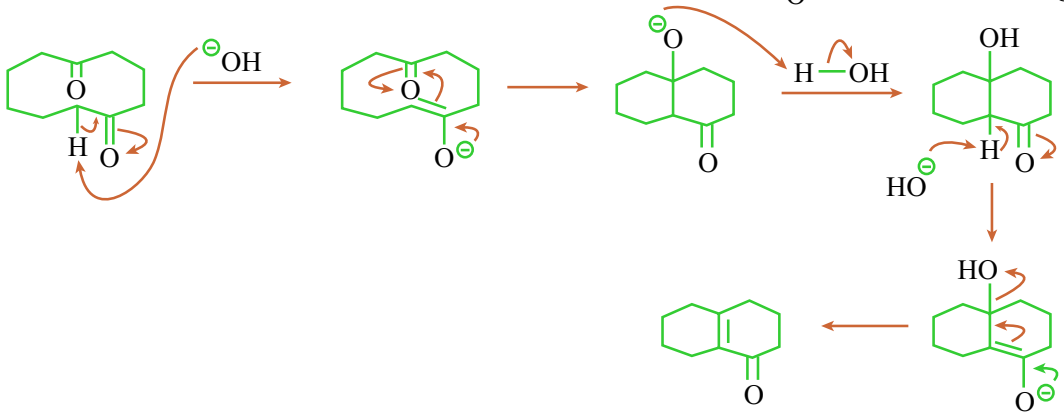
5.13: Organic Chemistry II

11.

(a)

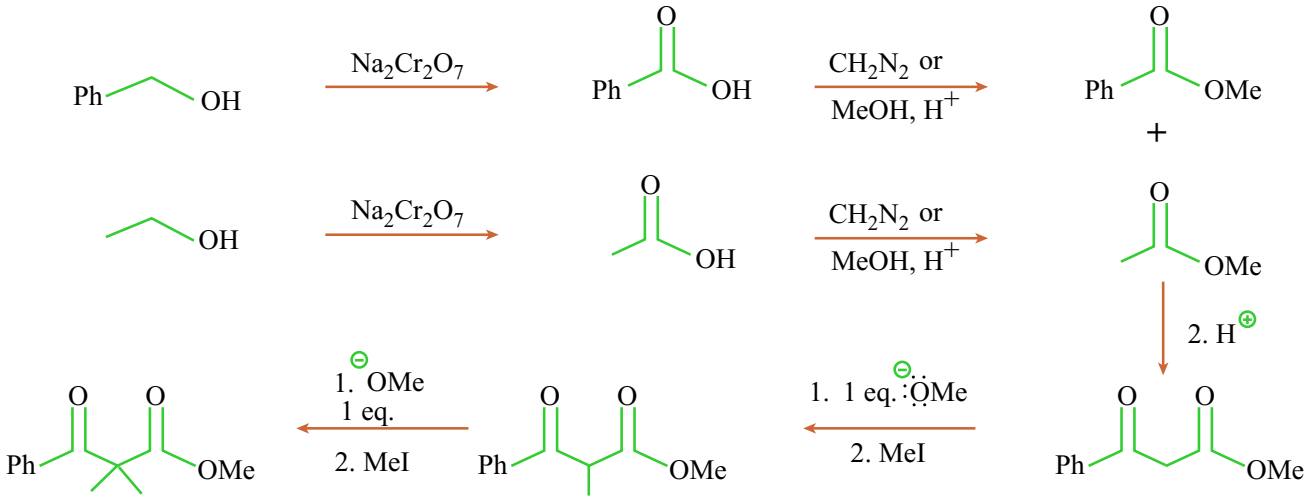


(b)

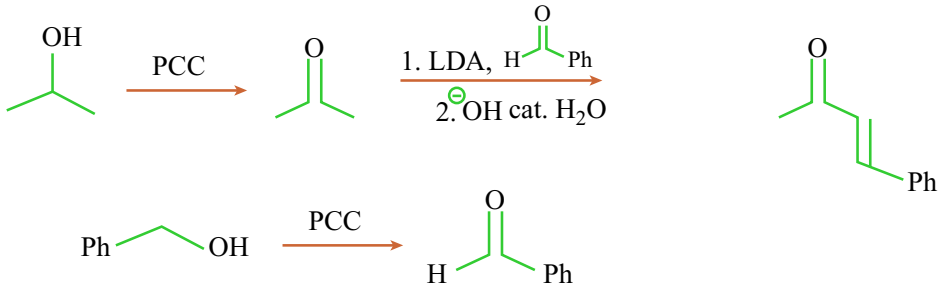


12.

(a)

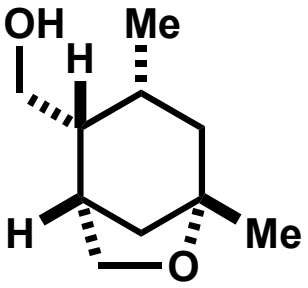


(b)



Figures by MIT OCW.

3. (22 points total) Using retrosynthetic analysis, propose a synthesis of the molecule to the right (**A**)**.** You may use any reagents you wish, as long as your **starting materials** and any other reagent that is used to install a **carbon** that is found in the final product (target molecule **A**) have **no more than 6 carbon atoms.** For example, 1,3-butadiene and benzene would be acceptable, but benzyl bromide ($PhCH_2Br$) would not be.



target molecule (**A**)

Write your synthesis in the "forward" direction, showing all Steps and reagents necessary. (You may include solvents, but you are not required to do so.) **Draw a box around or circle Your final synthesis.**

Hint: Use a Diels-Alder reaction.

