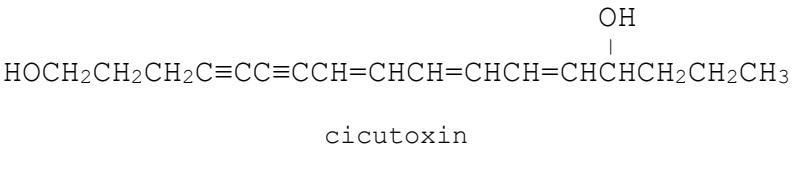
Chapter 9
Alkynes

So far we have explored the chemistry of two functional groups. In Chapters 6 and 7 alkyl halides functioned as electrophiles because of their good leaving groups, halide ions. In contrast, nonpolar π bonds conferred nucleophilicity to alkenes in Chapter 8. In this chapter our third functional group, the carbon-carbon triple bond of alkynes, will often react similarly to alkenes. In addition, alkynes will provide our first versatile way to extend the carbon skeleton of organic molecules.

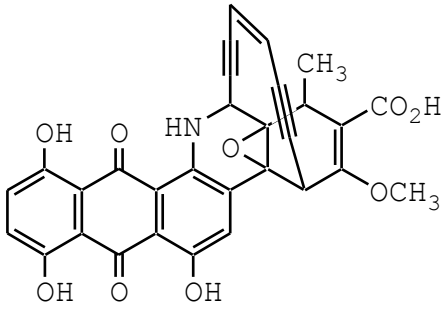
9.1 Notable Alkynes

Alkynes are not nearly as plentiful in daily life as alkenes. Nonetheless, some interesting molecules contain the carbon-carbon triple bond. Ethyne (also known as acetylene) is the smallest and commercially the most important alkyne. It furnishes the fuel for the oxyacetylene torch with the hottest flame (3000°C) of any fueled by a hydrocarbon. In the natural world metabolites containing the carbon-carbon triple bond protect their organisms from harm. For example, actinomycete bacteria create the antibiotic mycomycin, which contains two alkyne functional groups, as well as alkene double bonds and a carboxylic acid. Safflowers synthesize a triple alkyne that defends their roots from nematodes. Cicutoxin can cause convulsions in cattle that eat water hemlock. An arrangement of alkene and two alkyne functional groups, recently found in several natural products such as dynemicin A, correlates with potent activity against cancer cells.

ethyne (acetylene) | mycomycin | safflower triyne



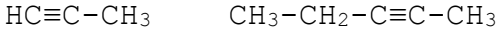
cicutoxin



dynemicin A

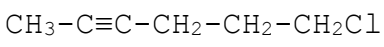
9.2 Nomenclature of Alkynes

The systematic IUPAC rules for naming alkynes follow the three basic rules for alkanes (Section 2.2A) but replace the *-ane* suffix with *-yne*. As with alkenes (Section 8.2), the longest chain containing the triple bond is numbered to give the lower possible number to the first of the multiply (doubly or triply) bonded carbons. For example:

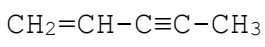


propyne

2-pentyne

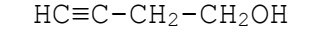


6-chloro-2-hexyne
(not 1-chloro-4-hexyne)



1-penten-3-yne
(not 4-penten-2-yne)

An exception to the above numbering rule can occur if a group of higher priority, such as an alcohol or carbonyl compound, is present. Such a group demands the lower possible number:



3-butyn-1-ol
(not 1-butyn-4-ol)

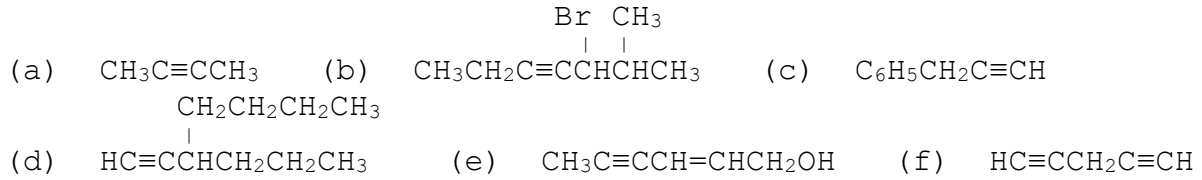
Diynes and triynes have two and three carbon-carbon triple bonds, respectively:

1,3-butadiyne

1,3,5-heptatriyne

Puzzle 9.1

Name these compounds:

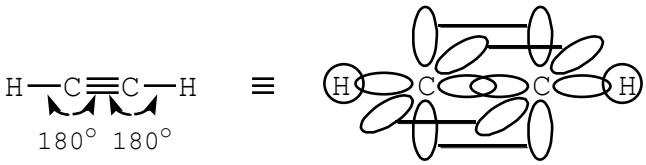


Puzzle 9.2

Draw structures for the compounds with these names:
(a) 3-chloropropyne (b) 1-cyclobutyl-2-butyne (c) 2,6-octadien-4-yne
(d) 4,4-diiodo-1-pentyn-3-ol

9.3 Structural Features of Alkynes

An alkyne features a carbon-carbon triple bond, whose structure we have already investigated:

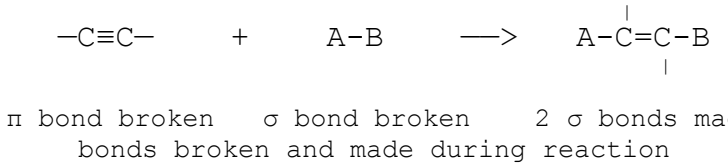


ethyne

The triple bond comprises one σ and two π bonds (Section 1.2C). With two σ bonds, each triply bonded carbon has two repelling electron pairs and *sp* hybridization. Consequently, the bond angle at each carbon is 180°, and the four atoms closest to the triple bond lie in a straight line (Section 1.6C).

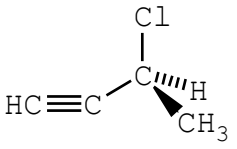
Because the six overlapping orbitals of the triple bond bind their nuclei more closely, the length of the triple bond is only 120 pm, versus 134 pm and 153 pm for the lengths of carbon-carbon double and single bonds, respectively (Table 1.5, Section 1.7A). Not only is the triple bond the shortest carbon-carbon bond, but it also is the strongest: 962 kJ/mol versus 682 and 368 kJ/mol for double and single bonds, respectively (Table 1.6, Section 1.8).

This great strength of the triple bond as a whole should not deceive us into thinking that the triple bond is unreactive. The bond energy represents the combined strength of the three bonds, not the strength of individual bonds. How much energy would be needed to break just one π bond in the triple bond while preserving a double bond? According to the bond energies of the triple and double bonds, approximately 962 - 682 = 280 kJ/mol would be needed. This individual π bond energy is not very large and, indeed, is much smaller than the 368 kJ/mol strength of a carbon-carbon single bond. Thus, despite its overall strength the carbon-carbon triple bond can react readily:

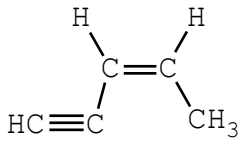


The total number of bonds remains constant during reaction. Yet, π bonds are generally weaker than σ bonds because the sideways overlap of parallel *p* orbitals in a π bond is smaller than the head-on overlap of orbitals in a σ bond (Section 8.3B). Therefore, forming the two new σ bonds in the addition product generally supplies more than enough energy to break one π bond of the alkyne and a σ bond of reactant AB. Consequently, like alkenes, alkynes have exothermic and thermodynamically favorable addition reactions.

What opportunities for stereoisomers does the alkyne triple bond provide? Because of the linear arrangement of the groups attached to the carbons of the triple bond, *E* and *Z* diastereomers are not possible for alkyne triple bonds, unlike alkene double bonds. Furthermore, without a tetrahedral atom the carbon-carbon triple bond cannot furnish a chiral atom. As a result, the alkyne group itself provides no stereoisomers. Of course, if a substituent on the triple bond contains a chiral atom, a double bond, or a ring, then stereoisomers could arise. For example:



(*S*)-3-chloro-1-butyne



(*Z*)-3-penten-1-yne

Puzzle 9.3 ———————————————————————————————

(a) Find an alkyne that is a stereoisomer because of a ring.
(b) Draw and name one of its stereoisomers.

Puzzle 9.4 ———————————————————————————————

Radio astronomy has detected cyanodecapentayne (below) near the star CW Leonis.

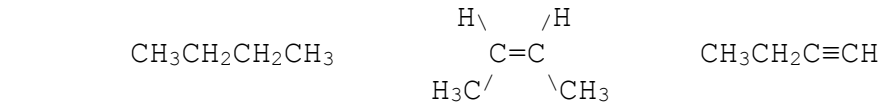
HC≡C-C≡C-C≡C-C≡C-C≡C-C≡N

(a) What is the hybridization of each carbon in this molecule?
(b) What is the overall shape of this molecule?

9.4 Physical Properties of Alkynes

If an alkyne has no polar substituents on its triple bond, all of its bonds are practically nonpolar. Thus, like simple alkanes and alkenes, simple alkynes are nonpolar molecules.

Because the only intermolecular forces among nonpolar compounds are dispersion forces, the boiling points of alkynes resemble those of alkanes and alkenes of similar size and dispersion forces. For example:



	butane	(*Z*)-2-butene	1-butyne
bp:	0°C	4°C	8°C

Note that the strong *intramolecular* triple bond does not affect the boiling point of 1-butyne very much, because covalent bonds are not broken during boiling.

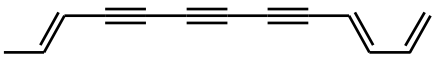
Like other nonpolar compounds simple alkynes dissolve well in nonpolar solvents and poorly in very polar water.

Puzzle 9.5 ———————————————————————————————————

Rank 1-butyne, 1-pentyne, and 1-butanol by boiling point. Explain your ranking.

Puzzle 9.6 ———————————————————————————————————

The following triyne is found in sunflowers and protects their roots from nematodes.



What kind of solvent could efficiently extract it from ground sunflower roots? Name an example of this kind of solvent.

