Bio-organic Chemistry

Chemistry 452

Section: E100

Term: 2010 Fall

Instructor: Dr. E. Plettner

Discussion Topics: General Course Description:

This course will provide a brief overview of natural products and their biosynthetic origin. The course will begin with the synthetic building blocks and strategies used in living systems. Next, we shall cover primary metabolic pathways and later move on to complex secondary metabolites. Behind the bewildering complexity and variety of natural product biosyntheses there are a few elegant recurring patterns, which we shall highlight.

Topics:

1. Biochemical "reagents"

nucleotide triphosphates, nicotinamide cofactors, flavins, coenzyme A, lipoic acid, pyridoxamine/pyridoxal, thiamine phosphate, biotin, folate, vitamin B12, S-adenosyl methionine

2. Primary metabolism: carbohydrates

2.1 glycolysis

2.2 TCA cycle

2.3 pentoses, tetroses

2.4 carbon fixation from CO2

3. Nucleic acids

3.1 DNA/RNA structure and replication (brief overview)

3.2 nucleotide biosyntheses pyrimidines, purines,
2'deoxyribonucleotides

4. Proteins and peptides

4.1 ribosomal

4.1.1 amino acid activation; transfer RNA

4.1.2 translation

4.1.3 post-translational modifications (brief overview)

4.2 non-ribosomal

cases: siderophores, §-lactam antibiotics, nitrile-containing products, glucosinolates

Bio-organic Chemistry

5. Fatty acids

5.1 biosynthesis (elongation, desaturation)

5.2 fatty acid derivatives

5.2.1 alkanes and aliphatic pheromones

5.2.2 prostaglandins

5.2.3 thromboxanes

5.2.4 leukotrienes

6. Polyketides and phenolics

6.1 polyketide synthases: comparison to fatty acid synthases

6.2 cases: erythromycin (open-chain procursor, release, post-PKS enzymes), avermectin, brevetoxin A (polyethers), lovastatin, phenolics

6.3 overview of polyketides diversity

7. Terpenes

7.1 general introduction, classification

7.2 electrophilic condensation reaction

7.3 precursor formation: mevalonate pathway

7.4 precursor formation: 1-deoxyxylulose-5-phosphate pathway

7.5 modifications

7.5.1 head-to-head condensation

7.5.2 cyclization

7.5.3 functionalization

8. The Shikimate pathway: another route to phenolics

9. Alkaloids

9.1 biologically accessible sources of N

9.2 amino acid biosynthesis

9.2.1 glutamate family

9.2.2 serine family

9.2.3 aspartate family

9.2.4 pyruvate family

9.2.5 aromatic family

Bio-organic Chemistry

9.2.6 histidine

9.3 alkaloid biosynthesis

9.3.1 derived from amino acids (ornithine, lysine, tyrosine, tryptophan, anthranilic acid and histidine)

9.3.2 derived from nicotinic acid

9.3.3 derived from acetate

9.3.4 derived from purine

Grading: 20% Midterm Exam (open book)

40% Term Paper

40% Final Exam (open book)

Required Texts: Medicinal Natural Products: A Biosynthetic Approach, by Paul M. Dewick, John Wiley & Sons (2002).

Other useful references:

1)Natural Products: Their Chemistry and Biological Significance, by J. Mann, R.S. Davidson, J.B. Hobbs, D.V. Banthorpe and J.B. Harborne, Longman (1994)

2)Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, Edited by G. Michal, J. Wiley & Sons and Spektrum Akademischer Verlag, ISBN 0-471-33130-9

Recommended Texts: None

Materials/Supplies: None

Prerequisite/Corequisite: CHEM 282, CHEM 380, CHEM 381, and a basic metabolism course (MBB 221) or their equivalents from another university. A more advanced metabolism course, such as MBB 321 is also a strong asset for this course, but is not required if the other basic requirements have been met. A brief conversation with the instructor is required prior to registration.

Notes: None