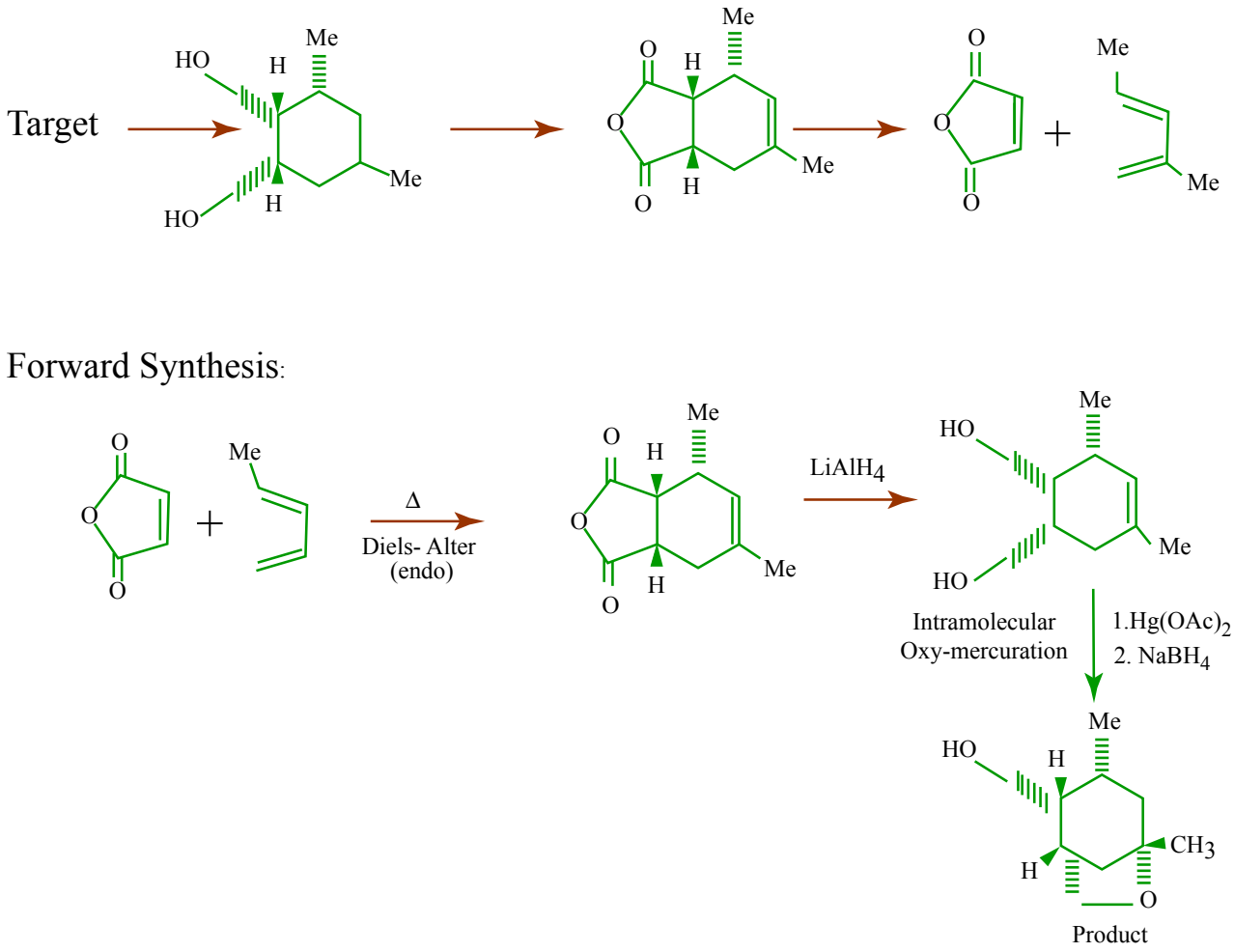


Figure by MIT OCW.

Massachusetts Institute of Technology

5.13: Organic Chemistry II

8. Synthesize the indicated compounds from the allowed starting materials shown below. All of the carbons of the target compounds should be derived from the allowed starting materials.

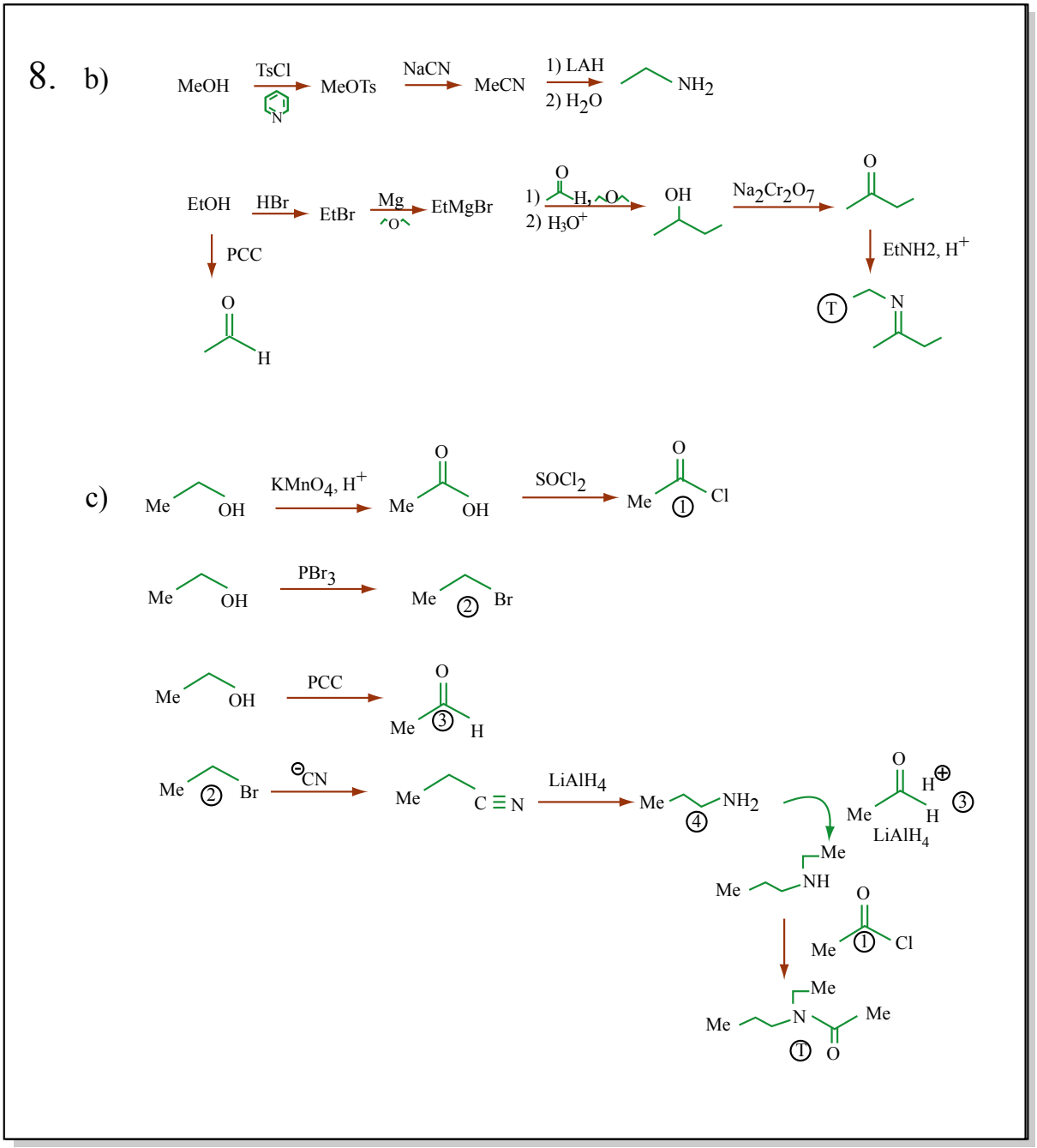


Figure by MIT OCW.