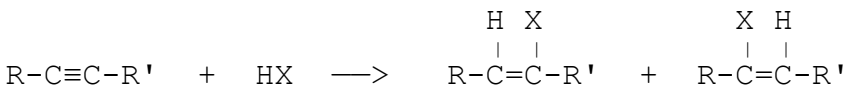
———————————————————————————————————————

9.5 Reactions of Alkynes

For the most part, alkynes react similarly to alkenes. This is not surprising because alkynes also have a nucleophilic region rich in electron density: the triple bond with six electrons. Four of these electrons occupy π bonds, well removed from nuclei and readily accessible to another reactant. In addition, breaking a relatively weak π bond to form an additional σ bond is thermodynamically favorable (Section 9.3). Finally, without a formal or even partial charge, a simple alkyne is soft. With its soft nucleophilicity the alkyne triple bond resembles the alkene double bond. Consequently, it adds electrophiles, especially strong or soft ones, in reactions analogous to those of alkenes.

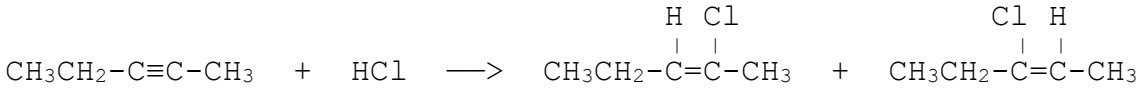
9.5A Addition Reactions with Hydrogen Halides

Hydrogen halides (HX) are strong acids that add to alkene double bonds to make alkyl halides (Section 8.8A). Therefore, it is not surprising that they also add to alkyne triple bonds.

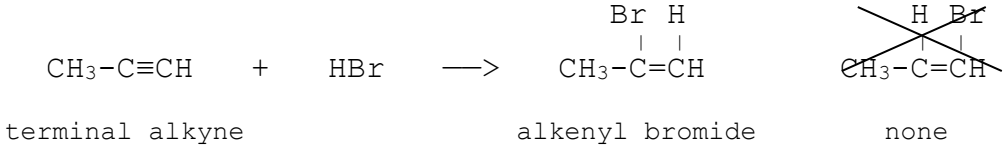


An alkyne substituted with two different alkyl groups gives a mixture of both possible

constitutional isomers of the alkenyl (i.e., vinylic) halide, where the halogen is directly bonded to a doubly bonded carbon. For example:

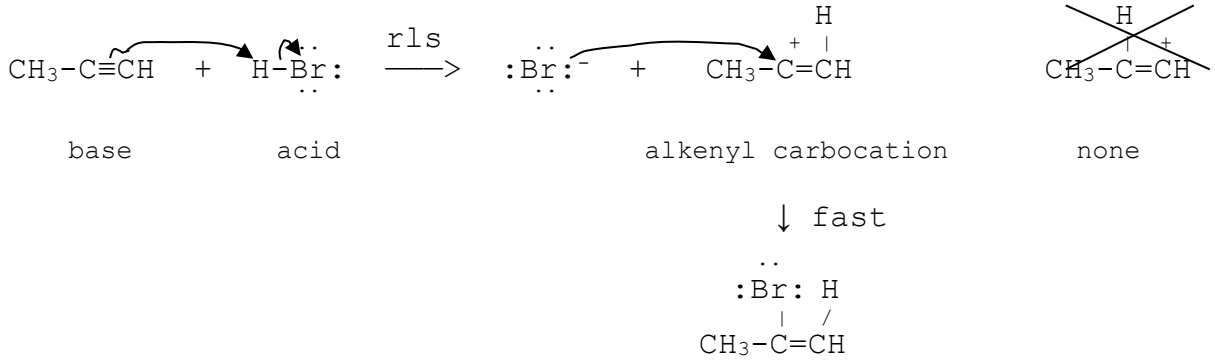


A **terminal alkyne** with the triple bond at the end of a carbon chain is regioselective (Section 8.8A) by yielding only one of the two possible constitutional isomers. For example:



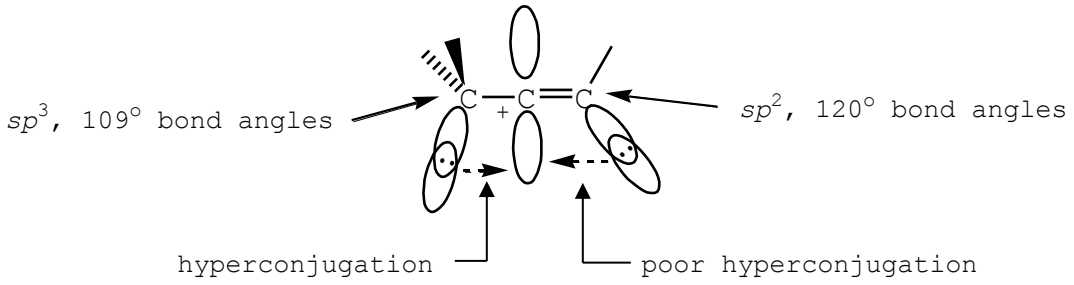
Thus, by adding hydrogen to the triply bonded carbon with more hydrogens, hydrogen halides add to alkynes according to Markovnikov's rule (Section 8.8A).

The mechanism, of course, explains this regioselectivity:



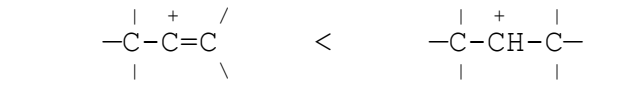
This mechanism is exactly analogous to alkene addition of a hydrogen halide. Only the more stable alkenyl (i.e., vinylic) carbocation with more alkyl substituents forms in the rate-limiting step (rls). In the first carbocation above, a methyl group stabilizes the cation carbon by hyperconjugation (Section 6.5B). Without such an alkyl group the second carbocation is less stable.

Furthermore, hyperconjugation explains the instability of alkenyl carbocations relative to simple carbocations:



A carbon that is hybridized sp^2 offers poor hyperconjugation to an adjacent carbocation. Perhaps the 120° bond angles on the sp^2 carbon are too wide to allow much interaction between the single

bonds of this carbon and the empty *p* orbital of the carbocation. Accordingly, alkenyl carbocations are not as stable as simple carbocations with the same number of carbon substituents:



alkenyl carbocation < 2° carbocation

stabilities of carbocations

Thus, despite the greater electron density, nucleophilicity, and energy at its triple bond, an alkyne does not add a hydrogen halide any faster than the corresponding alkene. The energy-reaction diagrams of Figure 9.1 illustrate the compensation:

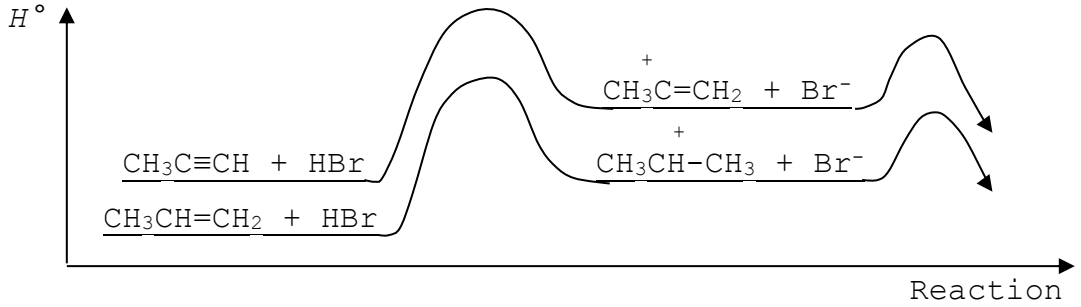
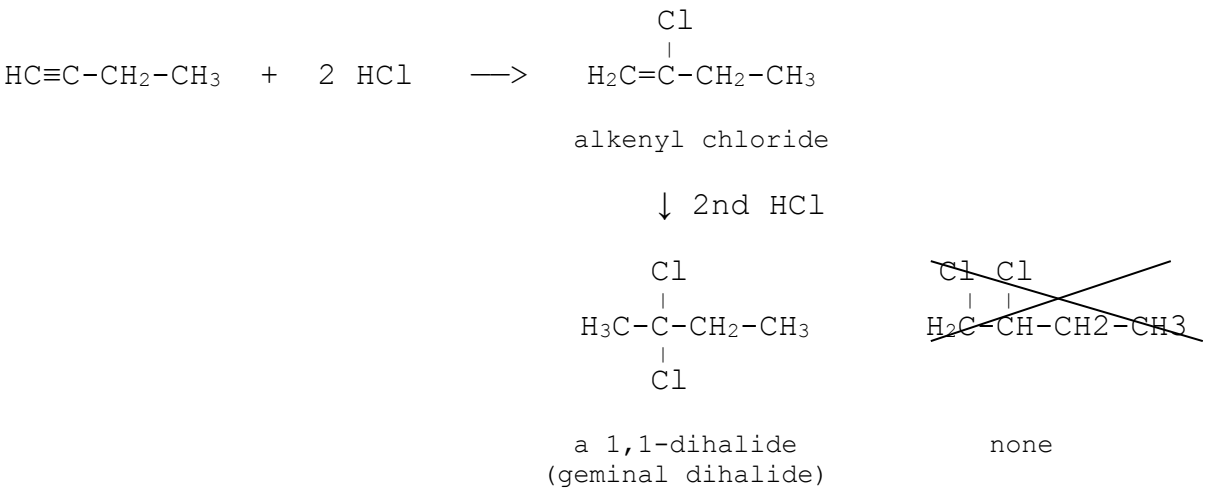


Figure 9.1 Energy-reaction diagrams for analogous alkyne and alkene reactions.

The higher energy of the alkenyl carbocation intermediate and presumably the transition state leading to it compensates for the higher energy of the alkyne. Consequently, the two reactions have roughly the same activation energies for their rate-limiting steps and so roughly the same rates.

