Name:_____ **Points:**_____

Prof. K. C. Nicolaou **Final Exam**

CHEM 151 - Molecules that Changed the World **March 19, 2009**

UCSD, Department of Chemistry and Biochemistry

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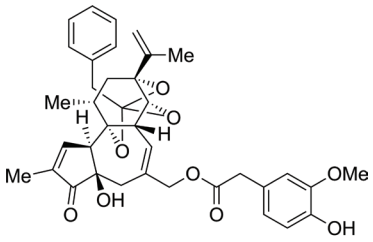
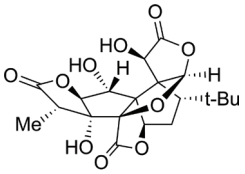
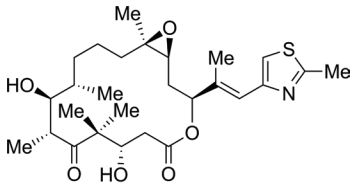
1. Match the following **names** with the appropriate **structure**: ginkgolide B, amphotericin B, rapamycin, brevetoxin B, Taxol®, palytoxin, calicheamicin γ_1^I, epothilone B, vancomycin, resiniferatoxin (20 points)



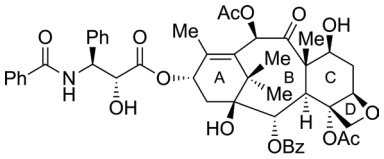
resiniferatoxin



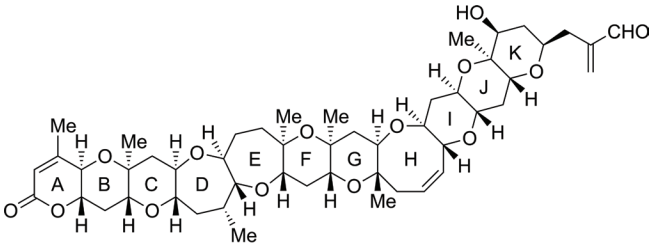
ginkoglide B



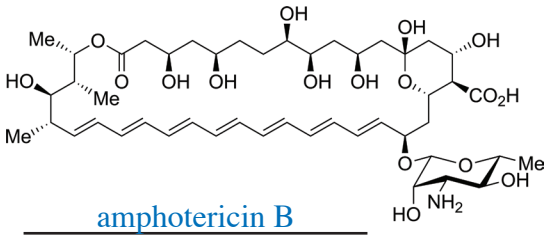
epothilone B



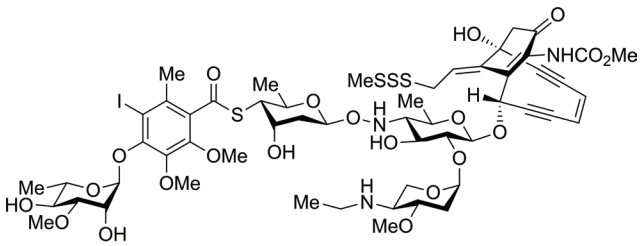
Taxol®



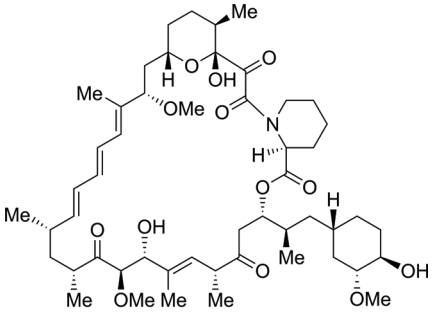
brevetoxin



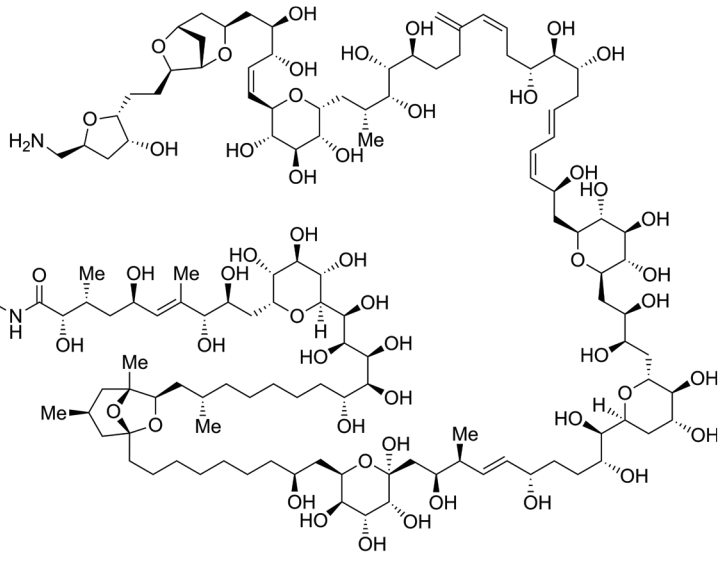
amphotericin B



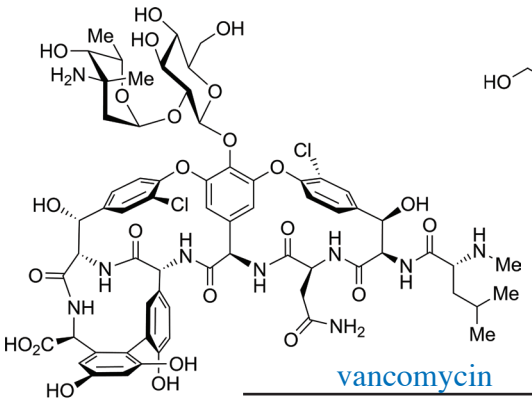
calicheamicin



rapamycin



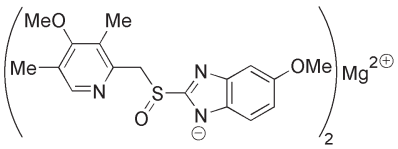
palytoxin



vancomycin

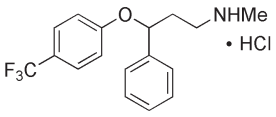
2. Match each of the following **medicines** with the appropriate molecular **structure** and **mechanism of action**: Nexium®, AZT (Retrovir®), Valium®, Viagra®, Prozac® (15 points)

Molecular Structure



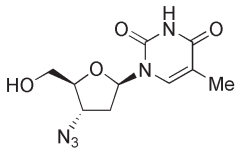
Nexium®

E IV



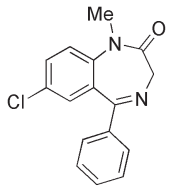
Prozac®

C I



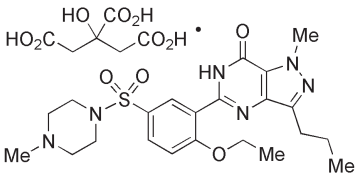
AZT

D V



Valium®

B III



Viagra®

A II

Mechanism of Action

A. Inhibits phosphodiesterase type5 (PDE5), an enzyme that cleaves and inactivates the messenger cyclic quanosine monophosphate (cQMP)

B. Binds to GABA receptors

C. Inhibits serotonin re-uptake, leading to higher levels of the neurotransmitter in the synapse

D. Inhibits the HIV enzyme reverse transcriptase

E. Blocks the $H^{\oplus}/K^{\oplus}$–ATPase, an enzyme that pumps acid into the stomach

Medical Indication