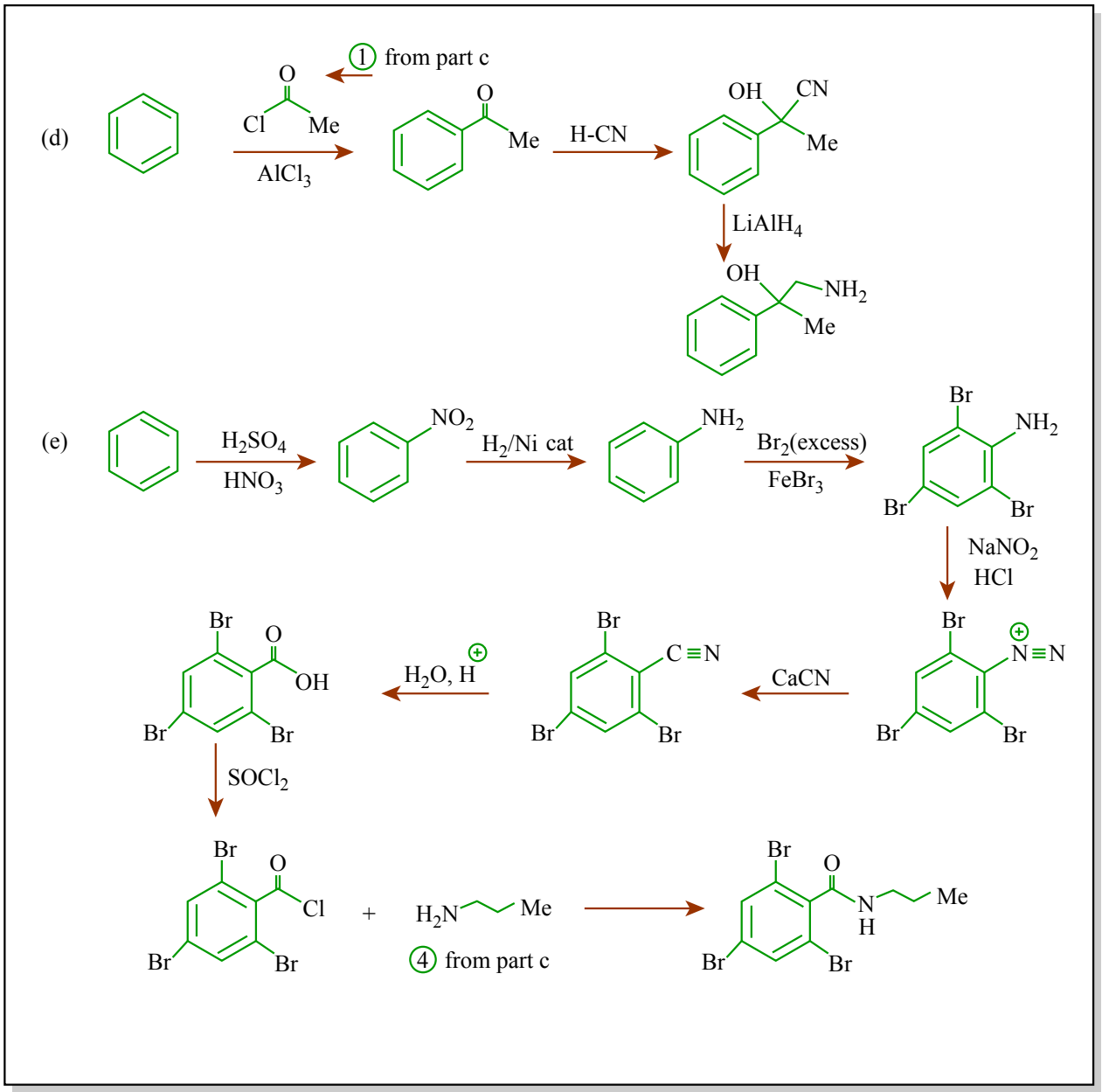
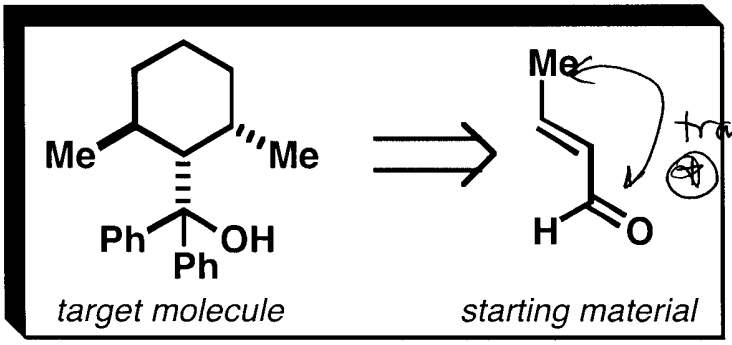
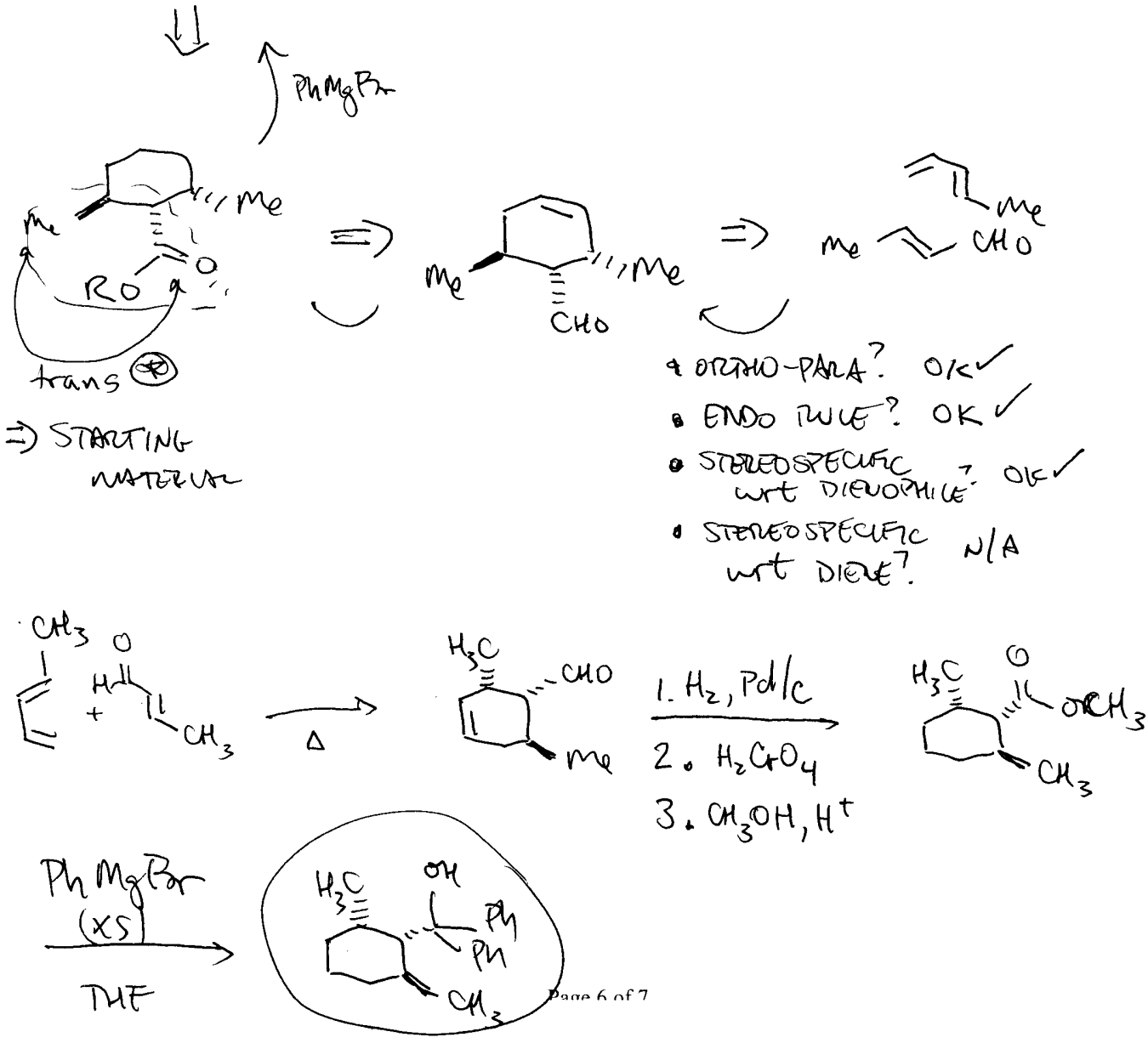


Figure by MIT OCW.

