Why Are Drugs So Expensive?

The average cost of launching a new drug is $1.2 billion. The manufacturer has to recover this cost quickly because the patent must be filed as soon as the drug is first discovered. Although a patent is good for 20 years, it takes an average of 12 years to bring a drug to market after its initial discovery, so the patent protects the discoverer of the drug for an average of eight years. It is only during the eight years of patent protection that drug sales can provide the income needed to cover the initial costs as well as to pay for research on new drugs.

Why does it cost so much to develop a new drug? The Food and Drug Administration (FDA) has high standards that must be met before a drug is approved for a particular use. An important factor leading to the high price of many drugs is the low rate of success in progressing from the initial concept to an approved product. In fact, only 1 or 2 of every 100 compounds tested become lead compounds. A lead compound is a compound that shows promise of becoming a drug. Chemists modify the structure of a lead compound to see if doing so improves its likelihood of becoming a drug. For every 100 structural modifications of a lead compound, only one is worthy of further study. For every 10,000 compounds that are worth further study (that is, to be evaluated in animal studies), only 10 will get to clinical trials.

Clinical trials consist of four phases:

- Phase I is the first use of the drug in humans, usually involving a small number of healthy volunteers. The primary goal of a phase I study is to explore the drug's safety at different dosages.
- Phase II studies are larger in size, and their volunteers have the condition the drug is meant to treat. Phase II studies investigate effectiveness, safety, and side effects.
- Large phase III studies, involving hundreds to thousands of patients, verify effectiveness and dosage while continuing to monitor adverse reactions.
- If the drug is approved for use, phase IV studies might be conducted. This phase looks for side effects that weren't detected in phases I, II, or III.

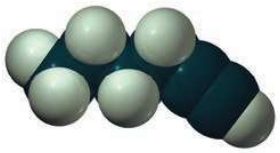
Approximately 1 of every 10 compounds entering clinical trials satisfies the stringent requirements needed to become a marketable drug.

7.1 THE NOMENCLATURE OF ALKYNES

Because of its triple bond, an alkyne has four fewer hydrogens than an alkane with the same number of carbons. Therefore, while the general molecular formula for an acyclic alkane is C_nH_{2n+2},

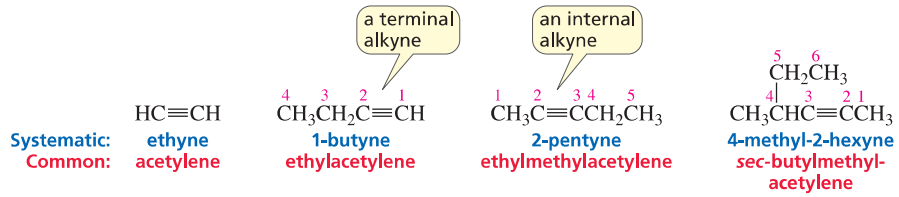
- the general molecular formula for an acyclic alkyne is C_nH_{2n-2}.
- the general molecular formula for a cyclic alkyne is C_nH_{2n-4}.

The systematic name of an alkyne is obtained by replacing the "ane" ending of the alkane name with "yne." Analogous to the way compounds with other functional groups are named, the longest continuous chain containing the carbon–carbon triple bond is numbered in the direction that gives the functional group suffix as low a number as possible (Sections 3.6, 3.7, and 5.2). If the triple bond is at the end of the chain, the alkyne is classified as a **terminal alkyne.** Alkynes with triple bonds located elsewhere along the chain are **internal alkynes.**



1-hexyne
terminal alkyne

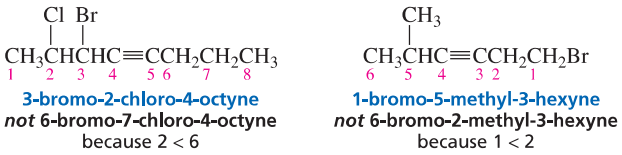
3-hexyne
internal alkyne



In common nomenclature, alkynes are named as *substituted acetylenes.* The common name is obtained by stating the names of the alkyl groups (in alphabetical order) that have replaced the hydrogens of acetylene. Acetylene is an unfortunate common name for an alkyne because its "ene" ending is characteristic of a double bond rather than a triple bond.

LEARN THE STRATEGY

If counting from either direction leads to the same number for the functional group suffix, the correct systematic name is the one that contains the lowest substituent number. If the compound contains more than one substituent, the substituents are listed in alphabetical order.



PROBLEM 1 ♦

Name the following:

a. $BrCH_2CH_2C{\equiv}CCH_3$

b. $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}H{-}C{\equiv}C{-}CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$

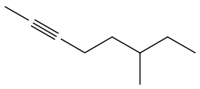
c. $CH_3OCH_2C{\equiv}CCH_2CH_3$

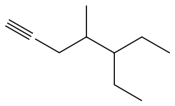
d. $CH_3CH_2\underset{\displaystyle CH_2CH_2CH_3}{\underset{|}{C}}H{-}C{\equiv}CH$

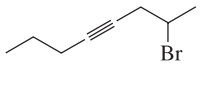
USE THE STRATEGY

PROBLEM 2 ♦

Name the following:

a. 

b. 

c. 