I. antidepressant drug

II. erectile dysfunction drug

III. antianxiety drug

IV. anti-ulcer drug

V. anti-AIDS drug

3. Name three (3) major **pharmaceutical** companies and two (2) successful **biotechnology** companies as well as five (5) **biologic drugs**, indicating the **medical indication** for each (15 points).

Major pharmaceutical companies:

1. Merck
2. Pfizer
3. Novartis

Biotechnology companies:

1. Genentech
2. Amgen

Biologic drugs:	Indication:
1. Insulin (Humalin®)	diabetes
2. Herceptin®	anticancer
3. Enbrel®	anti-arthritis
4. Epogen®	anti-anemia
5. Humira®	anti-arthritis
other biologics mentioned in Chapter 34	

4. Name five (5) **natural products** used as medicines and indicate their **medical indication** (10 points).

Natural Product:	Indication:
1. Amphotericin B	antifungal
2. Taxol®	anticancer
3. Vancomycin	antibiotic
4. Erythromycin	antibiotic
5. Calicheamicin	anticancer
Epothilone	anticancer
Penicillin	antibiotic
other natural products or derivatives	

5. Name one **Nobel Laureate** associated with the following (20 points):

1. Fundamental studies on the biochemistry of nucleic acids with particular regard to recombinant DNA — P. Berg

2. Contributions concerning the determination of base sequences in nucleic acids — W. Gilbert & F. Sanger

3. Development of methodology for chemical synthesis on a solid matrix — R. B. Merrifield

4. Discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material (the genetic code). — F. Crick, J. Watson, M. Wilkins

5. Contributions to carbocation chemistry — G. Olah

6. Fundamental contributions to the establishment of oligonucleotide-based, site-directed mutagenesis and its development for protein studies — M. Smith

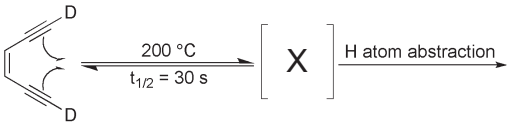
7. Conformation and its application in chemistry — D. H. R. Barton & O. Hassel

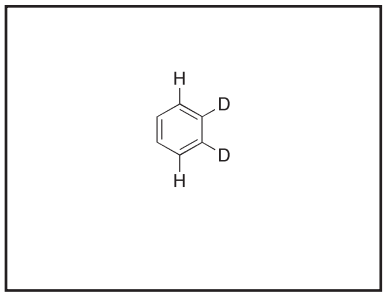
8. Research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances — L. Pauling