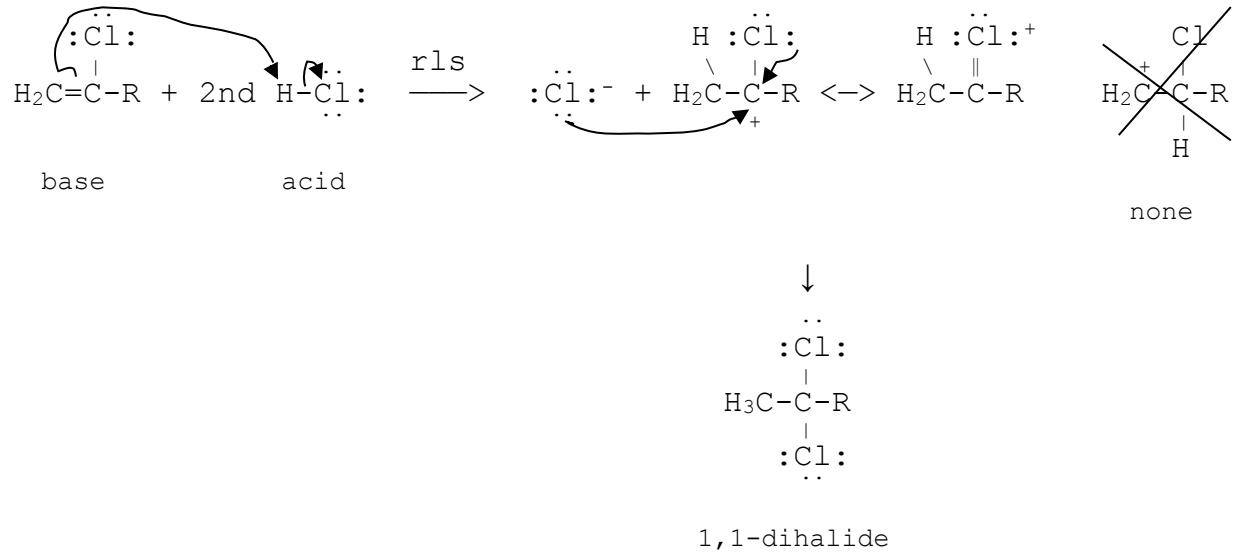
The alkenyl halide product of the addition reaction contains a carbon-carbon double bond, which, like simple alkenes, is vulnerable to further addition by excess hydrogen halide. For example:



The final product is a dihalide. Yet, this dihalide differs from the dihalide produced by halogenation of an alkene, which yields a 1,2-dihalide (i.e., vicinal dihalide) with the two halogens

attached to adjacent carbons (Section 8.10A). Here the product is a 1,1-dihalide (i.e., **geminal dihalide**) with halogens on the same carbon. Note that the numbering is relative and not IUPAC.

Why is the 1,2-dihalide constitutional isomer not produced? Let us inspect the mechanism for the answer:



The second chlorine becomes geminal because resonance with the first chlorine stabilizes the preferred carbocation intermediate. The alternative carbocation cannot be stabilized by resonance (verify this) and so is not produced in the rate-limiting step.

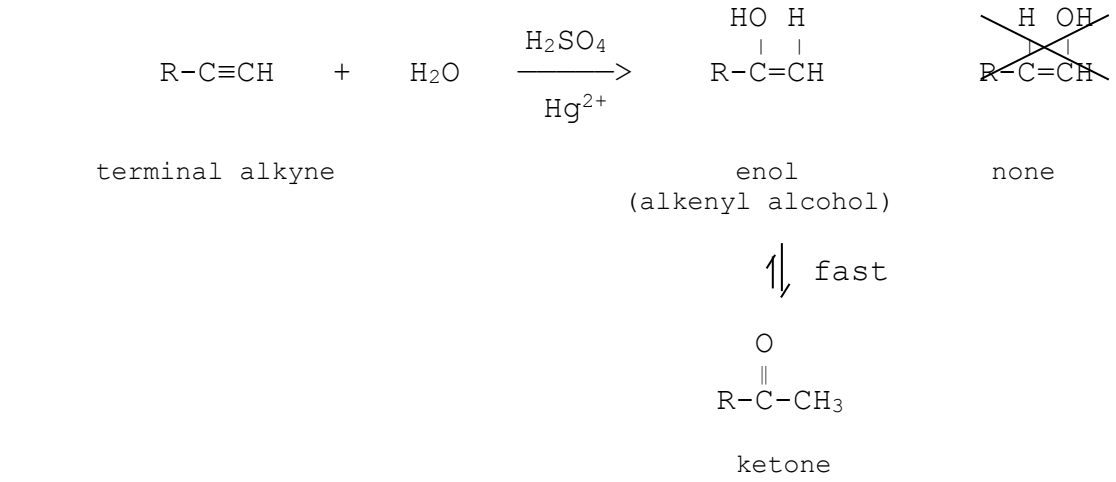
We have seen that the addition of hydrogen halides to alkynes can yield either alkenyl halides or, with an excess of hydrogen halide, a 1,1-dihalide.

Puzzle 9.7

(a) Draw the mechanisms for the reactions of two equivalents of hydrogen iodide with 2-pentyne.
(b) What is the hybridization of the cationic carbon in the first carbocation intermediate?

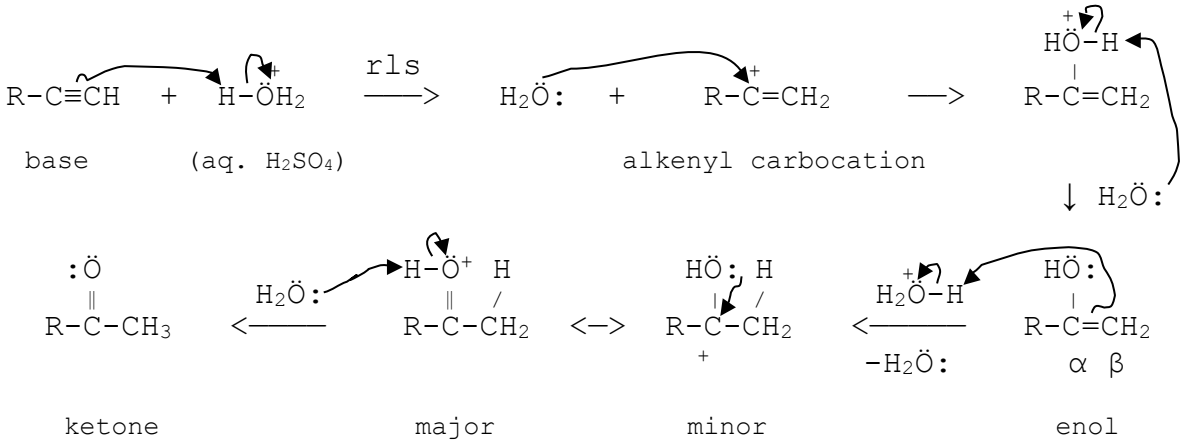
9.5B Addition Reaction with Aqueous Acid

In Section 8.8B we found that aqueous sulfuric acid hydrates alkenes to alcohols. Because water is too weakly acidic to protonate a weakly basic alkene, a strong acid is needed to catalyze the hydration. Likewise, an alkyne is a weak base that needs a strong acid to catalyze hydration. Actually, in addition to the acid a mercuric salt, such as mercuric sulfate ($HgSO_4$), is normally needed to catalyze this addition of water:

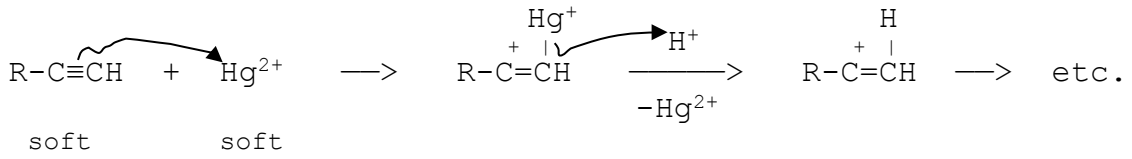


Note the regioselective addition that gives one enol isomer according to Markovnikov's rule: the hydrogen adds to the carbon with more hydrogens (Section 8.8A). In Section 5.5A an enol (i.e., alkenyl alcohol) was encountered in equilibrium with its ketone constitutional isomer by way of an enolate anion under basic conditions. This equilibrium favored the more stable ketone over the more energetic enol. Here, the acidic conditions of aqueous sulfuric acid promotes the same fast equilibrium or tautomerization (Section 5.5A), which favors the normally more stable ketone.

Let us examine the mechanisms to understand how both the hydration reaction and the subsequent tautomerization occur:



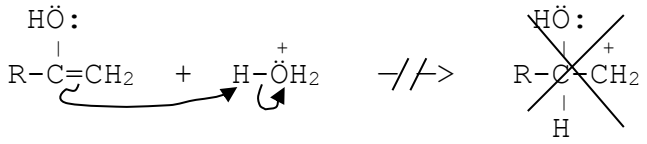
Consistent with Markovnikov's rule, the alkenyl carbocation with more alkyl substituents forms. Because this alkenyl carbocation intermediate is less stable than the corresponding alkyl carbocation from alkene hydration (Section 9.5A), this reaction needs mercuric ion as an additional catalyst. The mercuric ion may react with the alkyne:



The large size and resulting softness of the mercuric ion electrophile well suit the alkyne nucleophile, whose lack of charge makes it soft like alkenes (Section 9.5). Thus, the mercuric ion

catalyzes the addition reaction better than the acid, which is a hard electrophile (Section 4.8). A proton subsequently displaces the mercury ion.

After water adds to the carbocation, the resulting enol quickly gains and loses protons during tautomerization. Only the doubly bonded carbon β to the hydroxy group adds a proton so that resonance can stabilize the cation intermediate. Protonation of the other doubly bonded carbon would yield a primary carbocation incapable of resonance.



1° carbocation
no resonance

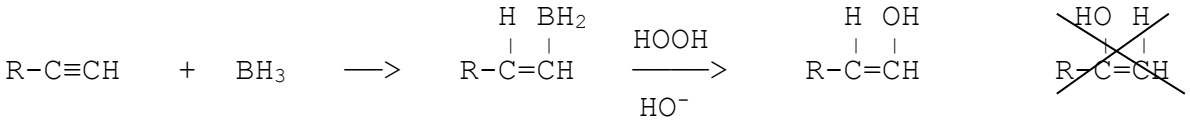
Finally, the cation's oxygen loses a proton to obtain the ketone. Reflecting the hydration and isomerization, the ketone product has two hydrogens and one oxygen (the elements of water) more than the original alkyne.

