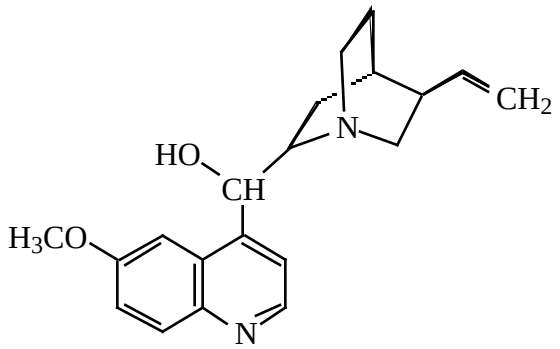
Chem 4563 Organic Qualitative Analysis
Introduction

1. What is the analysis of organic compounds?

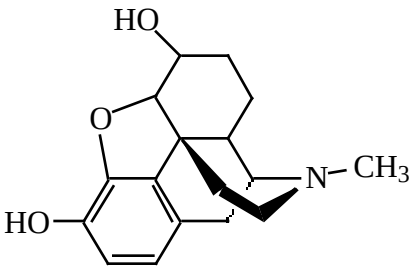
The characterization of organic compounds is the flip side of organic synthesis or natural product isolation Without a method to determine the structure of a compound either synthesized or isolated, no progress is possible in the field of organic chemistry.

There are now over three million known organic compounds, with many more new ones being added every year. The chemical and physical properties of these compounds is determined by their structure. Thus it very important that organic chemists be able to rapidly and accurately determine the structure of compounds.

Nowadays, modern spectroscopic techniques have greatly simplified the task of structure determination. Prior to the introduction of modern instrumental methods, structure elucidation was a tedious and time consuming task, but great achievements were made. The determination of chemical structure involves a logical and systematic scheme. The elaborate but rigorous structural logic to be found in the histories of some structural studies present fascinating examples which we will briefly illustrate. Consider the somewhat complex structures of quinine and morphine:

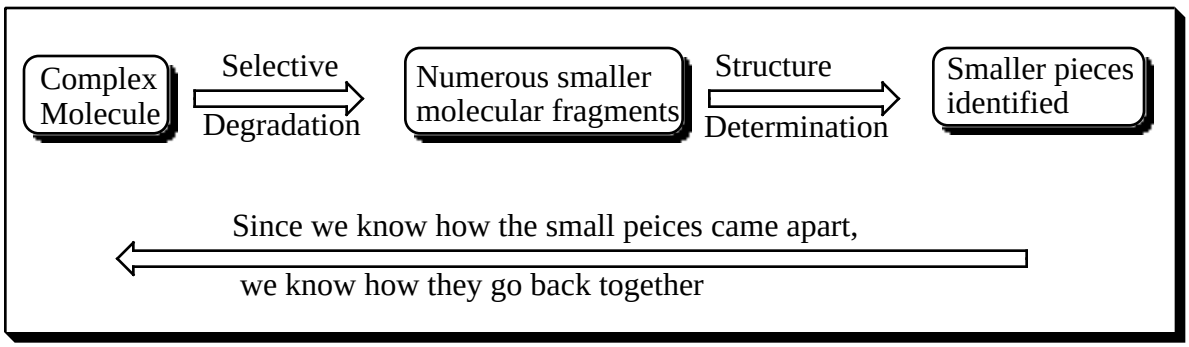


QUININE - first isolated from the bark of the chinchona tree in 1639. Structure determined in 1902

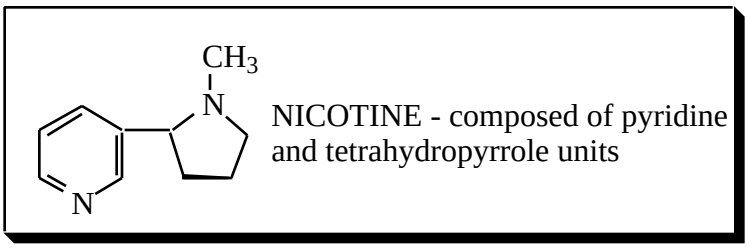


MORPHINE - first isolate from poppy seed in 1885. Structure determined in 1906

The structures of both compounds were determined entirely by chemical degradation methods. This involves breaking down a complex molecule, by a selective breaking of chemical bonds, into simpler pieces. We then determine the structure of the simpler fragments, and because we know what kinds of bonds were originally broken, we can then reconstruct the complex molecule. In a way this last step is like solving a jigsaw puzzle.



An example of this process can be seen the structure determination of nicotine, first carried out in 1896.