5. (20 points) In the space provided, propose an efficient synthetic route to the *target molecule* shown in the box from the *starting material* shown next to it. Assume that your "stockroom" of available reagents includes **any inorganic compounds**, **benzene**, **triphenylphosphine**, and **any** organic compound containing **3** or fewer carbon atoms. Your synthesis should provide a way to control the **relative stereochemistry** of the target molecule (but not the **absolute stereochemistry**). Write your synthesis in the **forward direction**, showing all necessary reagents and relevant reaction conditions for each step.





(3) (12 points) Please provide an efficient synthesis of the indicated target compound. All of the carbons of the target compound must come from ethyl acetate and 1, 5-dibromopentane.

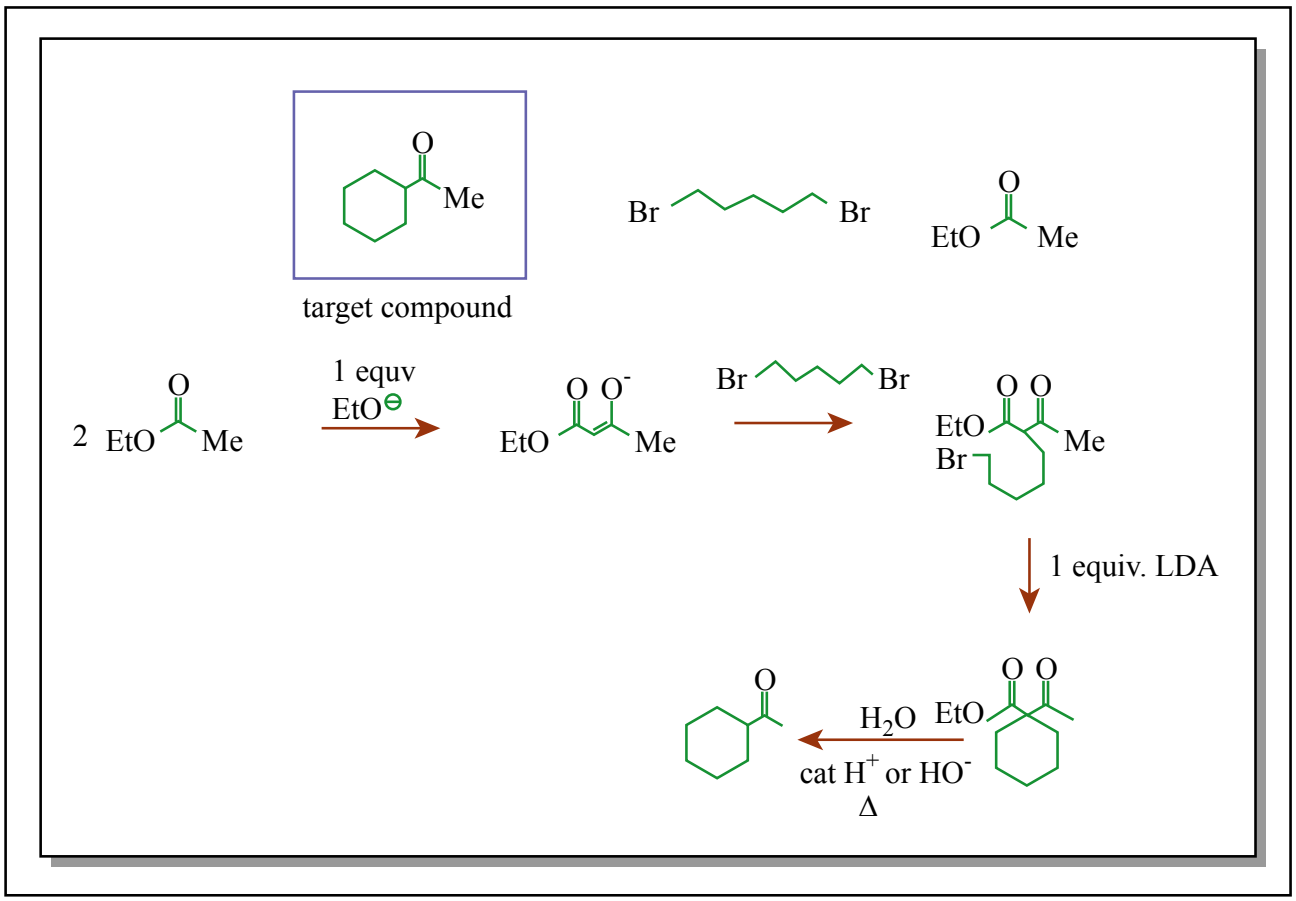
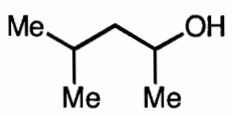
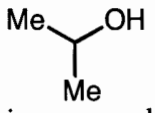


Figure by MIT OCW.

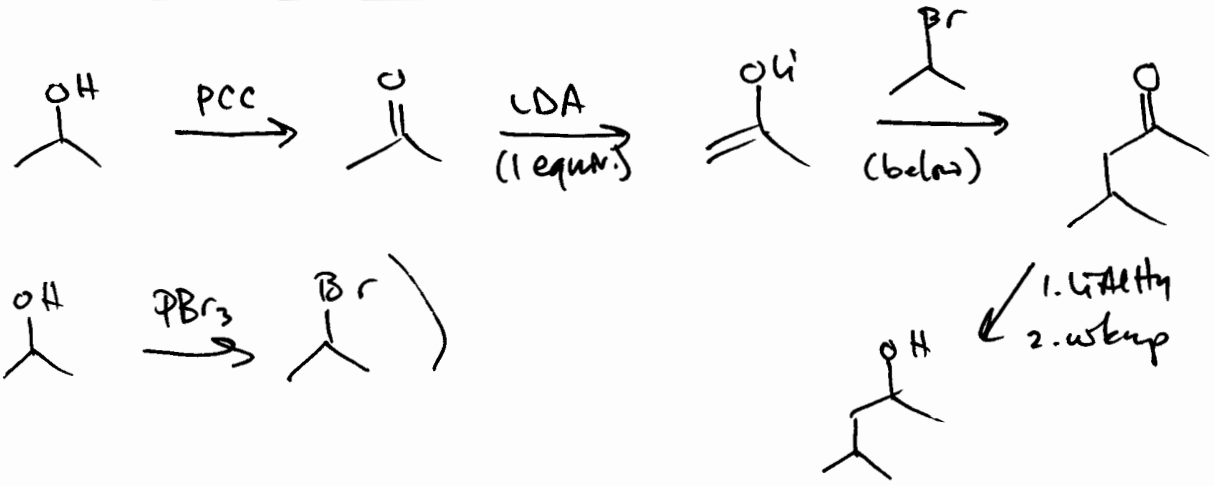
10. Please provide a synthesis of the indicated compound. All of the carbon atoms should be derived from isopropanol.