Puzzle 9.8 ———————————————————————————————————————

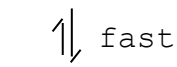
(a) How many alkyne constitutional isomers can be hydrated in aqueous acid to yield the ketone, 2-butanone?
(b) Draw the mechanism for one such hydration.

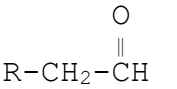
9.5C Addition Reaction with Borane

Just as hydroboration can lead to the hydration of an alkene in an anti-Markovnikov direction, so it allows anti-Markovnikov hydration of a terminal alkyne.



terminal alkyne — enol (alkenyl alcohol) — none





aldehyde

Hydration with borane and then basic hydrogen peroxide yields only one enol isomer. This isomer contradicts Markovnikov's rule because the hydrogen adds to the triply bonded carbon with no

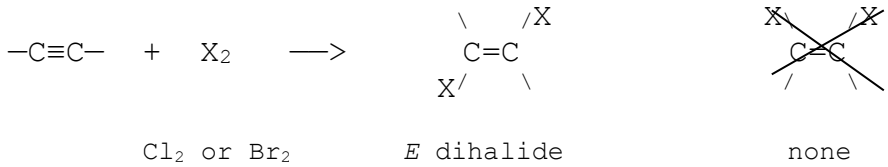
hydrogens. As in Sections 5.5A and 9.5B, the enol tautomerizes to the more stable carbonyl isomer, here an aldehyde. Thus, hydration with borane and hydrogen peroxide provides a carbonyl product different from the ketone produced by aqueous acid hydration.

Puzzle 9.9

(a) What is the final organic product from the treatment of 1-butyne with borane and then with basic hydrogen peroxide?
(b) What is the final organic product from the treatment of 1-butyne with aqueous acid and mercuric sulfate?

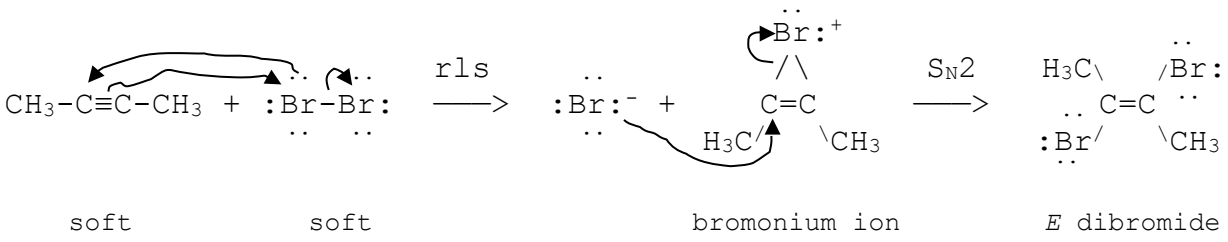
9.5D Addition Reactions with Halogens

The halogens chlorine and bromine add to alkenes to give 1,2-dihalides (i.e., vicinal dihalides) (Section 8.10A). This reaction goes readily because both the halogen electrophile and the alkene nucleophile are soft. Similarly, chlorine and bromine add to alkynes to form alkenyl dihalides:



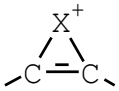
Just as for alkene halogenation, the addition is anti so that only the trans, *E* dihalide stereoisomer is produced, not the cis, *Z* diastereomer.

The mechanism explains the stereoselectivity. For example:

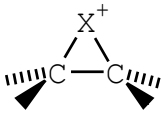


In the first step the softness of the alkyne nucleophile matches the softness of the bromine electrophile. The second step of the mechanism is S_N2 with inversion of configuration at the substituted carbon and the resulting *E* product.

This halogenation of an alkyne proceeds more slowly than the halogenation of a corresponding alkene. One can explain the rate difference by comparing the intermediate products of the two rate-limiting steps:



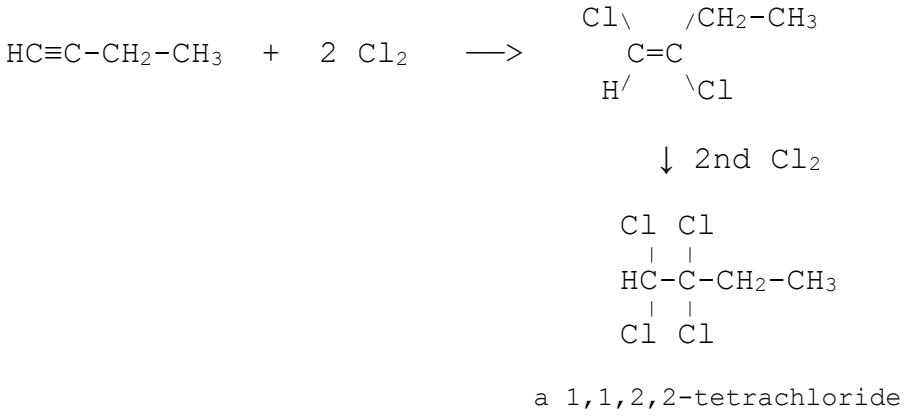
*sp*² C's
intermediate from alkyne halogenation



*sp*³ C's
intermediate from alkene halogenation

The bridged halonium ion from alkyne halogenation has more ring strain because its sp^2 carbons prefer a 120° bond angle, farther from the geometric requirements of a three-membered ring. The preferred 109° bond angles of the sp^3 carbons of the second intermediate cause less ring strain and faster attainment of this intermediate.

With a second equivalent of the halogen electrophile, the dihalogenated alkene product can react further. For example:



a 1,1,2,2-tetrachloride

Double halogenation provides a 1,1,2,2-tetrahalide final product. The number of equivalents of halogen reactant determines the number of halogens in the final product.

Puzzle 9.10

Draw the mechanism of the reaction of one equivalent of chlorine with 2-pentyne.

Puzzle 9.11

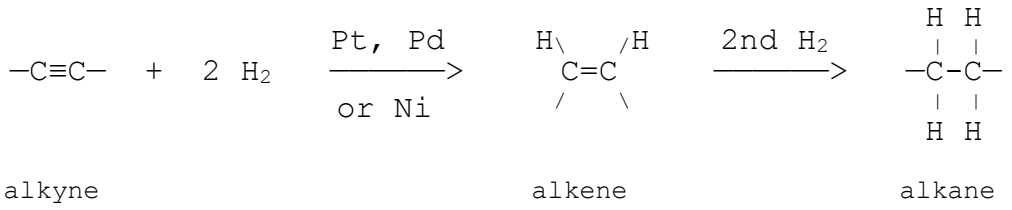
A qualitative analysis test for alkenes involves the discoloration of bromine (Puzzle 8.23, Section 8.10A). The same test works for alkynes: add a brownish dichloromethane solution of bromine to a solution of the unknown compound. Organic compounds are generally colorless unless they have many double bonds alternating with single bonds.

(a) Describe the color changes when a solution of 2-pentyne is treated with a dichloromethane solution of bromine.

(b) By high-resolution mass spectrometry (Section 2.4A), an unknown compound is found to have the molecular formula C_6H_{10}. A solution of the unknown becomes brown when first treated with a dichloromethane solution of bromine, but then becomes colorless again. What can you conclude about the unknown's structure?

9.5E Addition Reactions with Hydrogen

Three different hydrogenation reactions reduce alkynes to alkenes or alkanes. Once again, reactions with alkynes resemble those with alkenes. Platinum, palladium, and nickel, the heterogeneous catalysts that aid the addition of hydrogen to an alkene, also promote the addition of two equivalents of hydrogen to the two π bonds of an alkyne:



These reactions are reductions because carbon-hydrogen bonds replace carbon-carbon bonds (Section 8.12). Complete reduction of the alkyne to the alkane is our second way of deleting functionality from a molecule. Hydrogenation of an alkene was our first way (Section 8.7A).

The mechanism for this hydrogenation is uncertain but presumably resembles that for alkene hydrogenation (Section 8.7A). Certainly, the alkyne is the nucleophile and the metal catalyst is the electrophile.

We can get a quantitative sense of the difference in energies of alkenes and alkynes by comparing the heats of hydrogenation for ethene and ethyne:

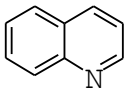
$H_2C{=}CH_2 + H_2 \longrightarrow H_3C{-}CH_3 \qquad \Delta H^\circ = -136 \text{ kJ/mol}$

$HC{\equiv}CH + 2\ H_2 \longrightarrow H_3C{-}CH_3 \qquad \Delta H^\circ = -311 \text{ kJ/mol}$

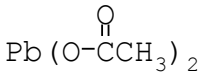
The exothermic nature of these reactions is not surprising because stronger carbon-hydrogen σ bonds form at the expense of weaker carbon-carbon π bonds breaking (Sections 8.3B and 9.3). In the first reaction one carbon-carbon π bond and one hydrogen-hydrogen σ bond break while two carbon-hydrogen σ bonds form. In the second reaction twice as many of those bonds break and form. Yet, the enthalpy change more than doubles! Hydrogenating the first π bond of ethyne releases 311 - 136 = 175 kJ/mol, whereas hydrogenating the second π bond of ethyne releases only 136 kJ/mol. This matches our intuitive expectations that a π bond in an alkyne triple bond, where six electrons reside, is more reactive than the π bond in an alkene double bond of less electron density. In fact, an alkyne is inherently more nucleophilic than an alkene.

Yet, we have seen additions of acids to alkynes that generate less stable alkenyl carbocations (Sections 9.5A and 9.5B) and alkyne halogenations that generate less stable cyclic halonium ions (Section 9.5D). These more energetic intermediates keep alkynes no more reactive than alkenes, as displayed in Figure 9.1 (Section 9.5A). In contrast, hydrogenations involve neither carbocations nor three-membered rings, and alkynes' inherently greater nucleophilicity generally makes them more susceptible to hydrogenations than alkenes.