A substituent receives the lowest possible number only if there is no functional group suffix or if counting from either direction leads to the same number for the functional group suffix.

PROBLEM 3 ♦

What is the molecular formula for a monocyclic hydrocarbon with 14 carbons and 2 triple bonds?

PROBLEM 4 ♦

Draw the condensed and skeletal structures for each of the following:

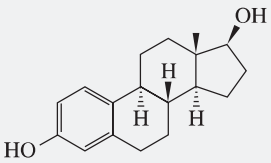
a. 1-chloro-3-hexyne
b. cyclooctyne
c. isopropylacetylene
d. *sec*-butylisobutylacetylene
e. 4,4-dimethyl-1-pentyne
f. dimethylacetylene

PROBLEM 5

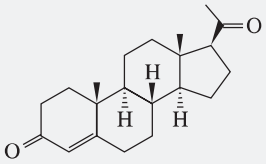
Draw the structures and give the common and systematic names for the seven alkynes with molecular formula C_6H_{10}.

Synthetic Alkynes Are Used for Birth Control

Estradiol and progesterone are naturally occurring female hormones. Because of their ring structures, they are classified as steroids (Section 3.16). Estradiol is responsible for the development of secondary sex characteristics in women—it affects body shape, fat deposition, bones, and joints. Progesterone is critical for the continuation of pregnancy.

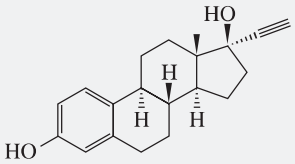


estradiol

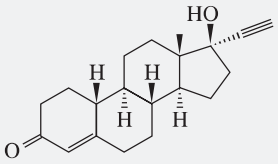


progesterone

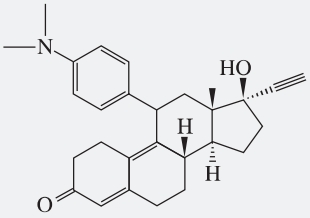
The four compounds shown next are synthetic steroids that are used for birth control; each contains an alkyne functional group. Most birth control pills contain ethinyl estradiol (a compound structurally similar to estradiol) and a compound structurally similar to progesterone (such as norethindrone). Ethinyl estradiol prevents ovulation, whereas norethindrone makes it difficult for a fertilized egg to attach to the wall of the uterus.



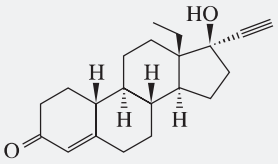
ethinyl estradiol



norethindrone
Aygestin®



mifepristone
RU-486
Mifegyne®

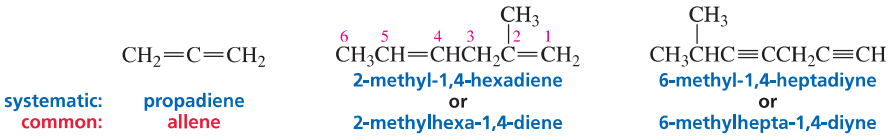


levonorgestrel
Norplant®

Mifepristone and levonorgestrel are also synthetic steroids that contain an alkyne functional group. Mifepristone, also known as RU-486, induces an abortion if taken early in pregnancy. Its name comes from Roussel-Uclaf, the French pharmaceutical company where it was first synthesized, and from an arbitrary lab serial number. Levonorgestrel is an emergency contraceptive pill. It prevents pregnancy if taken within a few days of conception.

7.2 HOW TO NAME A COMPOUND THAT HAS MORE THAN ONE FUNCTIONAL GROUP

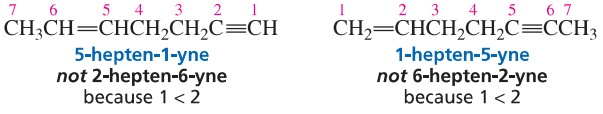
We saw how compounds with two double bonds are named (Section 5.2). Similar rules are followed for naming compounds with two triple bonds, using the ending "diyne."

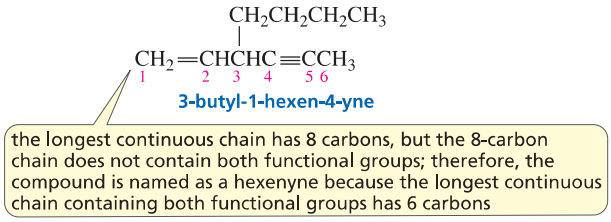


LEARN THE STRATEGY

1. To name an alkene in which the second functional group is not another double bond but has a functional group suffix, find the longest continuous chain containing both functional groups and put both suffixes at the end of the name. Put the "ene" ending first, with the terminal "e" omitted to avoid two adjacent vowels.
2. The number indicating the location of the first-stated functional group is usually placed before the name of the parent chain. The number indicating the location of the second-stated functional group is placed immediately before the suffix for that functional group.
3. If the two functional groups are a *double bond* and a *triple bond,* number the chain in the direction that produces a name containing the lower number. Thus, in the following examples, the lower number is given to the alkyne suffix in the compound on the left and to the alkene suffix in the compound on the right.