Target:

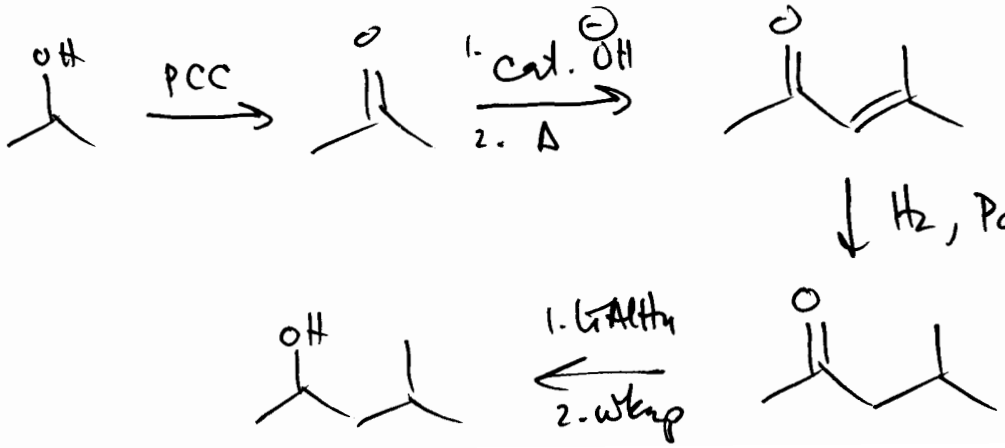




isopropanol



OR



9. Provide synthesis for the following compounds. All of the carbons in the target molecules should be derived from the allowed starting materials. You may use any common reagents.

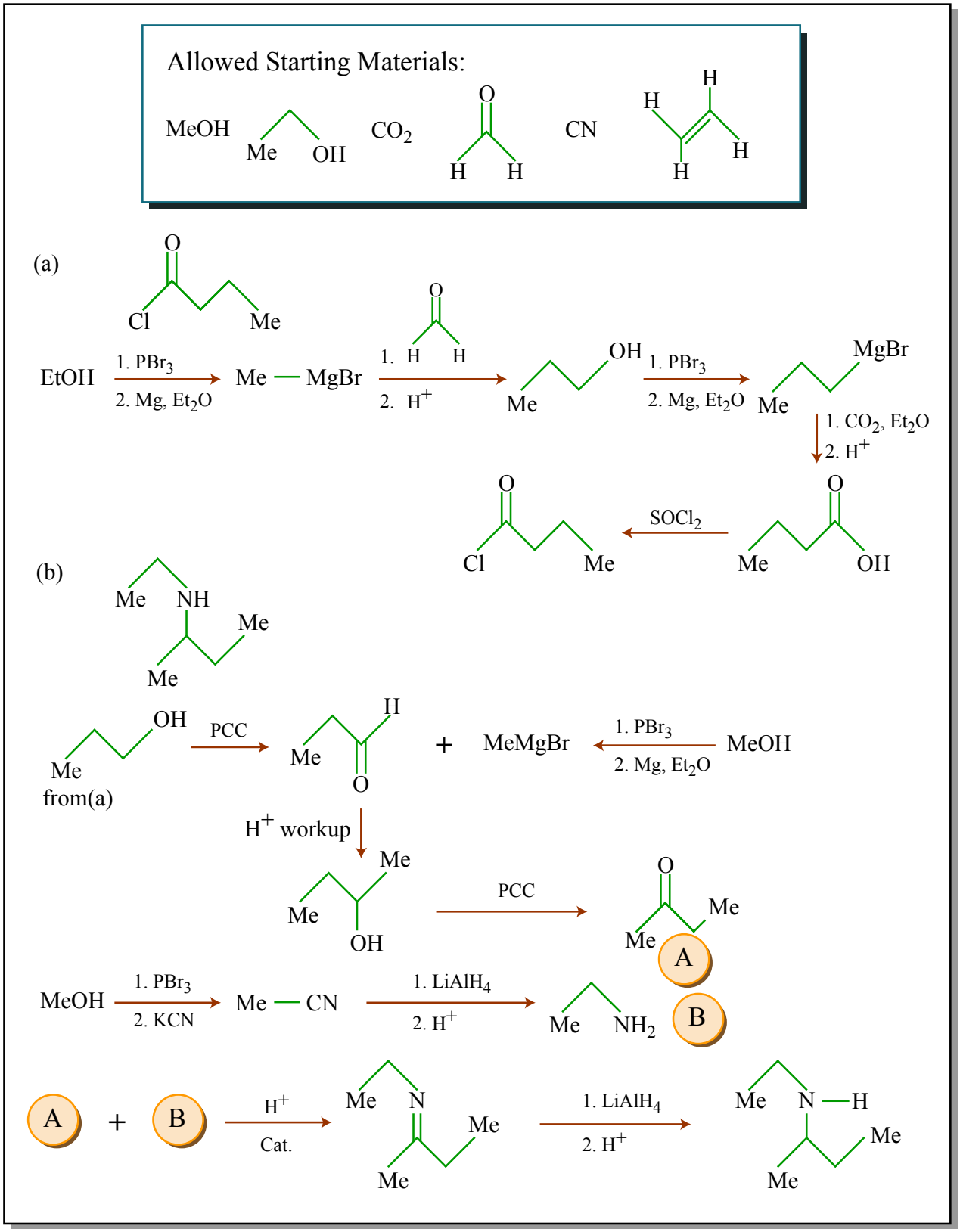


Figure by MIT OCW.

(5) (12 points) Please provide an efficient synthesis of the indicated target compound. All of the carbons of the target compound must come from acetone and diethyl malonate.

