

MIT OpenCourseWare
<http://ocw.mit.edu>

5.111 Principles of Chemical Science
Fall 2008

For information about citing these materials or our Terms of Use, visit: <http://ocw.mit.edu/terms>.

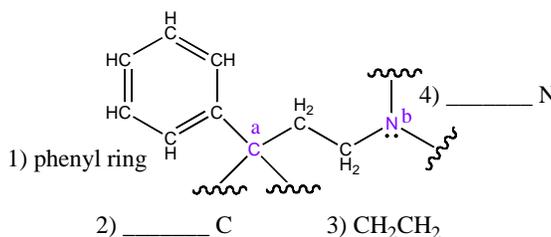
Hybridization (review of material from lectures 15 and 16)

See lecture 15 and lecture 16 (pages 1-2) for hybridization.

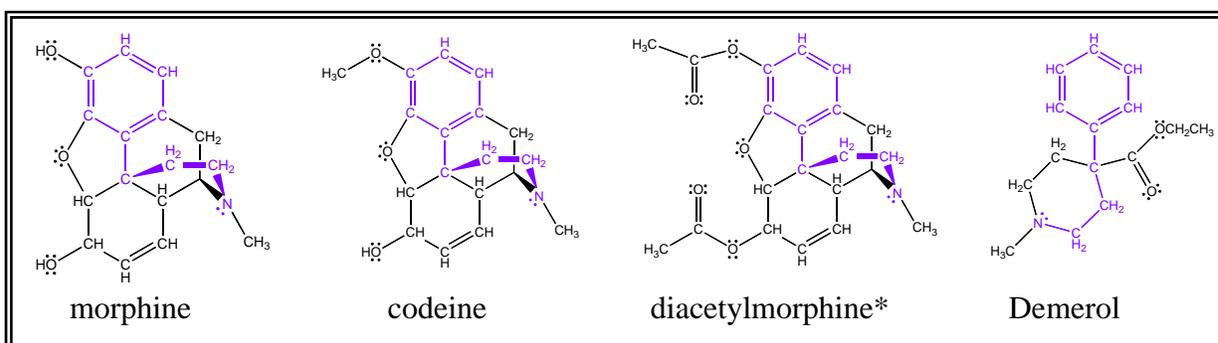
Example from page 1 of Lecture 17 notes: Identifying molecules that follow the “morphine rule”

Morphine, a potent and addictive analgesic (“painkiller”), and related molecules share a characteristic set of four features called the morphine rule:

- 1) a phenyl ring
- 2) an sp^3 hybridized carbon atom
- 3) a CH_2-CH_2 sequence
- 4) an sp^3 hybridized nitrogen atom



These structural elements are responsible for the bioactivity of morphine and other molecules that are pharmacologically similar to morphine. Examples are shown below with the “morphine rule” features highlighted in purple.



These molecules fit into a pain receptor in the brain, mimicking the action of endorphins, which are natural pain relievers produced by the body. Endorphins do not have all of the elements of the morphine rule, but do have significant structural similarities.

- Pure morphine was first isolated in 1803. The chemical structure was determined in 1925. Two hundred years later, morphine and related compounds remain the most potent painkillers known. Unfortunately, morphine is also highly addictive.
- Codeine is less addictive, but also less effective. It is approximately a tenth as strong as morphine.
- Diacetylmorphine was synthesized in 1898 by Bayer (the company best known for Bayer’s aspirin). Diacetylmorphine is much more potent than morphine, and this potency initially masked some major side effects. Bayer marketed this as a “hero” drug. We now know it as the “hero” derived name heroin, and few people associate it with the company Bayer.
- Until the 1980’s, Demerol was thought to be a safer alternative to morphine. While Demerol is less addictive than morphine, it can have dangerous side effects, including seizures, and has become much less widely used.

This example is based on Chapter 13 of **Napoleon's Buttons: How 17 Molecules Changed History** by Penny LeCouteur and Jay Burreson. The morphine rule can be used as a VSEPR or as a hybridization example.