Can hydrogenation of an alkyne be stopped at the alkene product before adding a second equivalent of hydrogen? It should be possible to find conditions strong enough for the hydrogenation of the more reactive alkyne but too weak for the hydrogenation of the less reactive alkene product. Indeed, such conditions have been discovered: palladium catalyst "poisoned" (i.e., partially deactivated) with either quinoline or lead acetate. (Similarly, lead in leaded gasoline can poison catalysts in automobile catalytic converters.)



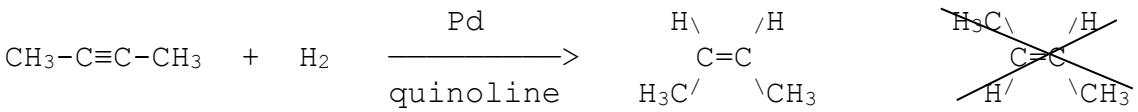
quinoline



lead acetate

poisons for metal catalysts

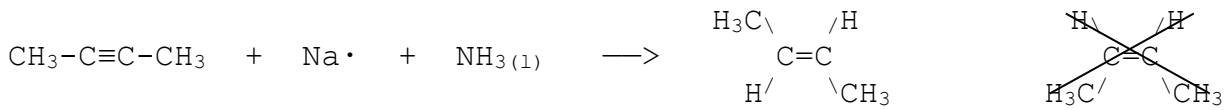
For example:



2-butyne (*Z*)-2-butene none

This reaction is not only selective to stop after yielding the alkene, but also stereoselective to yield only the *Z* diastereomer by syn addition.

To complement this syn addition a different set of reagents has been found. An alkali metal, usually sodium or lithium, in liquid ammonia solvent adds one equivalent of hydrogen anti to an alkyne. For example:



2-butyne metal (*E*)-2-butene none

This stereoselective reaction produces only the *E* diastereomer of the alkene.

The mechanism involves free radicals, having unpaired electrons. This very different mechanism accounts for the very different stereochemistry. By adding its single valence electron, the alkali *metal* reduces the alkyne. In contrast, alkali metal *salts* do not react. As a protic solvent (Section 6.5C), ammonia not only provides a suitable medium, but also adds hydrogens as protons to the alkynes.

These two methods of partially hydrogenating alkynes are synthetically important because they allow selection of whichever alkene stereoisomer might be desired.

Puzzle 9.12 ———————————————————————————————

Show the reactants and organic products for all reactions in a synthesis of the most stable, unbranched pentene stereoisomer of formula C_5H_{10} from an alkyne.

Puzzle 9.13 ———————————————————————————————

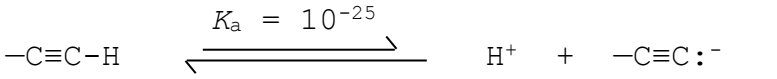
Section 9.1 indicated that ethyne combusts in oxygen with the hottest flame of any fueled by a hydrocarbon. Why should ethyne burn hotter than ethane or ethene?

———————————————————————————————

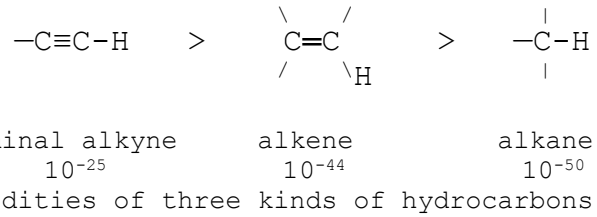
9.5F Terminal Alkynes as Acids

To take full advantage of the stereoselective reactions of the preceding section, we need to understand the synthetic capabilities of alkynes, to be explored in Section 9.6. And to realize these synthetic possibilities we must appreciate the acidity of terminal alkynes. Such electrophilic acidity contrasts with the nucleophilicity of alkynes and alkenes, examined earlier in this and the previous chapters.

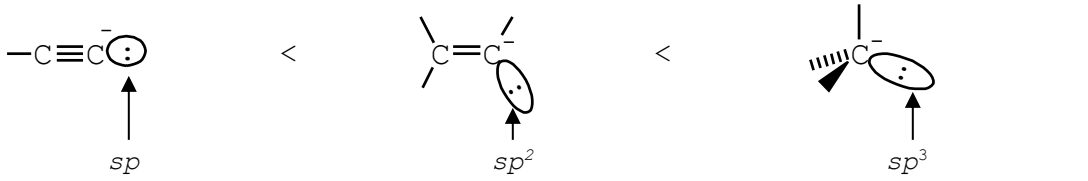
Consider the dissociation of a terminal alkyne acid to a proton and its conjugate base, called an **acetylide ion:**



With a K_a of 10^{-25}, which is much less than 10^{-7}, a terminal alkyne is a very weak acid like other hydrocarbons. Yet, a terminal alkyne is a much stronger acid than other simple hydrocarbons. The K_a values in Table 4.1 (Section 4.2) allow us to rank the acidities of three kinds of hydrocarbons:

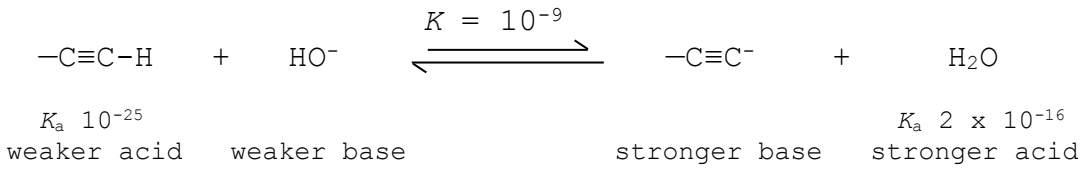


Why are terminal alkynes so much more acidic than alkenes or alkanes? Let us examine the three conjugate bases, where structural factors are more obvious:



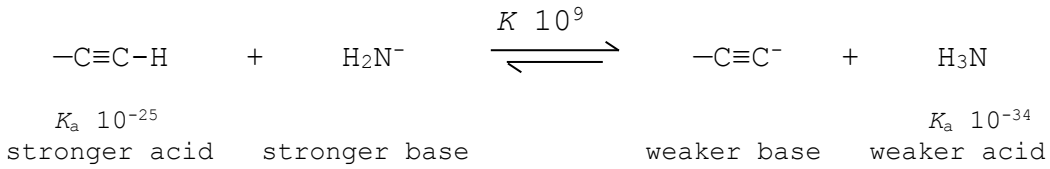
As discussed in Section 4.9F, hybridization is the key. In an *sp* orbital the base electron pair of the acetylide ion is repelled and destabilized by only one other electron pair of the carbanion carbon, the σ electron pair of the triple bond, and this repulsion is 180° away. At the other extreme, three electron pairs only 109° away repel and destabilize the base electron pair of an alkyl carbanion. The least repulsion and destabilization make the acetylide ion the least basic of these carbanions and the terminal alkyne the most acidic of the three types of hydrocarbons.

What reagent efficiently removes a proton from a terminal alkyne? As a weak acid, a terminal alkyne requires a strong base. Would hydroxide ion work? Consider the acid-base equilibrium:



The stronger acid and base are products, so the reactants predominate at equilibrium. Indeed, the equilibrium constant is much smaller than 1: $K = 10^{-25}/(2 \times 10^{-16}) = 10^{-9}$. So hydroxide ion, although a strong base, is not strong enough to deprotonate a terminal alkyne.

An even stronger base is needed, one whose conjugate acid has a K_a less than 10^{-25}, the K_a of the alkyne. A common choice is **amide ion,** H_2N^-, the conjugate base of ammonia:



With the stronger acid and base as reactants, the equilibrium constant is larger than 1: $K = 10^{-25}/10^{-34} = 10^9$. Products properly predominate at equilibrium.

Puzzle 9.14

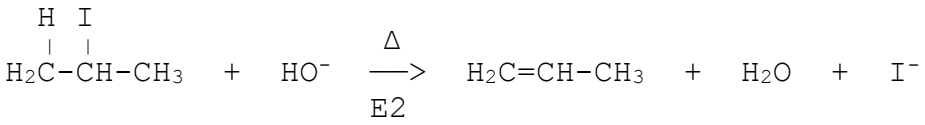
Explain the relative acidities of these two acids, the conjugate acids of a ketone and an alcohol:

9.6 Syntheses of Alkynes

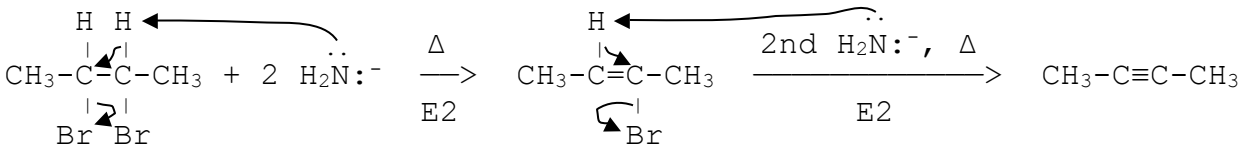
Organic synthetic reactions come in two types: transformation of one functional group to another, and extension of carbon skeletons. Both types of syntheses are very important. The reactions examined in this and previous chapters have generally exemplified functional group transformations. For example, E2 elimination reactions change an alkyl halide to an alkene. Now, we will consider two ways of preparing alkynes, which illustrate both types of reactions, including our first important method of extending carbon skeletons.