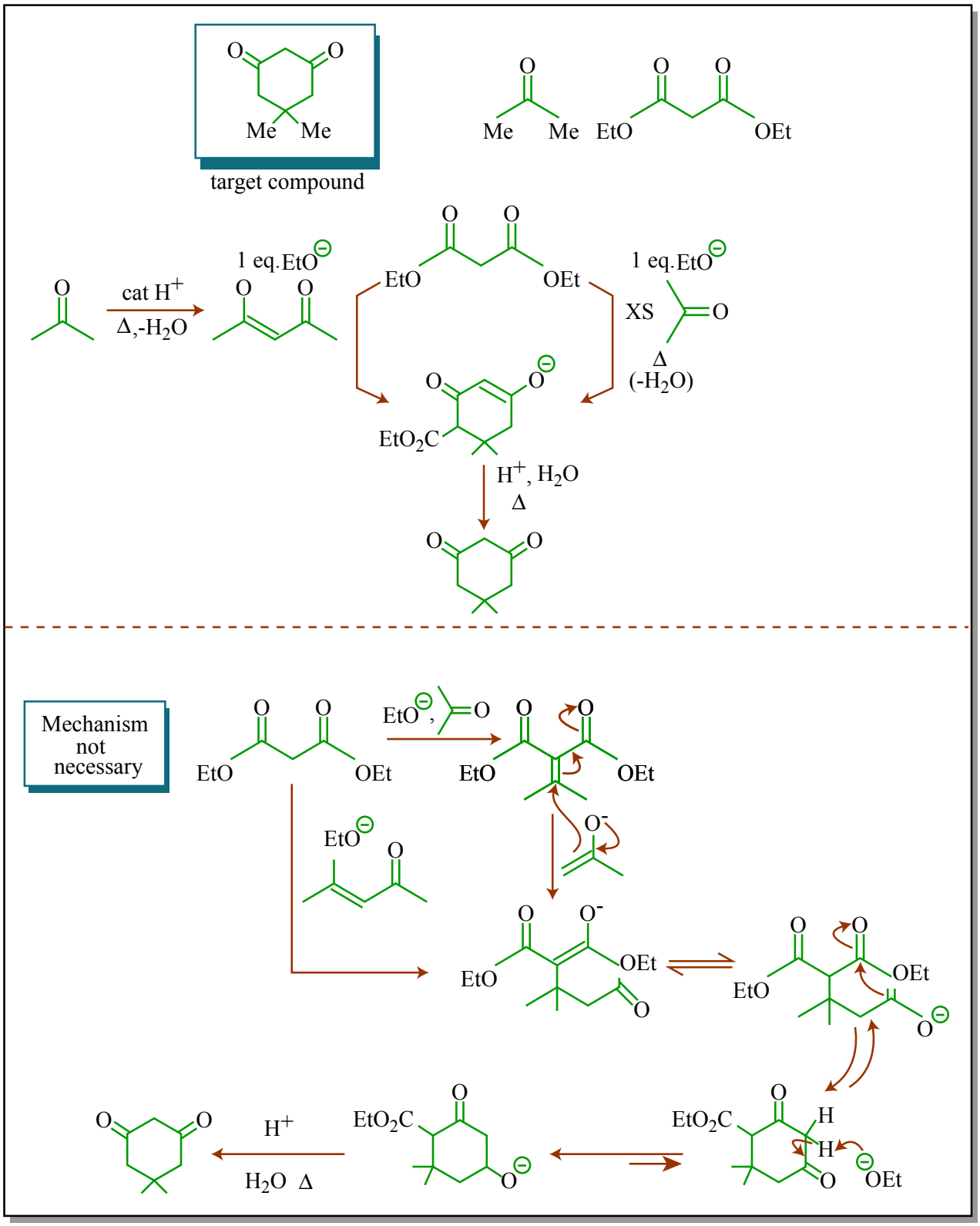


Figure by MIT OCW.

(4) (12 points) Please provide an efficient synthesis of the indicated target compound. All of the carbons of the target compound must come from the three illustrated alcohols.

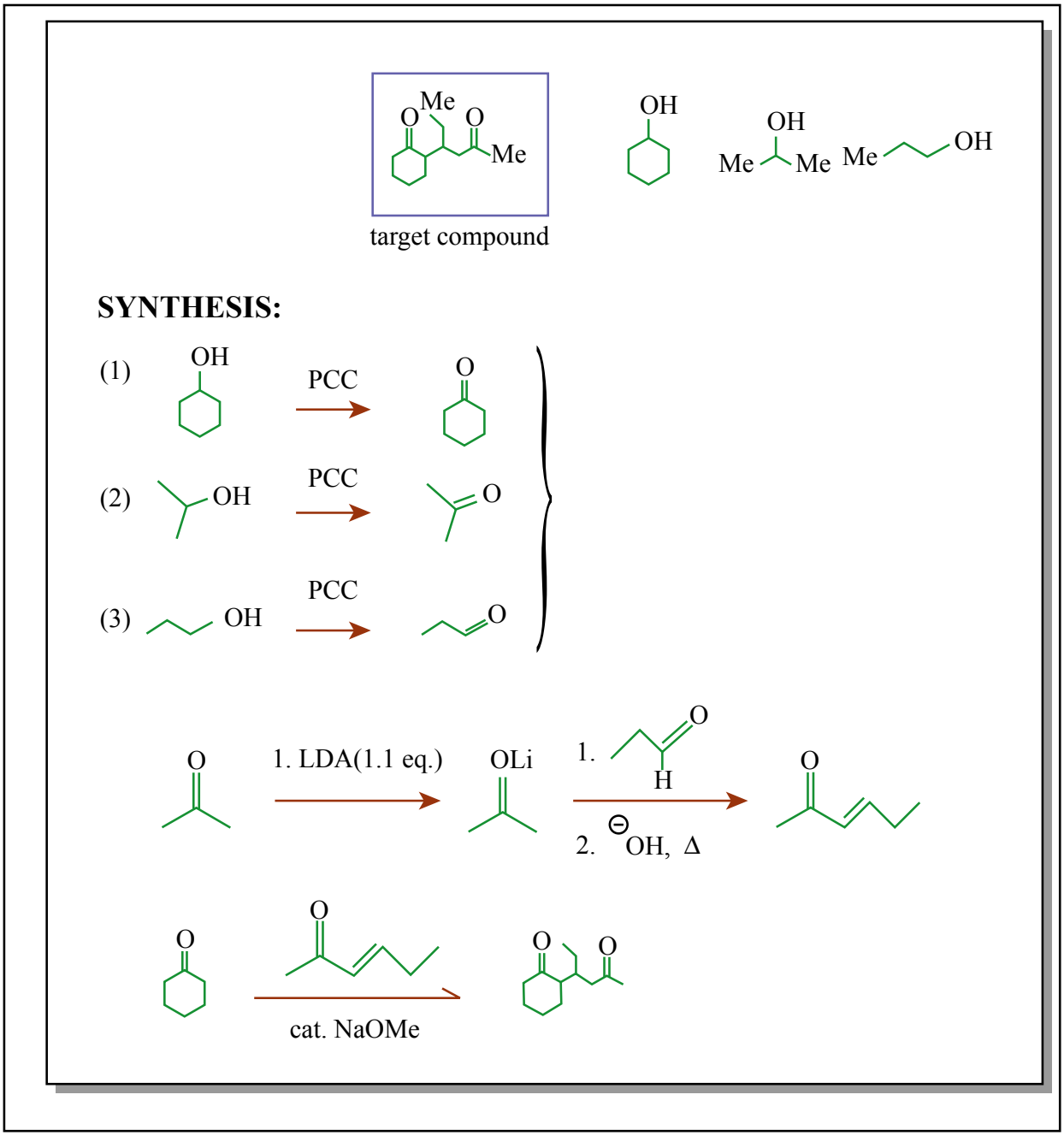
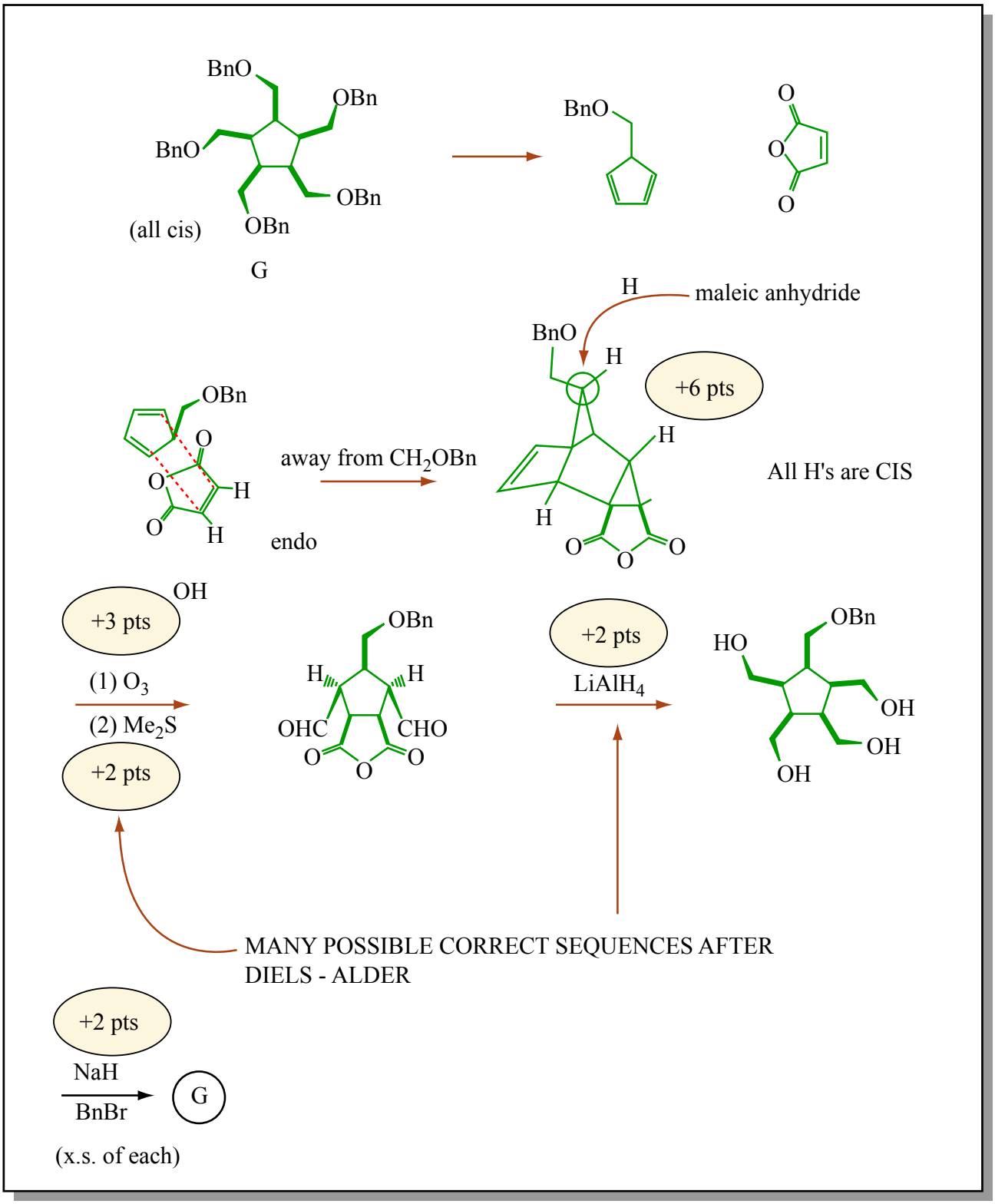


