Nature abounds with nitrogen compounds, many of which occur in plants and are referred to as **alkaloids**. Structural formulas for some representative alkaloids and other nitrogen containing natural products are displayed below, and we can recognize many of the basic structural features listed above in their formulas. Thus, Serotonin and Thiamine are 1º- amines, Coniine is a 2º-amine, Atropine, Morphine and Quinine are 3º-amines, and Muscarine is a 4º-ammonium salt.

![Structural formulas for some representative alkaloids and other nitrogen containing natural products](image)

The reader should be able to recognize indole, imidazole, piperidine, pyridine, pyrimidine & pyrrolidine moieties among these structures. These will be identified by pressing the "Show Structures" button under the diagram.

Nitrogen atoms that are part of **aromatic rings**, such as pyridine, pyrrole & imidazole, have planar configurations (sp² hybridization), and are not stereogenic centers. Nitrogen atoms bonded to carbonyl groups, as in caffeine, also tend to be planar. In contrast, atropine, coniine, morphine, nicotine and quinine have stereogenic pyramidal nitrogen atoms in their structural formulas (think of the non-bonding electron pair as a fourth substituent on a sp³ hybridized nitrogen). In quinine this nitrogen is restricted to one configuration by the bridged ring system. The other stereogenic nitrogens are free to assume two pyramidal configurations, but these are in **rapid equilibrium** so that distinct stereoisomers reflecting these sites cannot be easily isolated.

It should be noted that structural factors may serve to permit the resolution of pyramidal chiral amines. Two examples of such 3º-amines, compared with similar non-resolvable analogs, are shown in the following diagram. The two nitrogen atoms in Trögers base are the only stereogenic centers in the molecule. Because of the molecule's bridged structure, the nitrogens have the same configuration and cannot undergo inversion. The chloro aziridine can invert, but requires a higher activation energy to do so, compared with larger heterocyclic amines. It has in fact been resolved, and pure enantiomers isolated. An increase in angle strain in the sp²-hybridized planar transition state is responsible for the greater stability of the pyramidal configuration. The rough estimate of angle strain is made using a C-N-C angle of 60º as an arbitrary value for the three-membered heterocycle.

![Structural formulas for Trögers base and chloro aziridine](image)

Of course, quaternary ammonium salts, such as that in muscarine, have a tetrahedral configuration that is incapable of inversion. With four different substituents, such a nitrogen would be a stable stereogenic center.
A Structure Formula Relationship

Recall that the molecular formula of a hydrocarbon \((C_nH_m)\) provides information about the number of rings and/or double bonds that must be present in its structural formula. In the formula shown below a triple bond is counted as two double bonds.

\[
\text{Rings} + \text{Double Bonds in a } C_nH_m \text{ Hydrocarbon} = \frac{(2n + 2 - m)}{2}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Formula</th>
<th>Revised Formula</th>
<th>Calculated Rings + C=Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coniine</td>
<td>(C_8H_{17}N)</td>
<td>(C_9H_{18})</td>
<td>1</td>
</tr>
<tr>
<td>Nicotine</td>
<td>(C_{10}H_{14}N_2)</td>
<td>(C_{12}H_{16})</td>
<td>5</td>
</tr>
<tr>
<td>Morphine</td>
<td>(C_{17}H_{19}NO_3)</td>
<td>(C_{18}H_{20})</td>
<td>9</td>
</tr>
</tbody>
</table>

This molecular formula analysis may be extended beyond hydrocarbons by a few simple corrections. These are illustrated by the examples in the table above, taken from the previous list of naturally occurring amines.

- The presence of oxygen does not alter the relationship.
- All halogens present in the molecular formula must be replaced by hydrogen.
- Each nitrogen in the formula must be replaced by a CH moiety.

Contributors