9. Work on the structure of proteins, especially that of insulin — F. Sanger

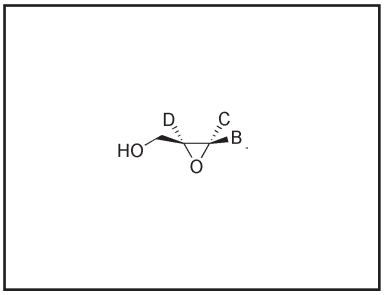
10. Invention of the polymerase chain reaction (PCR) method — K. B. Mullis

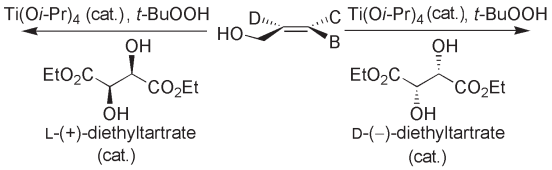
6. **Name** (type of reaction and scientist associated with it) each of the following reactions and give the **structure** of the product (in box) in each case (20 points).

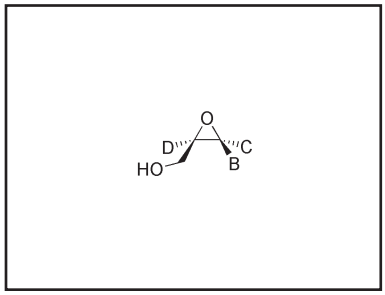




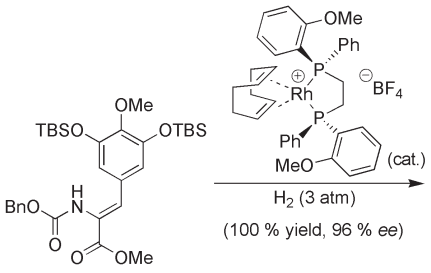
1. Bergman cycloaromatization
(R. Bergman)

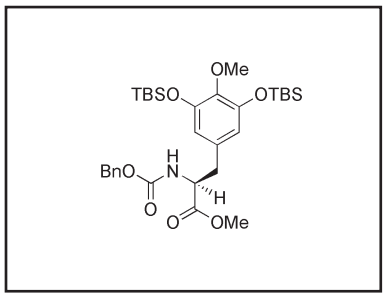




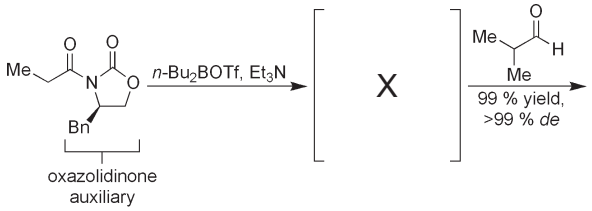


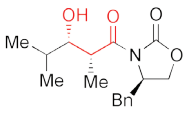
2. Sharpless asymmetric epoxidation
(T. Katsuki and K. B. Sharpless)



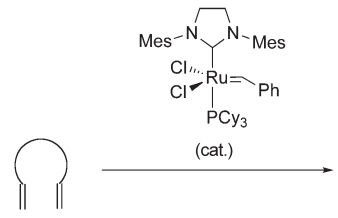


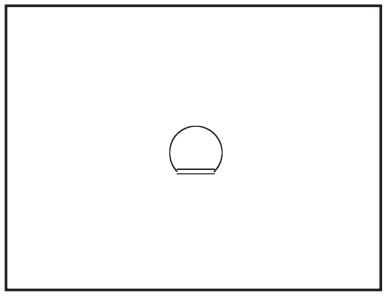
3. Asymmetric hydrogenation
(W. Knowles, H. Kagan, R. Noyori)





4. Evans aldol reaction





5. Olefin metathesis
(Y. Chauvin, T. J. Katz, R. Schrock, R. Grubbs, N. Calderon)

7. In the box below, describe (150 words or less) the **Drug Discovery and Development Process** indicating the roles played by **biologists and biochemists**, **medicinal chemists**, **process chemists**, **pharmacologists**, and **medical doctors** (20 points).

The modern drug discovery and development process is a long and costly endeavor starting with biology and proceeding through chemistry and pharmacology and ending with clinical trials and approval by the appropriate government authorities. Biologists and biochemists discover the cause of a disease (pathogenesis) and validate a biological target. They then develop a biological assay to test compounds for inhibition or binding. Medicinal chemists then begin their search for lead compounds which they then optimize through structural modifications to a drug candidate with the appropriate potency and selectivity as well as other desireable characteristics. Process chemists streamline or develop a new synthesis of the drug candidate for pilot and large scale production of the drug candidate. Pharmacologists test the drug candidate both in vitro and in vivo for toxicity and other pharmacological properties such as solubility, absorption, metabolic stability and bioavailability. If passed these stages, the compound will then be elevated to the status of clinical candidate and enter clinical trials which are conducted by medical doctors (I for safety; II for efficacy in small number of patients; and III for efficacy and possible side effects in a larger number of patients). Finally, approval by FDA (in the USA) signals success and clinical use for the public.