Figure by MIT OCW.

6. (15 points) Propose a synthesis of **G** from **H**, maleic anhydride, and benzyl bromide (BnBr = $PhCH_2Br$). (All of the substituents on the five-membered ring in **G** are cis to one another, and your synthesis must establish this relative configuration.) Your synthesis must use **H**, maleic anhydride, and BnBr. You may use any other reagents in addition to these. Write your synthesis **neatly** in the forward direction, and for each transformation, write the **reagents** necessary over the arrow.



Massachusetts Institute of Technology

5.13: Organic Chemistry II

8. Synthesize the indicated compounds from the allowed starting materials shown below. All of the carbons of the target compounds should be derived from the allowed starting materials.

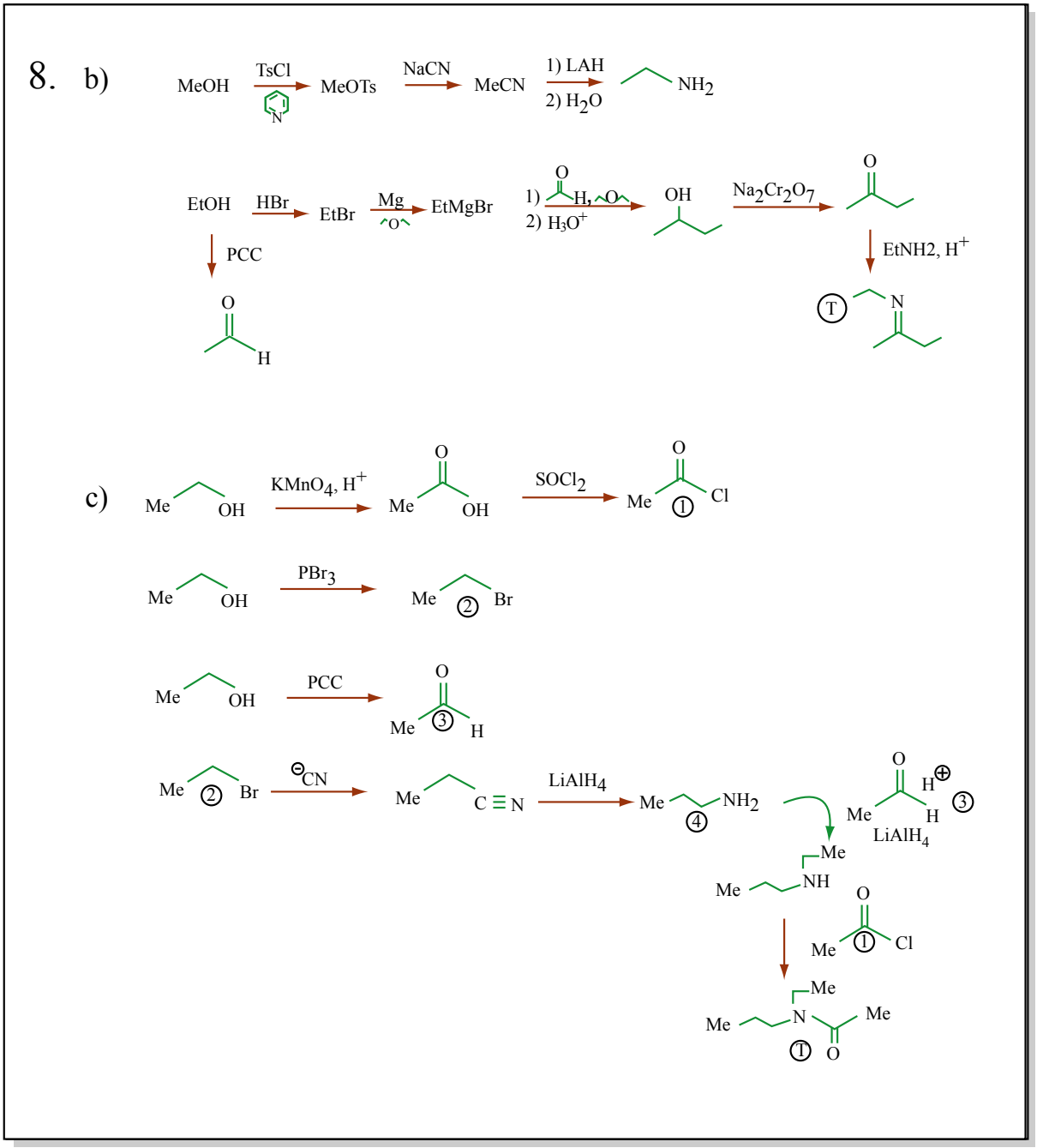


Figure by MIT OCW.

