A Few Common Observations...

Organic chemistry is typically taught from a chemical point of view
Organic chemistry is the one course EVERYONE has heard of and many DREAD taking
Organic chemistry is usually a “make it or break it” class for pre-med students

Does it have to be this way?

ABSOLUTELY NOT!!!

You can learn the same material that has been taught semester after semester at universities around the world but from a medical/biological point of view
**Organic Chemistry and Medicine**

**Organic** 
\(\text{ôr-}'g\-\text{a}-\text{nık}\) **adj**: 1. of, relating to, or arising in a bodily organ; 2. of, relating to, or containing carbon compounds; 3. relating to, being, or dealt with by a branch of chemistry concerned with the carbon compounds of living beings and most other carbon compounds.

**Chemistry** 
\(\text{ˈke-\text{mə-strē}}\) **n**: a science that deals with the composition, structure, and properties of substances and with the transformations that they undergo.

**Medicine** 
\(\text{ˈme-də-sən}\) **n**: 1. a substance or preparation used in treating disease; 2. the science and art dealing with the maintenance of health and the prevention, alleviation, or cure of disease.
Organic Chemistry and Medicine

**MEDICINE**
- History and Physical Exam
  - Differential Diagnosis
    - Order labs and Procedures
      - Diagnose and Treat

**ORGANIC CHEMISTRY**
- Review Literature
  - Synthetic Strategy
    - Run Model Reactions
      - Synthesize Molecule
The format of the lectures will be as follows:

**Presentation of Case Study**
- Ex. 24 year old female presents to the ED with...

**Discuss Functional Group(s)/Reaction(s)**
- How this functional group/reaction(s) relates to the disease
Organic Chemistry and Medicine

Medicine

Blood, Plasma, Serum
- Alanine aminotransferase (ALT, GPT at 30°C)
  - Reference Range: 8-20 U/L
- Aspartate amino transferase (AST, GGT at 30°C)
  - Reference Range: 25-125 U/L
- Bilirubin, serum (adult)
  - Total: 0.1-1.0 mg/dL
  - Direct: 0.0-0.3 mg/dL
  - Reference Range: 0.1-1.0 mg/dL
- Calcium, serum (Total)
  - Reference Range: 8.6-10.2 mg/dL
- Cholesterol, serum
  - Reference Range: 140-250 mg/dL
- Creatinine, serum (Total)
  - Reference Range: 0.6-1.1 mg/dL
- Electrolytes, serum
- Sodium
  - Reference Range: 135-147 mEq/L
- Chloride
  - Reference Range: 95-105 mEq/L
- Potassium
  - Reference Range: 3.5-5.0 mEq/L
- Bicarbonate
  - Reference Range: 22-28 mEq/L
- Gases, arterial blood (room air)
  - P<sub>O</sub>2
    - Reference Range: 55-84 mmHg
  - P<sub>CO</sub>2
    - Reference Range: 35-45 mmHg
  - pH
    - Reference Range: 7.35-7.45
- Glucose, serum
  - Fasting: 70-110 mg/dL
  - Reference Range: <5 mg/mL
- Growth hormone - arginine stimulation
  - Proven stimulatory: >7 ng/mL
- Osmolality, serum
  - Reference Range: 275-295 mOsm/kg
- Phosphorus (alkaline), serum (p-NPP at 30°C)
  - Reference Range: 2.0-7.0 mg/dL
- Phosphorus (ionic), serum
  - Reference Range: 0-4.5 mg/dL
- Proteins, serum
  - Reference Range: 6.0-7.8 g/dL
- Albumin
  - Reference Range: 2.5-5.5 g/dL
- Globulins
  - Reference Range: 2.3-3.5 g/dL
- Urea nitrogen, serum (BUN)
  - Reference Range: 7-18 mg/dL
- Uric acid, serum
  - Reference Range: 2.0-8.2 mg/dL
- Cerebrospinal fluid
  - Glucose
    - Reference Range: 40-70 mg/dL

Hematologic
- Erythrocyte count
  - Male: 4.3-5.9 million/mm³
  - Female: 3.5-5.5 million/mm³
- Hematocrit
  - Male: 41-52%
  - Female: 36-46%
- Hemoglobin, blood
  - Male: 13.5-17.5 g/dL
  - Female: 12.0-16.0 g/dL
Organic Chemistry and Medicine

Biology

[Diagram showing organic chemistry and biology pathways]
Organic Chemistry and Medicine

Organic Chemistry

\[
\begin{align*}
\text{2-propanol} & \xrightarrow{\text{K}_2\text{Cr}_2\text{O}_7, \ H_2\text{SO}_4, \ 70^\circ} \text{propanone} \\
\text{2-butanol} & \xrightarrow{\text{KMnO}_4, \ H_2\text{SO}_4, \ 80^\circ} \text{2-butanone} \\
\text{2-butanol} & \xrightarrow{\text{CrO}_3, \ \text{CH}_3\text{COOH}, \ 80^\circ} \text{2-butanone}
\end{align*}
\]
Organic Chemistry and Medicine