9.6A Alkynes from 1,2-Dihalides

Just as most reactions of alkynes strongly resemble reactions of alkenes, so one synthesis of alkynes parallels a standard method of making alkenes: E2 elimination reactions. To synthesize the one π bond of an alkene, an alkyl halide is heated with a strong base (Section 7.2A). For example:



To create the *two* π bonds of an alkyne, an alkyl *di*halide, normally a 1,2-dihalide or a 1,1-dihalide, is heated with a strong base, usually hydroxide, alkoxide, or amide ion. A succession of two E2 reactions ensues. For example:



1,2-dibromide base alkenyl bromide alkyne

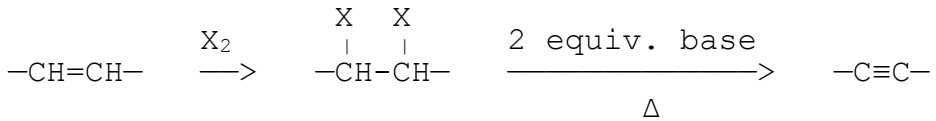
The second elimination reaction requires a higher temperature or stronger base (e.g., amide ion) than the first. Why? It is harder for a leaving group to leave a doubly bonded, sp^2 carbon than a singly bonded, sp^3 carbon:

bonding e⁻ pair closer to C bonding e⁻ pair farther from C

relative leaving abilities of L

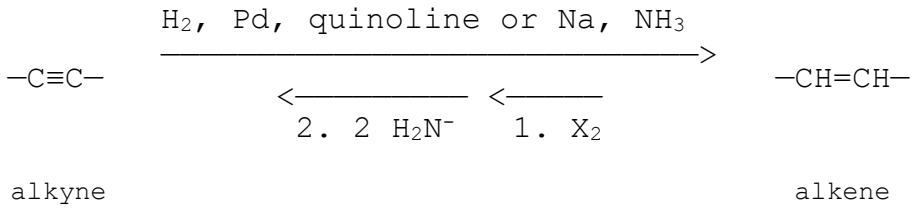
The doubly bonded carbon uses a smaller sp^2 orbital to share the bonding electron pair with the leaving group. Consequently, this electron pair is closer to the doubly bonded carbon and is less easily removed by the leaving group. This handicap for leaving groups on sp^2 carbons is general and will be encountered again in Sections 14.5A, 16.2C, 18.2D, and 18.5D.

The 1,2-dihalides needed for synthesizing alkynes are most conveniently prepared by halogenating alkenes (Section 8.10A). Thus the synthetic scheme can begin with an alkene:



alkene 1,2-dihalide alkyne

Consequently, we have the useful synthetic couple that can interconvert an alkyne and an alkene:

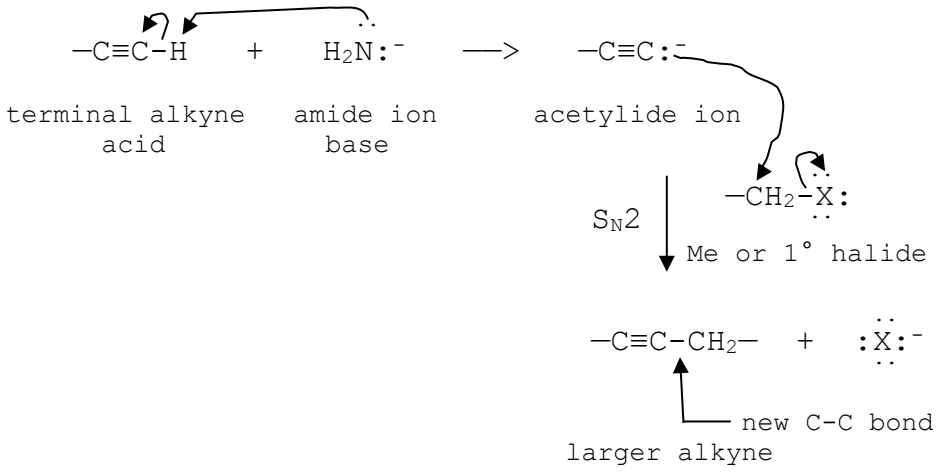


Puzzle 9.15

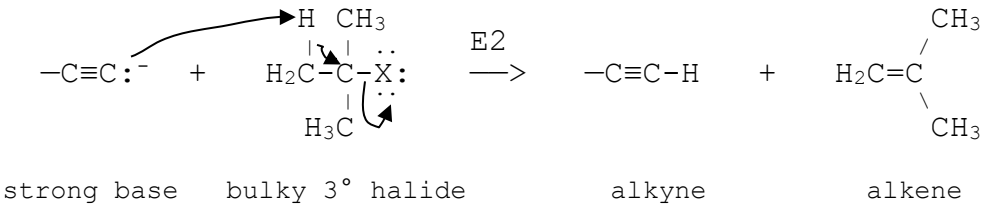
(a) Show the reactants and organic products for all reactions in a synthesis of propyne from 2-chloropropane. Hint: generate an alkene.
(b) Show the reactants and organic products for all reactions in a synthesis of 2-chloropropane from propyne.

9.6B Alkynes from Smaller Alkynes

Alkynes can also be made from smaller terminal alkynes:

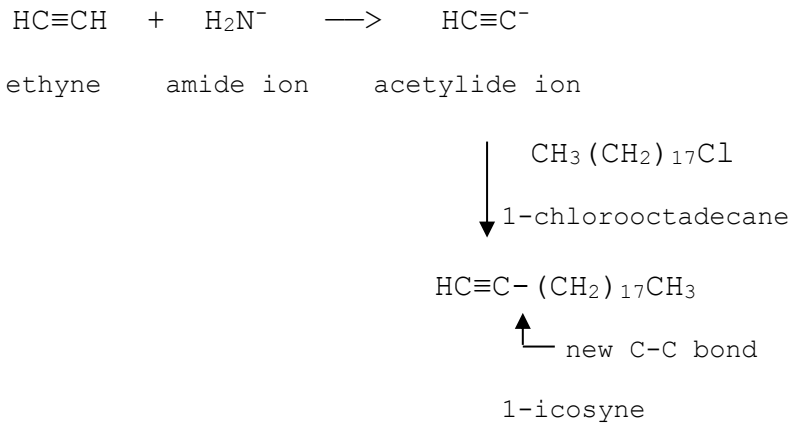


First we must convert the terminal alkyne, a weak nucleophile, into the strong nucleophile, acetylide ion. Acetylide ion is a strong nucleophile by two criteria. It is a strong base because its conjugate acid, the terminal alkyne, is a weak acid ($K_a = 10^{-25}$). Secondly, its nucleophilic carbon is not bulky. Consequently, acetylide ion is a strong enough nucleophile for an S_N2 reaction with an electrophilic alkyl halide (Section 6.4C). In the process a new carbon-carbon σ bond is formed. The alkyl halide itself should not be too bulky, or else the strongly basic acetylide ion would cause too much E2 elimination (Section 7.5B):



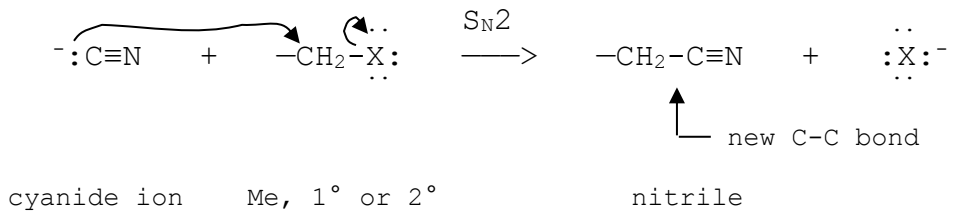
This undesirable elimination reaction would form an alkene and the original alkyne instead of a new larger alkyne. To inhibit this competing E2 reaction and to encourage the desired S_N2 reaction, a methyl or primary alkyl halide is needed.

Overall, we have outlined a synthesis of an alkyne with a larger carbon skeleton from a smaller alkyne. The increase in size depends solely on the size of the methyl or primary halide, which can have any number of carbons. Thus, alkynes of any size can be constructed. For example, a twenty-carbon alkyne could be made from ethyne:



The 18-carbon alkyl chloride can be readily made from the plentiful 18-carbon fatty acid, stearic acid (Section 14.8A).

To fully appreciate the synthetic utility of this method of making large alkynes, we should realize that no other reaction studied so far can lengthen the carbon skeleton by any number of carbons. (Other methods will be established later.) Consider the logic behind the above synthetic scheme: *a carbon nucleophile joins a carbon electrophile, forming a carbon-carbon σ bond*. Among electrophiles studied so far, only alkyl halides in S_N2 reactions and carbocations in S_N1 reactions have carbon atoms that attract nucleophiles. Yet, by limiting competition from elimination reactions, S_N2 reactions surpass S_N1 reactions in synthetic usefulness (Section 6.8). Therefore, alkyl halides are the preferred electrophiles. (Chapters 10, 12, and 14 will present other carbon electrophiles.) We have examined various reagents with nucleophilic carbon atoms: alkenes, alkynes, cyanide ion, Grignard (and organolithium) reagents, and acetylide ions. The first two nucleophiles are too weak to react with an alkyl halide in the preferred S_N2 reaction. A cyanide ion is nucleophilic enough to react by S_N2 but adds only one carbon to the skeleton:



Grignard reagents do not react cleanly with alkyl halides (Section 6.9). For now, that leaves only acetylide ions with the capability of lengthening the carbon skeleton of an alkyl halide by any specified number of carbons.

Puzzle 9.16

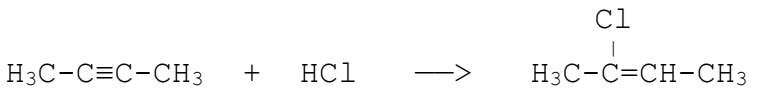
Show the reactants and organic products for all reactions in the synthesis of 2-pentyne from ethyne and any other reagents.

Puzzle 9.17

2-Methylheptadecane is a sex attractant emitted by tiger moths. Outline a synthesis of this chemical from ethyne and any other reagents.

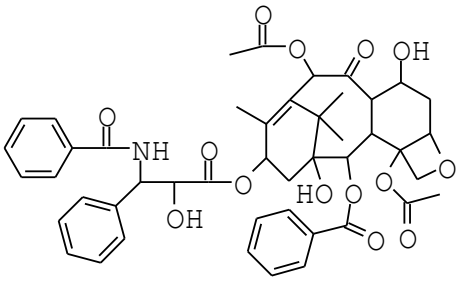
9.6C Synthetic Strategies with Alkynes

Some organic syntheses require only one reaction. These straightforward syntheses normally involve simple functional group transformations and are easy to design. Thus, an outline of a synthesis of 2-chloro-2-butene from an alkyne, is simply this reaction:

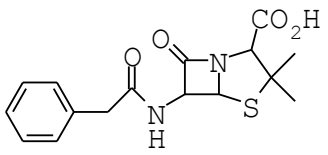


2-butyne 2-chloro-2-butene

Yet, many other syntheses are less direct and demand more than one reaction, so that one may not easily imagine the reaction sequence from starting materials to final product. Such syntheses pose some of the most interesting problems in organic chemistry. Many famous organic chemists have won their fame by synthesizing large, complex organic molecules by many, sometimes dozens of reactions in proper sequence. Often the complex molecule targeted for synthesis is a natural product with important biological properties. Prime targets are drugs and **pheromones**, which are chemical signals issued by one organism to influence another. Sex attractants are one kind of pheromone. The laboratory synthesis may be important because the natural source cannot satisfy human demand. For example, taxol was a critically scarce cancer drug from the bark of a rare yew tree, until organic chemists recently developed a laboratory synthesis. Also, variations on the synthesis of a natural product can prepare analogues of the natural compounds with improved biological activity. A classic example is the synthesis of natural penicillin, which led to the related syntheses of more effective penicillin analogues.