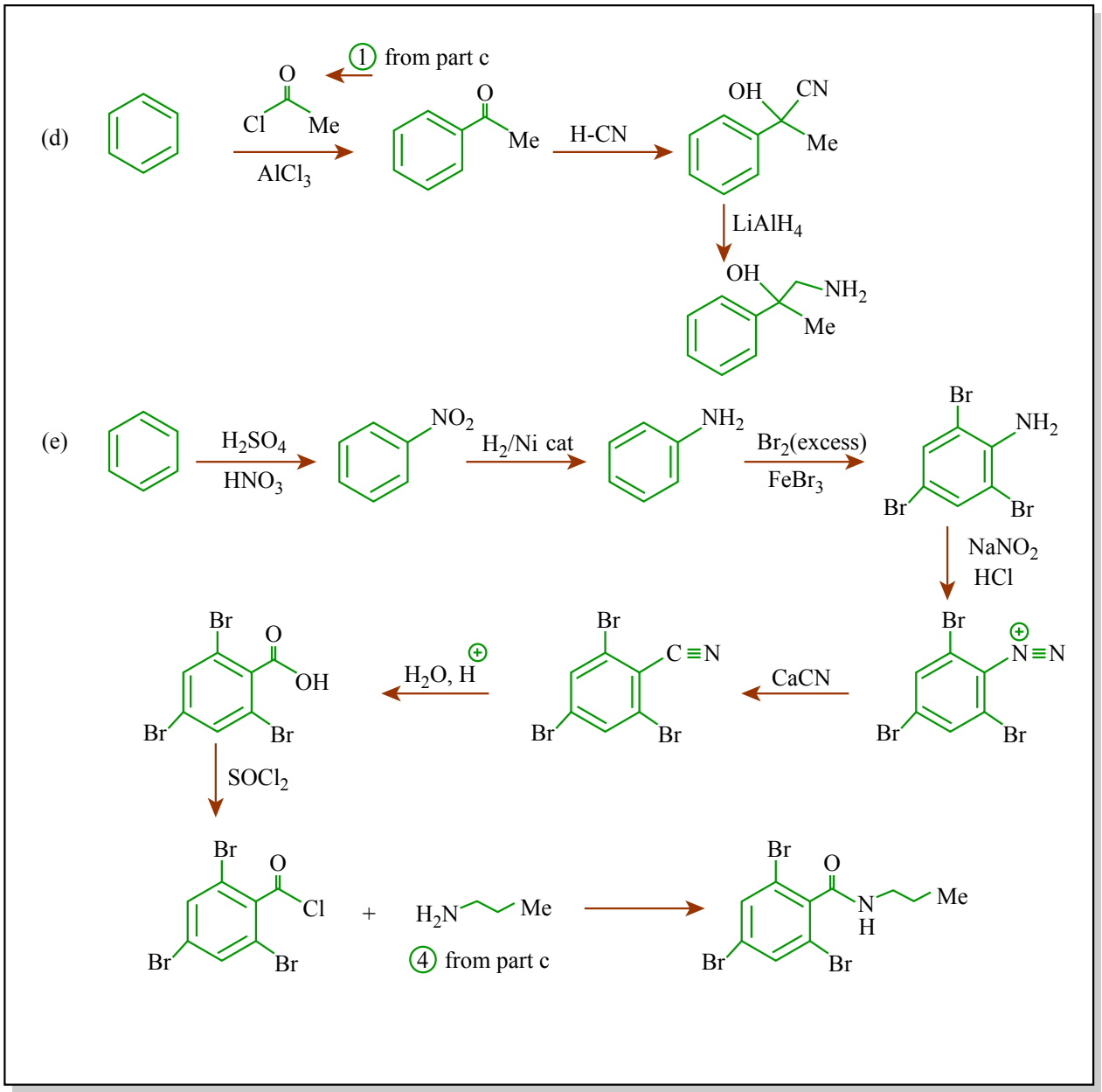


Figure by MIT OCW.

5. (11 points each, 22 points total) Please provide syntheses for **only two of the three** indicated compounds. All the carbon atoms should be derived from the allowed starting materials. You may use any common reagents.

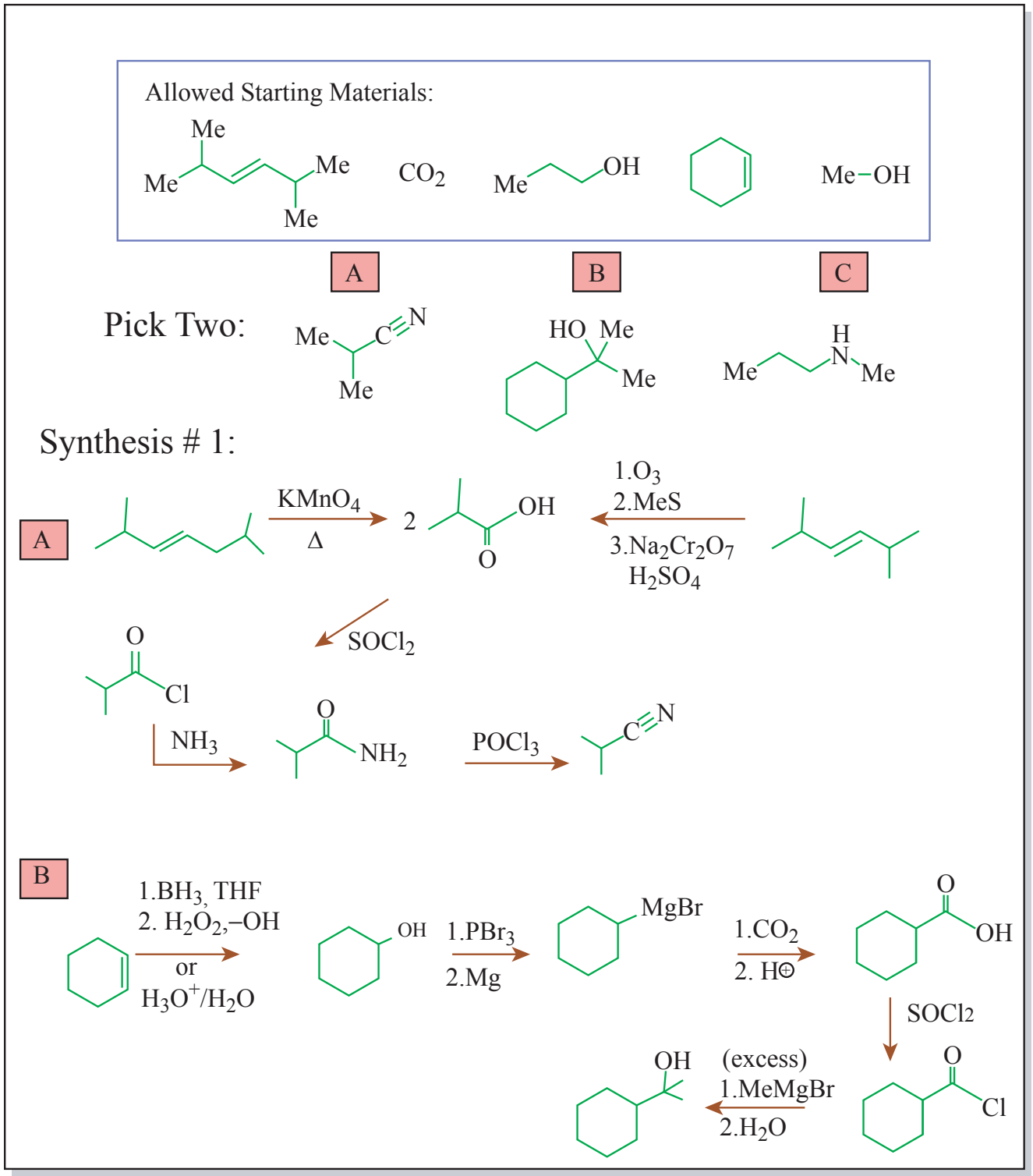


Figure by MIT OCW.

Name_____