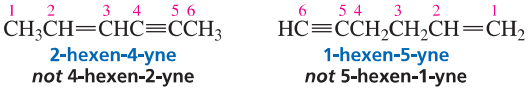
When the functional groups are a double bond and a triple bond, the chain containing both groups is numbered in the direction that produces the name containing the lowest possible number, regardless of which functional group gets the lower number.





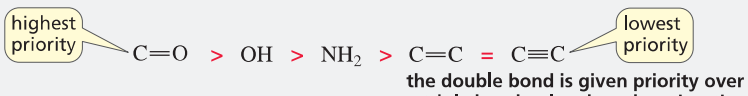
4. If the same low number is obtained in both directions, number the chain in the direction that gives the double bond the lower number.

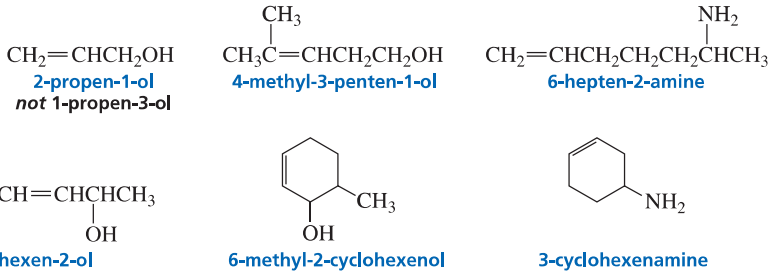
If there is a tie between a double bond and a triple bond, the double bond gets the lower number.



5. If the second functional group suffix has a higher priority than the alkene suffix, number the chain in the direction that assigns the lower number to the functional group with the higher-priority suffix. (The relative priorities of functional group suffixes are shown in Table 7.1.) The higher-priority functional group is assumed to be at the 1-position in cyclic compounds.

Table 7.1 Priorities of Functional Group Suffixes





Number the chain so that the lowest possible number is given to the functional group with the higher priority.

PROBLEM 6 ♦

USE THE STRATEGY

Name the following:

a. $CH_2{=}CHCH_2C{\equiv}CCH_2CH_3$

b. $CH_3CH{=}\overset{\displaystyle CH_3}{\overset{|}{C}}CH_2CH{=}CH_2$

c. $CH_3CH_2CH{=}\overset{\displaystyle CH{=}CH_2}{\overset{|}{C}}CH_2CH_2C{\equiv}CH$

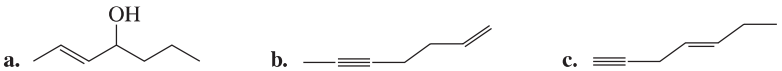
d. $HOCH_2CH_2C{\equiv}CH$

e. $CH_3CH{=}CHCH{=}CHCH{=}CH_2$

f. $CH_3CH{=}\overset{\displaystyle CH_3}{\overset{|}{C}}CH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2OH$

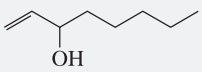
PROBLEM 7 ♦

Name the following:



How a Banana Slug Knows What to Eat

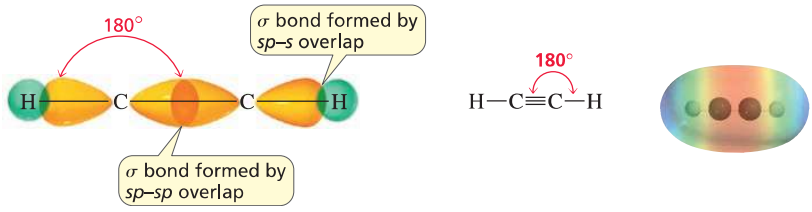
Many species of mushrooms synthesize 1-octen-3-ol, a repellent that drives off predatory slugs. Such mushrooms can be recognized by small bite marks on their caps, where the slug started to nibble before the volatile compound was released. People are not put off by the release of this compound because to them it just smells like a mushroom. 1-Octen-3-ol also has antibacterial properties that may protect the mushroom from organisms that would otherwise invade the wound made by the slug. Not surprisingly, the species of mushroom that banana slugs commonly eat cannot synthesize 1-octen-3-ol.



1-octen-3-ol

7.3 THE STRUCTURE OF ALKYNES

The structure of ethyne was discussed in Section 1.9, where we saw that each carbon is *sp* hybridized. As a result, each carbon has two *sp* orbitals and two *p* orbitals. One *sp* orbital overlaps the *s* orbital of a hydrogen, and the other overlaps an *sp* orbital of the other carbon, to form σ bonds. (The small lobes of the *sp* orbitals are not shown.) Because the *sp* orbitals are oriented as far from each other as possible to minimize electron repulsion, ethyne is a linear molecule with bond angles of 180°.



Recall that the two π bonds of a triple bond are formed by each of the two *p* orbitals on one *sp* carbon overlapping the parallel *p* orbital on the other *sp* carbon (see Figure 7.1 on the next page). The end result can be thought of as a cylinder of electrons wrapped around the σ bond.