

# Medicinal Chemistry 310

## Medicinal Chemistry and Drug Design

### Second Midterm Exam

April 9, 2007

Name: \_\_\_\_\_

**(Unless otherwise stated, all questions are 3.0 points)**

*N.P. Farrell*

1. To use Technetium (Tc) as an imaging agent we take advantage of which physico-chemical property?

- |                           |                      |
|---------------------------|----------------------|
| A) Paramagnetism          | C) $\gamma$ -emitter |
| B) Square-planar geometry | D) Soft Acid         |

2. Which element do the following properties describe?

Necessary for growth  
Functions include DNA transcription and replication  
Functions include cell ( $O_2^-$ ) regulation

- |       |       |
|-------|-------|
| A) Pt | C) Cu |
| B) Fe | D) Zn |

3. Which of the following is **NOT** a useful mustard anti-cancer drug?

- |                    |                     |
|--------------------|---------------------|
| A) Mechlorethamine | C) Iphosphamide     |
| B) Sulfur Mustard  | D) Cyclophosphamide |

4. Use of DNA microarrays allows

- A) correlation between gene expression and cytotoxicity of anti-cancer drugs
- B) DNA binding to be assessed
- C) Quantitation of interstrand crosslinks

5. Cisplatin binding to DNA produces:
- |                  |                    |
|------------------|--------------------|
| A) Strand breaks | C) Mutations       |
| B) DNA bend      | D) Left-handed DNA |
6. Nitroprusside,  $[\text{Fe}(\text{NO})(\text{CN})_5]^{2-}$  acts as a vasodilating agent through
- |                             |                                 |
|-----------------------------|---------------------------------|
| A) release of $\text{CN}^-$ | C) redox reactions of Fe        |
| B) release of NO            | D) strong binding to hemoglobin |

*A.T. Sneden*

7. How does taxol function as a drug?
- |  |
|--|
| A) By stabilization of mitosis.          |
| B) By inhibition of mitosis.             |
| C) By reduction of pain.                 |
| D) By reduction of inflammation.         |
| E) By stabilization of cardiac activity. |
8. Which pathway best represents the synthesis of aspirin?
- |   |
|---|
| A) Gaultheria procumbens $\rightarrow$ salicylaldehyde $\rightarrow$ salicin $\rightarrow$ acetylsalicylic acid |
| B) Spiraea tomentosum $\rightarrow$ methyl salicylate $\rightarrow$ salicin $\rightarrow$ acetylsalicylic acid  |
| C) Salix alba $\rightarrow$ salicin $\rightarrow$ methyl salicylate $\rightarrow$ acetylsalicylic acid          |
| D) Salix alba $\rightarrow$ salicin $\rightarrow$ salicylic acid $\rightarrow$ acetylsalicylic acid             |
| E) Salix alba $\rightarrow$ salicylic acid $\rightarrow$ methyl salicylate $\rightarrow$ acetylsalicylic acid   |
9. Which pair of plants below produce antimalarial compounds?
- |  |
|--|
| A) Cinchona succirubra and Artemisia annua     |
| B) Atropa belladonna and Erythroxylum coca     |
| C) Salix alba and Mentha piperita              |
| D) Papaver somniferum and Vinca rosea          |
| E) Catharanthus roseus and Cinchona succirubra |
10. Morphine is related to which other alkaloid?
- |                |              |
|----------------|--------------|
| A) taxol       | D) cocaine   |
| B) quinine     | E) oxycontin |
| C) scopolamine |              |

11. The main carbon skeleton of a diterpene contains:
- A) 10 carbon atoms.                      D) 25 carbon atoms.  
B) 15 carbon atoms.                      E) 30 carbon atoms.  
C) 20 carbon atoms.
12. An alkaloid is best defined as:
- A) A drug of abuse derived from a plant.  
B) A physiologically active compound containing a basic nitrogen in a complex structure  
C) A physiologically active compound containing an acidic nitrogen in a complex structure.  
D) A compound used to treat malaria derived from a plant. A physiologically active compound containing an acidic nitrogen in a complex structure.  
E) A toxic compound derived from a plant.

Q. Zhou

13. In the parallel synthesis of the benzodiazepine library, how many reaction wells are needed for 230 amino acids, 100 anthranilic acids and 280 alkylating agents?
- A) 230    D)  $230+100+280$   
B) 100    E)  $230 \times 100 \times 280$   
C) 280
14. In the combinatorial synthesis of iNOS inhibitors, if a split and mix method was used with 300 of R1 of 1st step, 400 of R2 of 2nd step and 200 of R3 of the last step, what is the number of final reaction wells?
- A) 300    D)  $300+200+400$   
B) 200    E)  $300 \times 200 \times 400$   
C) 400
15. After the *in vitro* screen of a kinase inhibitor library, there are four positive hits with the four component library of 110 of R1, 320 of R2, and 40 of R3. What is the total number of wells are required for the identification of a positive bead using the positional deconvolutional method?
- A) 110    D)  $110+320+40$   
B) 320    E)  $110 \times 320 \times 40$   
C) 40