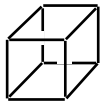
taxol



penicillin G

Other complex molecules are synthetic targets because they are expected to have

interesting chemical properties. An example is the molecule with the common, whimsical name of cubane:

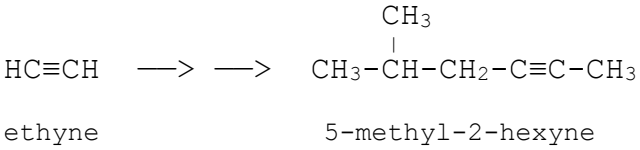


cubane

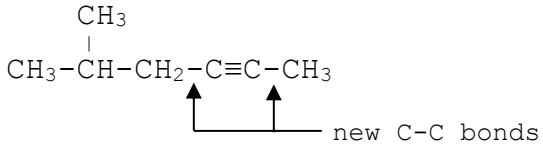
Cubane has been made despite the tremendous strain of six cyclobutane rings fused together.

Such difficult synthetic problems do not suit a first-year organic chemistry course, but puzzles throughout this text will frequently request outlines of multistep syntheses, some of which will prove very challenging. Having already acquired many functional group transformations and one method for enlarging carbon skeletons in our synthetic repertoire, let us develop some strategies for outlining reasonable multistep syntheses. Although organic synthesis is a somewhat personal exercise with different people developing different feasible schemes by different strategies, some general points are worth considering. Let us design syntheses of two molecules to establish a few general principles and to start developing one's own insights.

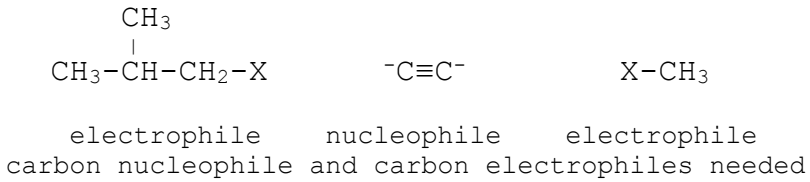
First, how could 5-methyl-2-hexyne be made from ethyne and any other reagents? A view of the overall problem helps:



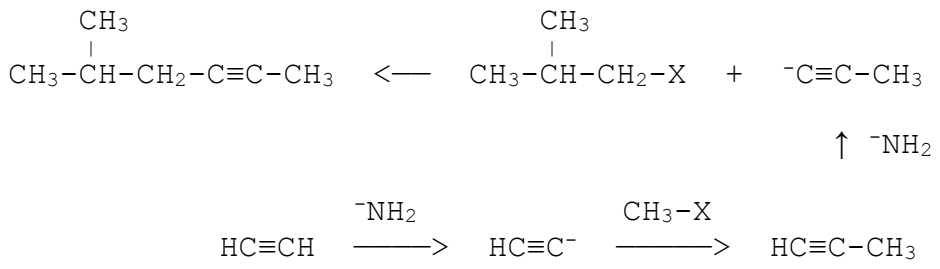
The two reaction arrows suggest multiple reaction steps. Reaction steps are distinct reactions, not mechanistic steps. When outlining syntheses, it is important to primarily consider reactions, and only secondarily mechanisms. Clearly, we will need not only functional group transformations but also carbon-carbon σ bond formations to extend the carbon skeleton from two to seven carbons. In designing syntheses one should first decide which, if any, carbon-carbon σ bonds must be made. In this case retaining the position of the triple bond throughout the synthesis is reasonable, so we should attach two alkyl groups to the ethyne skeleton by the carbon-carbon bonds shown:



Next, we show which carbon nucleophile and carbon electrophiles can make the desired carbon-carbon σ bonds:

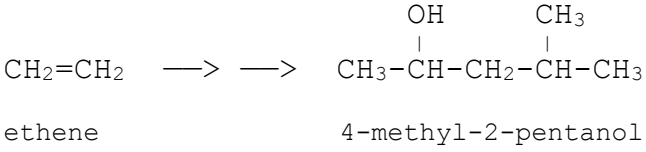


The nucleophile with two repelling negative charges so close together is not realistic, but suggests the necessary functionality at different points in the synthesis. Filling in the details of the synthesis is a personal matter. Some prefer to start at the beginning and work forward from derivative to derivative. Many start at the end and work backwards from **precursor** (i.e., forerunner) to precursor. Others find feasible derivatives and precursors along the way and work in both directions from these milestones. This time let us work backward from the end in a counterintuitive but often fruitful direction:

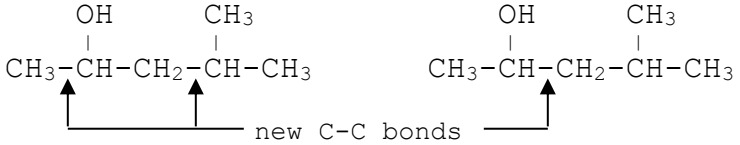


Alternatively, the two carbon-carbon bonds could have been formed in the opposite order.

A second puzzle further develops synthetic strategies with alkynes: make 4-methyl-2-pentanol from ethene and any other reagents. A picture is worth a thousand words:



Because the carbon skeleton of ethene must be extended, we first identify carbon-carbon σ bonds to form near the alcohol functional group. Two ways of attaching alkyl groups to the two-carbon unit from ethene should be considered:



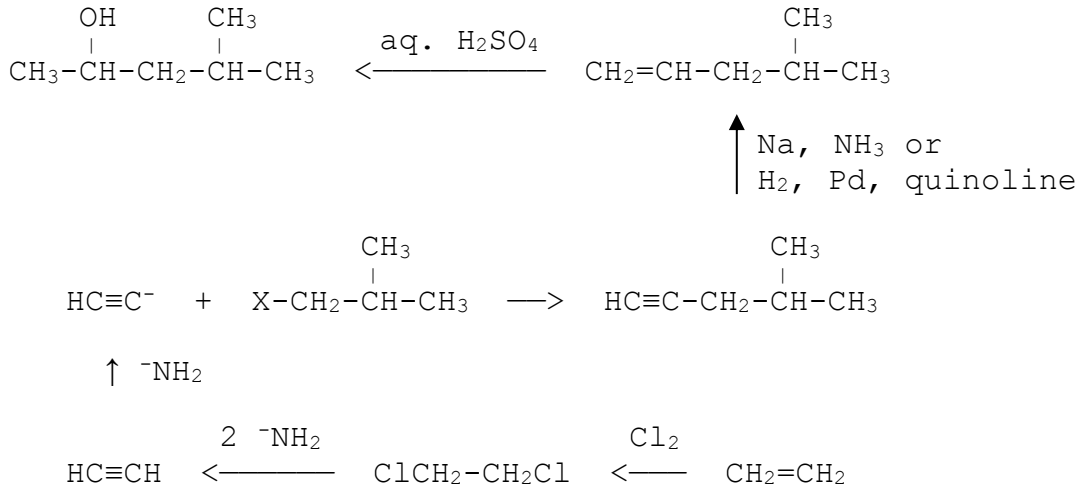
two methods of forming carbon skeleton

Before deciding between these two plans, we should take the next step and visualize the carbon nucleophiles and carbon electrophiles for the two methods:

carbon nucleophiles and carbon electrophiles for two methods

The first scheme uses an electrophilic secondary halide, which would undergo too much E2 reaction with acetylide ion (Section 9.6B). With a primary halide the second method suffers less from a competing E2 reaction. Furthermore, the second method needs fewer steps to build the

carbon skeleton, so this is the preferred way of joining carbon pieces. From here we look for precursors and derivatives of the milestones established along the route. Once again let us write the final scheme backwards to practice thinking in this unnatural but useful direction:



This synthesis shows not only how an alkyne can extend the carbon skeleton but also how various derivatives, such as alkenes and alcohols, can then be formed from the larger alkyne produced. The possibilities are endless!

Finally, let us formulate the few guidelines for complex syntheses that we have established.

1. If the carbon skeleton must be extended, find the carbon-carbon σ bonds to be formed near a functional group in the target molecule.

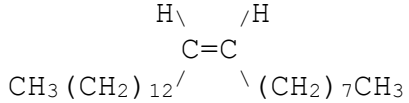
2. Identify the carbon nucleophiles and carbon electrophiles to form the requisite carbon-carbon σ bonds.

3. Seek feasible precursors of the ultimate product, the carbon nucleophiles, and carbon electrophiles, as well as derivatives of starting materials.

Thanks to alkynes, you can already create synthetic schemes for a wide array of molecules large and small.

