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Robert Burns Woodward

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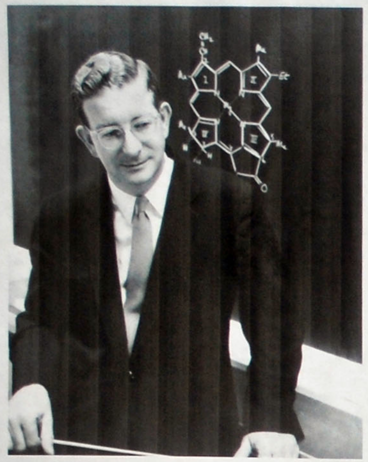


Robert Burns Woodward

"The greatest synthetic organic chemist of all time"
(Seeman, 2014)

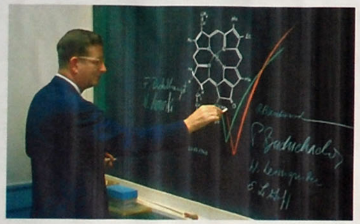
PERSONAL LIFE

Robert Burns Woodward was born on April 10th, 1917 to the parents of Margaret Burns and Arthur Woodward (1). His mother was a native of Glasgow, while his father was an English antecedent (1).

EDUCATION

- Attended primary and secondary public schools in Quincy, a suburb of Boston, Massachusetts (1).
- In 1933, Robert, at the age of 16, decided to enroll in the Massachusetts Institute of Technology (1).
- Mr. Woodward completed these degrees by the age of 20.
  - Bachelor of Science in 1936 & Doctor of Philosophy in 1937 (1).
- Began teaching immediately at the University of Illinois for a semester, but quickly returned to the east coast and Harvard in the Chemistry Department (2).

Robert Woodward passed away from a heart attack on July 8, 1979 in Cambridge, Mass (1).

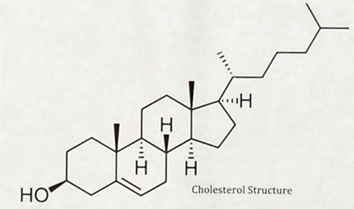


Presented by: Cody Reeley
CHEM 203 - Dr. Sonnichsen

Contributions

Synthesis of Cholesterol

- Cholesterol is a very important natural steroid that can be found in all body tissues of vertebrates (4).
- Robert Burns completed this synthesis in two years with the help of his team.
- Cholesterol is primarily synthesized from acetyl CoA through the HMG-CoA reductase pathway in the liver (~1 g/day), although other sites include the intestines, adrenal glands and reproductive organs (6).
  - Formal synthesis with 35 steps (5).
  - Best known for causing cardiovascular disease when present in elevated levels (WOM).
- Cholesterol has a molecular formula of $C_{27}H_{45}OH$ (5).
  - The hydroxyl (OH) group is polar, which makes this molecule an alcohol (5).
  - The 4-ring region is common for all steroid hormones (hydrocarbon rings) (5).
  - The combination of the steroid ring and alcohol group makes this a "sterol" (5).
  - Last region is hydrocarbon tail. The ring and tail region are non-polar, meaning they dissolve in fatty and oily substance, but don't mix well with water (5).

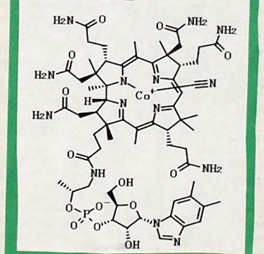


Cholesterol Structure

Synthesis of Vitamin B_{12}

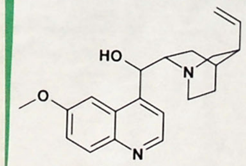
- Bacteria and algae produce Vitamin B_{12}, with common name cobalamin (7).
  - Water-soluble and involved in metabolism of every cells in the body, especially DNA synthesis and regulation (7).
- Deficiency can cause severe and irreversible damage to nervous system (7).
- This is a cobalt complex consisting of a 15-membered macrocycle. Additionally, 4 heterocyclic rings, 9 stereocenters, 6 amide side chains, and 1 carboxylic acid side chain (7).
- Woodward and Eschenmoser completed synthesis at Harvard through formal synthesis.
  - The first retrosynthesis step of the vitamin was based on the work of Bernhauer in 1960 (7).
- Important to society because this produced understanding in the form of
  - Synthetic Strategy, Woodward-Hoffman Rules, and Diastereoselective Synthesis (7).

vitamin B12



Synthesis of Quinine

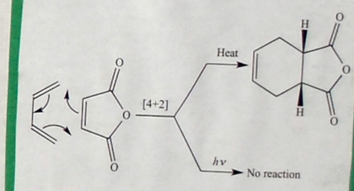
- Robert Woodward and Bill Doering completed a total synthesis of quinine in fourteen months (8).
  - Work began on the synthesis by looking at the form for attacking the quinolone moiety of quinine. Many chemists attempted to complete a total synthesis, but due to the complexities of the project, many were unsuccessful.
- Quinind is a medication used to treat malaria and bebesiosis. Additionally, found a flavor component of tonic water (bitter taste) (10).
- Publiished in 1944, the total synthesis was formal and included 17 linear steps (9).
  - Features an alcohol group as well as 4 stereocenters.
- The total synthesis of quinine opened the door to the advanced intermediate and d-quinotoxine in the field of science (8).



Quinine

Woodward-Hoffmann Rules

- A series of rules which predict whether a pericyclic process occurs under thermal or photochemical condition, as well as the stereochemical outcome of the reaction (11).
  - Based on the conservation of orbital symmetry (11).
- Can be used to understand electrolytic reactions, cycloadditions, sigmatropic reactions, and group transfer reactions (11).
- Original Rules
  - In an open-chain system containing 4n π electrons, the orbital symmetry of the highest occupied molecule orbital is such that a bonding interaction between the termini must involve overlap between orbital envelopes on opposite faces of the system and this can only be achieved in a conrotarty process (12).
  - In open systems containing (4n + 2) π electrons, terminal-bonding interaction within ground-state molecules requires overlap of orbital envelopes on the same face of the system, attainable only by disrotarty displacements (12).
  - In a photochemical reaction an electron in the HOMO of the reactant is promoted to an excited state leading to a reversal of terminal symmetry relationships and reversal of stereospecificity (12).



Rules able to predict that a (4+2) cycloaddition reaction is thermally allowed but photochemically forbidden.

Conclusion

Robert Burns Woodward was the master of organic syntheses and was able to accomplish more than anyone before him. He combined this mastery and systematic approach with the latest theories of the time on molecular structure and reaction mechanisms. Robert Woodward was awarded the Nobel Prize in Chemistry in 1965 for "outstanding achievements in the art of organic synthesis." Overall, Woodward's biggest contribution to chemistry would be his work on total syntheses. These include total synthesis of cholesterol, chlorophyll, colchicine, erythromycin, lysergic acid, quinine, reserpine, and vitamin B_{12}. Woodward's work allowed for labs today to perform these syntheses and provide education to the many chemists of the future.

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