Medicine

Organic Chemistry

\[ \text{OH} \]
\[ \text{CH}_3 - \text{CH} - \text{CH}_3 \] 2-propanol
\[ \xrightarrow{\text{K}_2\text{Cr}_2\text{O}_7, \ H_2\text{SO}_4, 70^\circ} \text{CH}_3 - \text{C} - \text{CH} \text{ propanone} \]

\[ \text{OH} \]
\[ \text{CH}_3 - \text{CH} - \text{CH}_3 \] 2-butanol
\[ \xrightarrow{\text{KMnO}_4, \ H_2\text{SO}_4, 80^\circ} \text{CH}_3 - \text{CH} - \text{C} - \text{CH}_3 \text{ 2-butane} \]

\[ \text{OH} \]
\[ \text{CH}_3 - \text{CH} - \text{CH}_3 \] 2-butanol
\[ \xrightarrow{\text{CrO}_3, \ CH_3\text{COOH}, 80^\circ} \text{CH}_3 - \text{CH} - \text{C} - \text{CH} \text{ 2-butane} \]
Case 1

A 30-year-old man is evaluated in the emergency department for complications of difficulty breathing, chills, and chest pain for the past 24 hours. He denies any previous history of medical problems. On physical examination, he appears ill. His temperature is 40°C (104°F), his blood pressure is 90/50 mm Hg, and his heart rate is 110/min. Cardiac examination reveals a 3/6 diastolic murmur; however, the patient denies any history of a murmur. ECG results are normal.

Diagnosis: Acute Endocarditis

How does this case relate to organic chemistry?
Treatment of Endocarditis

VANCOMYCIN

PENICILLIN

CEFTRIAXONE

GENTAMICIN

AMPICILLIN

NAFCILLIN

OXACILLIN
Penicillin

β-lactam structure is involved in the mechanism of action
Penicillin Mechanism of Action

Penicillin Binding Protein

- PBPs are all involved in the final stages of the synthesis of peptidoglycan, which is the major component of bacterial cell walls.
- Bacterial cell wall synthesis is essential to growth, cell division (thus reproduction) and maintaining the cellular structure in bacteria.
- Inhibition of PBPs leads to irregularities in cell wall structure such as elongation, lesions, loss of selective permeability, and eventual cell death and lysis.
Penicillin Mechanism of Action

Nucleophilic Attack on the Cyclic Amide Carbonyl Carbon
Biology sets the reaction up perfectly; however, this is not the case in a chemistry laboratory....
The Chemistry of Amides

Reactions formation:

1H NMR, 13C NMR, IR, MS
The Formation of Amides

\[ \text{R-C≡N} + \text{H}_2\text{O} \xrightarrow{\text{H}^+} \text{R-C}=\text{NH} \quad \xrightarrow{\text{H}^+} \text{R-C}(-\text{NH}_2) \]

Nitrile

\[ \text{CH}_3\text{C}-\text{Cl} + 2\text{NH}_3 \rightarrow \text{CH}_3\text{C}=\text{NH}_2 + \text{NH}_4^+\text{Cl}^- \]

Acid Chloride

\[ \text{CH}_3\text{C}(-\text{O})=\text{CH}_3 + 2\text{NH}_3 \rightarrow \text{CH}_3\text{C}=\text{NH}_2 + \text{CH}_3\text{C}(-\text{O})^\text{-} + \text{NH}_4^+ \]

Anhydride

\[ \text{CH}_3\text{C}(-\text{O})\text{C}(-\text{O})\text{C}(-\text{O})\text{CH}_3 + \text{NH}_3 \rightarrow \text{CH}_3\text{C}=\text{NH}_2 + \text{HO}-\text{CH}_2\text{CH}_3 \]

Ester
Mechanisms

\[
\text{Halides are great leaving groups}
\]
Mechanisms

\[
\text{R-C≡N} + \text{H}_2\text{O} \xrightarrow{\text{H}^+} \text{R-C=NH} \rightleftharpoons \text{R-C-NH}_2
\]

Regenerated acid catalyst
**$^{13}$C NMR and IR of Amide**

**$^{13}$C NMR spectra**
- Carbonyl carbon: 180 ppm
- Alkyl carbon: 20 ppm

**IR spectra**
- Carbonyl group: 1700 cm$^{-1}$
- N-H group: 3200 cm$^{-1}$

- Physicians obtain laboratory values and perform diagnostic tests
- Organic chemists obtain spectroscopic data and perform model reactions
The Chemistry of Amides

What compounds can we make from the amide functional group?
The Chemistry of Amides

\[
\text{CH}_3\text{C}\equiv\text{NH}_2 + \text{H}_2\text{O} \xrightarrow{\text{HCl}} \text{CH}_3\text{C}\text{OH} + \text{NH}_4^+ \text{Cl}^- \\
\text{Carboxylic acid}
\]

\[
\text{CH}_3\text{C}\equiv\text{NH}_2 \xrightarrow{1. \text{LiAlH}_4, \text{Et}_2\text{O}} \text{CH}_3\text{CH}_2\text{NH}_2 \\
\text{Amine}
\]

\[
\text{CH}_3\text{C}\equiv\text{NH}_2 + \text{Br}_2 + 2\text{NaOH} \rightarrow \text{CH}_3\text{NH}_2 + \text{CO}_2 \\
\text{Amine}
\]
Stability of Amides

Less electrophilic than other carbonyl functional group
Amides and Amino Acids

- Alanine
  \[ \text{H}_2\text{N}-\text{CHC}=\text{OH} \]
  \[ R = \text{CH}_3 \]
  \[ \text{Alanine} \]

- Arginine
  \[ \text{H}_2\text{N}-\text{CHC}=\text{OH} \]
  \[ R = \text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{C}=\text{NH}\text{NH}_2 \]
  \[ \text{Arginine} \]

- Lysine
  \[ \text{H}_2\text{N}-\text{CHC}=\text{OH} \]
  \[ R = \text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \]
  \[ \text{Lysine} \]
Amides and Amino Acids

Penicillin Binding Protein

G-coupled Protein Receptor

Na/K Channel