Time: 3 hours

This exam contains 12 pages,
counting the cover sheet.

Please answer all questions within these pages.
Scrap paper is provided for rough work, but will not be graded.
Part 1. Provide the product, starting material or reagents (as indicated) for 5 of the following 6 reactions. Specify the stereochemical outcome of the reaction wherever appropriate. If you attempt all 6, be sure to cross out the one you don’t want me to mark. Otherwise, I will go in order.

A. $\text{N} - \text{H} - \text{O}$

B. $\text{N} - \text{H} - \text{O}$

C. $\text{N} - \text{H} - \text{O}$

D. $\text{CO}_2\text{Me}$

E. $\text{O}$

F. $\text{O}$
Part 2. Provide a reasonable mechanism for 2 out of the following 3 transformations (here, and on the following two pages). If you attempt all 3, be sure to cross out the one you don’t want me to mark. Otherwise, I will go in order.

Leftovers... not just for lunch anymore!
In a recent Nature paper, Brian Stoltz published a beautiful synthesis of (-)-cyanthiwigin F that relied on a desymmetrization reaction as the key step. Provide mechanisms to account for the formation of 2 and 3. In words, briefly summarize how it is that Stoltz is able to “correct” the stereochemistry at the chiral quaternary centres, in proceeding from 2 to 3.

A.

\[
\text{not chiral} \quad \xrightarrow{\text{chiral ligand}^*} \quad \text{chiral!}
\]

1. NaH, toluene, reflux
2. K₂CO₃ / MeO, acetone, reflux

1:1 mixture of racemic:meso diastereomers

\(99\%\) enantiomeric excess

(R,R)-3

Cyanthiwigin F
In the presence of a photosensitizer and light (hv), oxygen (O₂) can participate in Diels-Alder reactions, which opens up all kinds of interesting synthetic possibilities. In 1993, Dale Boger (Scripps) synthesized isochorysohermidin from a bis-pyrrole precursor. Propose a **mechanism**, and comment on the expected **stereochemical outcome** for the reaction.

Note: the purpose of the photosensitizer and light is to generate singlet oxygen (oxygen in the ground state is a triplet). Don’t worry about this too much, though. You can just push arrows from O=O if that makes you happier.
In a synthesis of the briarellin diterpenes, Larry Overman formed the central bicycle by reacting precursors 1 and 2 in an efficient 2-step procedure. Propose a mechanism for the formation of 3.

Don't worry about the relative stereochemistry for this reaction.
Part 3. The following synthesis of (+/-)-isocycloseychellene was completed by Steven Welch’s group in 1985. Fill in the blanks corresponding to reagents or intermediates where indicated. For the two requested mechanisms (A and B), please write your responses on the subsequent pages. In a couple of cases, I have used blue circles to highlight where the molecule has been transformed. In other steps, I have left the products unannotated, so you will need to figure out for yourself what reaction has taken place.

Note: pay attention to regiochemical control in these reactions, but don’t worry too much about stereochemistry.
Space for mechanisms is provided on the next two pages.
Mechanism for Step A:
Mechanism for Step B:
Part 4. Propose an **enantioselective** synthesis for 2 out of the following 5 natural products. Your approach should begin with commercially available reagents. You can assume that you have access to:

(a) **simple** alkyl, alkenyl or alkynyl reagents with up to 4 carbon atoms, for example:

\[
\text{\textbf{Br}} \quad \text{or} \quad \text{\textbf{H}} \quad \text{or} \quad \text{\textbf{Li}} \quad \text{or} \quad \text{\textbf{Cl}} \quad \text{or} \quad \text{\textbf{O}}
\]

(b) aryl or heteroaryl molecules with a **maximum of 2 substituents**, for example:

\[
\text{\textbf{O}} \quad \text{\textbf{Me}} \quad \text{or} \quad \text{\textbf{N}}
\]

(c) **simple** 5- or 6-membered rings, for example:

\[
\text{\textbf{O}} \quad \text{\textbf{Cl}} \quad \text{or} \quad \text{\textbf{O}} \quad \text{\textbf{Me}}
\]

(d) other reagents or catalysts that we’ve seen in class.

You will **not** have access to organotin or organoborane compounds, so you’ll have to make those yourself.

Please write your final answers on the next two pages – I’ve also provided some scrap paper you can use for working through your ideas, but this will not be submitted with your exam so make sure you have something good in the allotted space.

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**Dizocilpine**  
( NMDA receptor antagonist )

**Cubane**  
( popular synthetic target from the 1960s )

**Cinerin I**  
( insecticide from pyrethrum flowers )

**Eucalyptol**  
( from eucalyptus ... duh )

**Domoic Acid**  
( responsible for amnesic shellfish poisoning )

*Come on ... you know you want to try cubane!*
Synthesis #1:
Synthesis #2:

END