Puzzle 9.18 ———————————————————————————————————————

Using ethyne and any other reagents, show the reactants and organic products for all reactions in an efficient synthesis of muscalure, the sex pheromone of the house fly:



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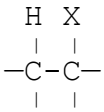
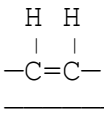
Chapter Summary

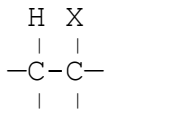
1. IUPAC rules provide a systematic method for naming alkynes, similar to the naming of alkenes.
2. Despite the overall strength of the triple bond, an alkyne's two π bonds are individually

weaker than a single carbon-carbon bond and vulnerable to reaction.
3. Simple alkynes, alkenes, and alkanes are nonpolar and insoluble in water. Their boiling points are similar if their sizes are similar.
4. Their lack of charge makes alkynes soft nucleophiles. Their addition reactions and mechanisms resemble those of alkenes, also soft nucleophiles.
5. In reacting with hydrogen halides and aqueous acid, alkynes follow Markovnikov's rule.
6. With their two π bonds, alkynes can add either one or two equivalents of hydrogen halides, halogens, and hydrogen.
7. Aqueous acid first hydrates an alkyne by Markovnikov's rule to an enol, which quickly isomerizes to a more stable carbonyl tautomer.
8. Borane and then basic hydrogen peroxide hydrates an alkyne to an enol that violates Markovnikov's rule. The enol then isomerizes to a more stable carbonyl tautomer.
9. An alkyne may add one equivalent of hydrogen either syn or anti, depending on the reagents.
10. Though weakly acidic, terminal alkynes are much more acidic than alkenes or alkanes. An amide ion removes a proton from a terminal alkyne to form the acetylide ion conjugate base.
11. Alkynes can be prepared in two ways: double E2 elimination of a 1,2-dihalide, and S_N2 substitution of an acetylide ion with a primary or methyl halide. The latter synthesis is our first versatile method of extending carbon skeletons.
12. The key to designing a synthesis that extends a carbon skeleton is identifying the carbon-carbon bond to be made and the carbon nucleophile and carbon electrophile to be used.

Reaction Summary

Reactants		Product	Section
Syntheses of alkynes			
	$2\ H_2N^-$ ⟶	$-C\equiv C-$	9.6A
	1. X_2 2. $2\ H_2N^-$ ⟶ ⟶	$-C\equiv C-$	9.6A
Reactions of alkynes			
$HC\equiv C-R$	HX ⟶		9.5A

Reactants		Product	Section
Reactions of alkynes (continued)			
HC≡C-R	2 HX ⟶	H X | | HC-C-R | | H X	9.5A
HC≡C–	aq H_2SO_4, Hg^{2+} ⟶	H O | ‖ HC-C– | H	9.5B
HC≡C–	1. BH_3 2. HOOH, HO^- ⟶	O H ‖ | HC-C– | H	9.5C
–C≡C–	X_2 ⟶ X = Cl or Br	X\ / C=C / \X	9.5D
–C≡C–	2 X_2 ⟶ X = Cl or Br	X X | | –C-C– | | X X	9.5D
–C≡C–	2 H_2, Pt ⟶	H H | | –C-C– | | H H	9.5E
–C≡C–	H_2, Pd, quinoline ⟶	H\ /H C=C / \	9.5E
–C≡C–	Na, NH_3 ⟶	H\ / C=C / \H	9.5E
HC≡C–	H_2N^- ⟶	$^-$C≡C–	9.5F
Reactions of acetylide ions			
$^-$C≡C–	–CH_2-X ⟶	–CH_2-C≡C–	9.6B

Reactants		Product	Section
Reactions of acetylide ions (continued)			
$^-C{\equiv}C-$		$HC{\equiv}C-$,	9.6B

Additional Puzzles

9.19 Name these compounds:
(a) $CH_3CH_2C{\equiv}CCHCl_2$ (b) $CH_3C{\equiv}CCH_2CHCl_2$ (c) $HC{\equiv}CCH_2CH{=}CHCH_3$
(d) $H_2C{=}CHCH_2C{\equiv}CCH_3$ (e) $CH_3CH_2C{\equiv}CC{\equiv}CCH_2OH$ (f) $HOCH_2CH_2C{\equiv}CC{\equiv}CCH_3$

9.20 Correct the mistake in each name and draw a structure for the corrected name:
(a) 3-butyne (b) 5-methyl-1-pentyne (c) 2-methyl-1-pentyne (d) 2-methyl-3-pentyne
(e) 5-hexen-2-yne (f) 2-hexen-5-yne (g) 1-butyne-3-ol

9.21 (a) Which bonds are broken and made in this reaction?

$$HC{\equiv}CH \;+\; 2\ H_2 \longrightarrow CH_3CH_3$$

(b) With the help of Table 1.5 (Section 1.8), estimate the enthalpy change.
(c) Is the enthalpy change favorable or unfavorable?

9.22 Why does 2-butyne have a higher boiling point (27°C) than 1-butyne (8°C)? Hint: consider the shapes of the molecules.

9.23 Draw the organic products when propyne reacts with these reagents. If it does not react, say so.
(a) Cl_2 (b) 2 Cl_2 (c) HBr (d) 2 HBr (e) Na, NH_3 (f) aqueous H_2SO_4, $HgSO_4$
(g) $CH_2{=}CH_2$ (h) $^-NH_2$ (i) H_2, Pd, quinoline (j) 2 H_2, Pt (k) $^-CH_3$ (l) $^-C{\equiv}N$
(m) BH_3; then HOOH, HO^-

9.24 Draw the organic products when 2-butyne reacts with these reagents. If it does not react, say so.
(a) Cl_2 (b) 2 Cl_2 (c) HBr (d) 2 HBr (e) Na, NH_3 (f) aqueous H_2SO_4, $HgSO_4$
(g) $CH_2{=}CH_2$ (h) $^-NH_2$ (i) H_2, Pd, quinoline (j) 2 H_2, Pt (k) $^-CH_3$ (l) $^-C{\equiv}N$
(m) BH_3; then HOOH, HO^-

9.25 Although hydrations of most alkynes in aqueous acid ultimately yield ketones, identify an alkyne that yields an aldehyde.

9.26 Show the reactants and organic products, including stereoisomers, for all reactions in an efficient synthesis of achiral 2,3-dichlorobutane from an alkyne.

9.27 Determine the missing molecules.

(a) $CH_2{=}CHC{\equiv}CCH_3 + H_2 + Pd + \text{quinoline} \longrightarrow ?$

(b) $C_6H_5C{\equiv}CH + ? \longrightarrow C_6H_5\overset{\overset{O}{\|}}{C}CH_3$

(c) $CH_3\overset{\overset{Br}{|}}{C}H{=}CCH_2CH_3 + HI \longrightarrow ?$

(d) $C_6H_5C{\equiv}CC_6H_5 + ? \longrightarrow (E)\text{-}C_6H_5CH{=}CHC_6H_5$

(e) $HC{\equiv}CCH_3 + {}^{-}NH_2 \longrightarrow ? \xrightarrow[?]{CH_3CH_2I} ? \xrightarrow{Br_2} ?$

(f) $CH_3CH{=}CH_2 + Cl_2 \longrightarrow ? \longrightarrow CH_3C{\equiv}CH$

9.28 (a) Draw the final organic product if 2,3-dimethyl-2-butene reacts with chlorine and the result reacts with two equivalents of sodium amide.
(b) Draw the mechanism and explain why an alkyne is not produced.

9.29 Treatment of 1,2-dibromocyclohexane with two equivalents of sodium amide yields 1,3-cyclohexadiene instead of an alkyne. Explain.

9.30 Show the reactants and organic products for all reactions in an efficient synthesis of 3,8-dimethyldecane from ethyne and any other reagents.

9.31 (a) How many hydrogens should all constitutional isomers of simple, acyclic five-carbon alkynes have?
(b) Draw and name all of these isomers.

9.32 Outline an efficient synthesis of each product from ethyne and any other reagents.
(a) (*E*)-3-heptene (b) 2,2-dichloropentane (c) 1,2-dibromo-1-butene (d) 1-nonanol
(e) 2-iodo-1-pentene

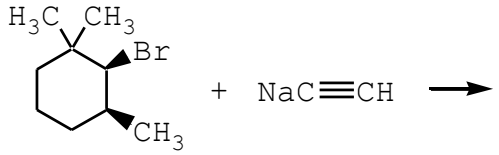
9.33 Determine **A**, **B**, and **C** in these reactions:

$$\mathbf{A} \xrightarrow[\text{quinoline}]{H_2,\ Pd} \mathbf{B} \xrightarrow[Pt]{H_2} \text{hexane}$$

$$\mathbf{B} \xrightarrow[2.\ Zn]{1.\ O_3} \mathbf{C} \text{ (the only organic product)}$$

9.34 Both cyclohexane and cyclohexene are easy to isolate and characterize. Yet, cyclohexyne has not been isolated and characterized. Explain in terms of geometry.

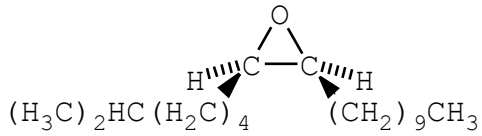
9.35 Hoping to obtain a large alkyne, a student combined these reactants at room temperature:



During the reaction she noted a gas bubbling from the reaction mixture. When she treated the remaining organic product with bromine in dichloromethane, the bromine's brown color dissipated. High-resolution mass spectrometry indicated the product had a formula of C_9H_{16}.
(a) Identify the large alkyne she hoped to get. (b) Identify the gas product.
(c) Identify the C_9H_{16} product.

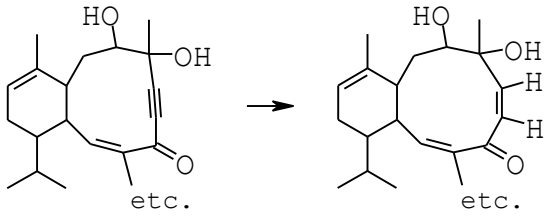
9.36 (*Z*)-9-Tricosene, the *Z* stereoisomer of $CH_3(CH_2)_7CH{=}CH(CH_2)_{12}CH_3$, is the sex pheromone of the female housefly. Show the reactants and organic products for all reactions in an efficient synthesis of this chemical from ethyne and any other chemicals.

9.37 Disparlure is the sex pheromone of the female gypsy moth:



Show the reactants and organic products for all reactions in an efficient synthesis of this chemical from ethyne and any other chemicals.

9.38 Eleutherobin is a promising anticancer agent from a Pacific sea coral. It has also been synthesized in the laboratory. During this synthesis the following selective hydrogenation was achieved:



(a) Is it surprising that conditions were found that allowed hydrogenation of the alkyne group without hydrogenation of either alkene group? Explain.
(b) What conditions might achieve this selective hydrogenation?