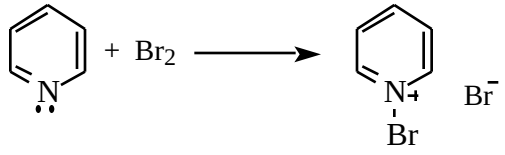
1. Combustion analysis determined the empirical formula to be C_5H_7N. The molecular formula can be any whole number multiple of this: i.e. C_5H_7N, $C_{10}H_{14}N_2$, $C_{15}H_{21}N_3$…

2. Freezing point depression showed the molecular weight to be 162, this gives a molecular formula to be $C_{10}H_{14}N_2$.

3. Index of hydrogen deficiency (unsaturation) of 5 indicates some combination of rings and multiple bonds.

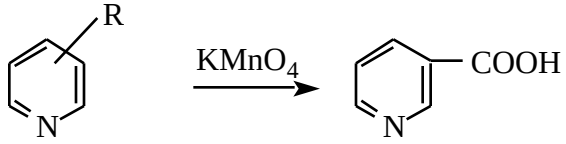
3. Multiple bonds determined by catalytic hydrogenation. Uptake of three equivalents of H_2 indicate three double bonds, character of uptake indicates they were in an aromatic ring.

5. The addition of Br_2 to the molecule formed a perbromide salt ($C_{10}H_{14}N_2Br_2$), this suggested the presence of a pyridine ring in structure



pyridinium
perbromide salt

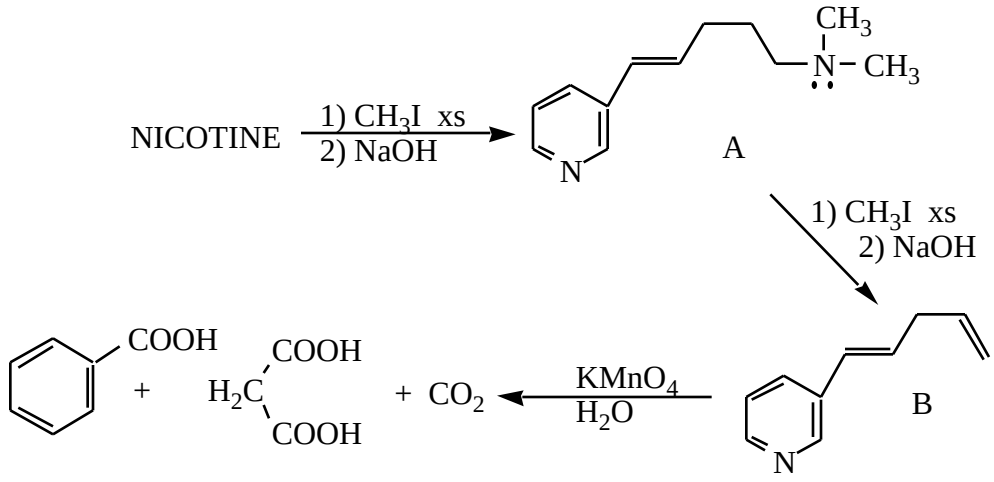
6. Oxidation of nicotine with refluxing, aqueous $KMnO_4$ forms 3-pyridine carboxylic acid. This indicates that the pyridine ring has a substituent at the 3-position.



Nicotine may be a substituted pyridine

3-pyridinecarboxylic acid
known compound, easily identified

7. Treatment of nicotine with excess methyl iodide followed by Hoffmann Elimination with NaOH gave compound A as shown. Compound A was again methylated and subject to Hoffmann Elimination to give B. The acyclic, non-aromatic double bonds were cleaved via oxidation with KMnO4 to give the three relatively simple compounds of 3-pyridine carboxylic acid, malonic acid and carbon dioxide. By determining what these final products were and working backwards (knowing which bonds were broken during the chemical reactions), it was determined that the pyridine substituent was a N-methyl pyrrole ring. This fits with the unaccounted $C_5H_{10}N$ from the molecular formula after removing the atoms of the pyridine ring.



Thus the structure elucidation of nicotine illustrates the standard pattern for structure determination of unknown compounds. The following sequence of steps is usually followed.

i. Determination of appearance and physical characteristics. i.e. color, odor mp, bp, density, refractive index.

ii. Determination of solubility characteristics.

iii. Qualitative determination of elements present.

iv. Quantitative determination of elements present. This allows the determination of an empirical formula.

v. Molecular weight determination. This allows the molecular formula to be obtained.

vi. Calculation of the Index of Hydrogen Deficiency. This gives the number of rings and or multiple bonds present in the compound.

vii. Determination of spectral characteristics: i.e.ir, nmr, ms, visible spectrum

viii. Determination of chemical characteristics by testing for various functional groups

ix. Chemical degradation to compounds of know/ or easily determined structure.

x. Unequivocal proof via derivative formation and comparison via mixed melting point with known compound.

READ: **"The Systematic Identification of Organic Compounds" Chapters 1 and 2 (pp 1-30).**