16. The requirement of the solid resin in the synthesis includes the following **EXCEPT**:
- A) high loading
  - B) high swelling in organic solvents
  - C) stability in the reaction conditions
  - D) fast release of intermediates in the early synthesis
  - E) physical durability
17. What are the advantages of the solid phase synthesis?
- A) Excess reagents can be used.
  - B) Products can be obtained at the last step by a simple cleavage step.
  - C) Easy purification by filtration.
  - D) Facile automation.
  - E) All of above.
18. After a library of compounds is achieved, the following steps are used to ensure the success of the synthesis **EXCEPT**:
- A) Purity of the compounds by HPLC analysis
  - B) Structural confirmation by NMR analysis
  - C) Mass analysis
  - D) Swelling analysis of the solid phase resin
  - E) Infrared spectroscopic analysis

*G.E. Kellogg*

19. The “fundamental” particle of quantum mechanics is the electron. What is the fundamental particle of molecular mechanics?
- A) Boson
  - B) Quark
  - C) proton
  - D) atom
  - E) functional group
20. The electrostatic term in a Molecular Mechanics Force Field is usually represented by a variation of:
- A) Tesla’s Law
  - B) Van der Waal’s Law
  - C) Coulomb’s Law
  - D) Van der Graaf’s Law
  - E) Newton’s 3<sup>rd</sup> Law

21. The most successful molecular modeling/computational chemistry technique (in terms of drug discovery and design) has been:
- A) 3D Database searching and mining
  - B) 3D QSAR, i.e., Comparative Molecular Field Analysis.
  - C) Quantum Mechanics
  - D) De Novo Drug design
  - E) None of the above
22. Quantum mechanics (QM) is not usually useful for “drug discovery” research because:
- A) it is difficult to understand the results of QM calculations.
  - B) biological molecules are too large for the programs currently in use.
  - C) there are no electrons in biological molecules.
  - D) the QM force field is not well parameterized for biological molecules.
  - E) all of the above.
23. Which of the following terms is **not** found in a molecular mechanics force field?
- A) Electrostatic (Coulombic) attractions and repulsions
  - B) Highest Occupied Molecular Orbital (HOMO) energy
  - C) Van der Waals (London) Forces
  - D) Bond Stretches and Angle Bends
  - E) All of these **are** found in molecular mechanics force field.
24. The two principal paradigms of computer-aided drug discovery are “Ligand-based design” and “Structure-based design”. Which of the following is an example of Ligand-based design?
- A) Virtual screening through docking and scoring
  - B) 3D data base searches against receptor target query
  - C) 3D QSAR such as Comparative Molecular Field Analysis
  - D) *De novo* design algorithms
  - E) None of these are Ligand-based design

*J.C. Hackett*

25. Drug-metabolizing cytochrome P450 enzymes are localized primarily to which cellular organelle?
- A) Nucleus  
B) Mitochondria  
C) Smooth Endoplasmic Reticulum  
D) Cell Membrane
26. Which prosthetic group interacts directly with, and is central to the activation of molecular oxygen by cytochrome P450?
- A) Iron Protoporphyrin IX  
B) Flavin Adenine Dinucleotide  
C) Nicotinamide Adenine Dinucleotide Phosphate  
D) Tetrahydrobiopterin
27. Which of the following pairs of proteins are responsible for shuttling electrons to mitochondrial cytochrome P450 enzymes?
- A) NADPH Cytochrome P450 Reductase/Cytochrome b5  
B) Adrenodoxin/Adrenodoxin Reductase  
C) Myoglobin/Hemoglobin  
D) Dihydropteridine Reductase/Galactose Oxidase
28. The majority of cytochrome P450-catalyzed oxidations proceed via which mechanism?
- A) Aldol condensation  
B) [2+2] cyclization  
C) Michael addition  
D) Hydrogen Atom Abstraction/Hydroxyl Radical Rebound
29. Which of the following is the predominant family of cytochrome P450 in human liver?
- A) CYP2D  
B) CYP2C  
C) CYP1A  
D) CYP3A



36. Clinically useful HIV protease inhibitors have which of the following functional groups replacing the normal substrate amide group:

- A) A thiol.
- B) An alcohol.
- C) A phosphonate
- D) A ketone

*Modeling Lab (G.E.K., J.C.H. and R.B.W.)*

37. When optimizing (minimizing) the structure of cyclohexane, why do some people get the “chair” form and some people get the “twisted boat” form?

- A) The computer program is wrong on some computers
- B) Structure generation relies on random number generation – a random sampling of conformers is always observed.
- C) Local minima are easier to reach than the global minimum.
- D) The people with the boat structures did not include charges in their model.
- E) The people with the boat structures did not minimize their energy long enough.
- F) None of the above.

38. The enzyme HIV protease has been discussed at several points throughout the course. Without molecular graphics it is difficult to appreciate its complex architecture. We looked at the structure of HIV-1 protease and one of its inhibitors on the graphics workstations. What structural feature(s) of the protease was/were used to design new inhibitors?

- A) the two-fold symmetry of HIV-1
- B) the hydrophobic pockets of HIV-1
- C) the dual aspartate residues at the center of the active site
- D) the movement of the “flaps”
- E) A) - C), but not D)
- F) A) - D)
- G) None of the above

39. After building and optimizing cyclohexane, we built and optimized:

- A) benzodiazepine
- B) catecholamine
- C) methamphetamine
- D) morphine
- E) nicotine
- F) lysergic acid diethylamide

40. While optimizing structures in the lab, we observed that molecular mechanics energy minimizations end when:

- A) number of planned iterations has been reached
- B) gradient,  $\Delta E/\Delta t$  (change in energy/iteration) has been reached
- C) desired molecular energy has been reached
- D) A) or B)
- E) A) or C)
- F) None of the above