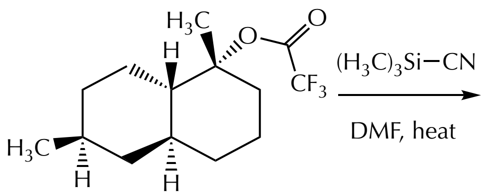
Thinking in Blue #9 - Both of these questions relate to generating an array of substitution and elimination products based purely on the definition of the reactions. The first question is from EQ 03.28C, and the second one did not make it into the book.

Trimethylsilyl cyanide [$(CH_3)_3Si$-CN] is a source of nucleophilic cyanide ion that, unlike sodium cyanide (NaCN), can dissolve readily in organic solvents. There are five different substitution and elimination products observed in the following reaction with compound W. What are they?



compound W

substitution product C1	substitution product C2

elimination product C3	elimination product C4	elimination product C5

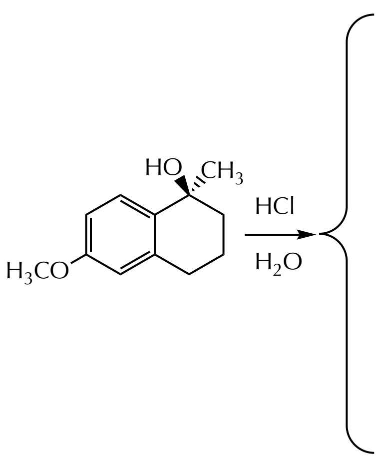
When compound W reacts with potassium tert-butoxide [$(CH_3)_3COK$], only three of these five products are observed. Of those three products, they can be ranked from major to minor based solely on the steric accessibility of the β-H that is being removed (more accessible = faster reaction). Using the C1 through C5 labels above, according to the products as you have entered them, rank the three anticipated outcomes from the reaction of compound W with potassium tert-butoxide as major to minor.

major > intermediate > minor

☐ > ☐ > ☐

enter the C1-C5 label

The following reaction produces two pairs of isomeric products derived from substitution and elimination pathways. Draw these pairs and indicate the stereochemical or structural relationship between them.



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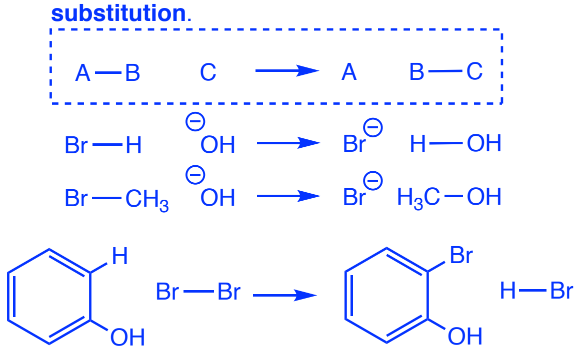
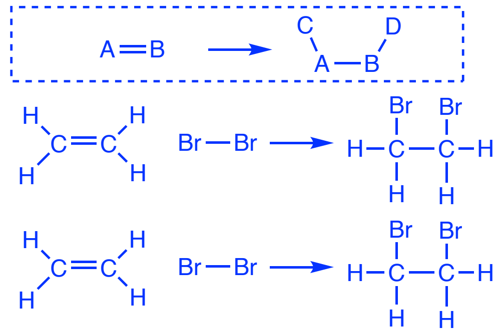
In the early stages of learning reaction chemistry, the fact that there are actually only a few fundamental classifications of chemical reactions is the most useful information. With only a few different kinds of bonds to deal with (sigma and pi), it is simply not surprising that the four fundamental types of reactions involve a change in connectivity between sigma and pi bonds.

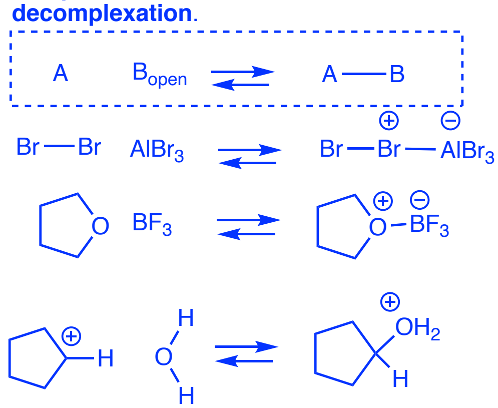
A reaction in which one sigma bond is broken and a new one is formed is called **substitution**.



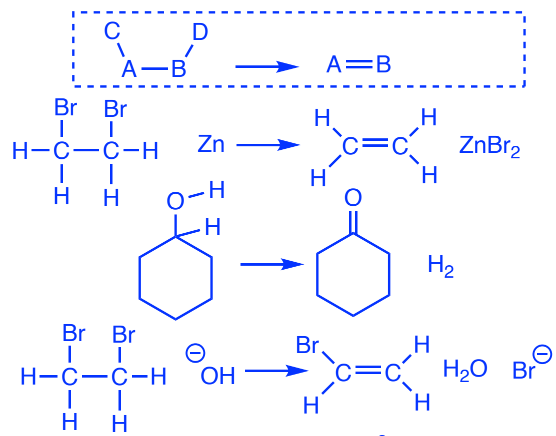
A reaction in which one pi bond is broken and 2 new sigma bonds are formed is called **addition**.



A reaction in which one sigma bond is formed from an open shell atom is a **complexation** reaction, and the reverse is **decomplexation**.

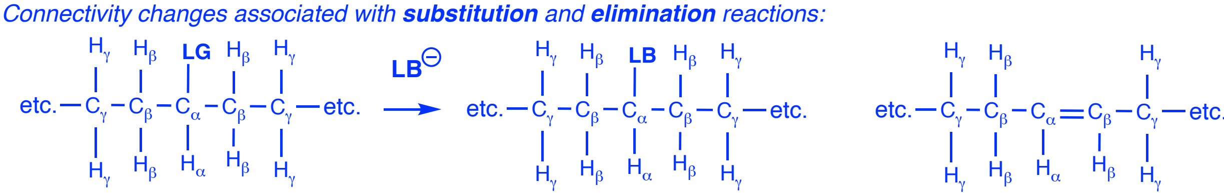


A reaction in which a pi bond is formed and 2 sigma bonds are broken is the opposite of addition, and called **elimination**.



Substitution and **elimination** reactions are always learned together because the reactivity of sp^3 carbon-electronegative atom bonds that can be easily broken (such groups are called leaving groups - LG; e.g., carbon-halogen bonds). The reaction with Lewis bases (LB) is usually a competition between substitution of the leaving group (sigma to sigma replacement) or elimination of the leaving group (loss of the sigma bonded LG and β-hydrogen to give a new pi bond).

*Connectivity changes associated with **substitution** and **elimination** reactions:*

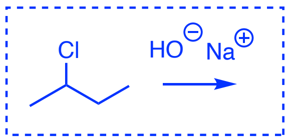


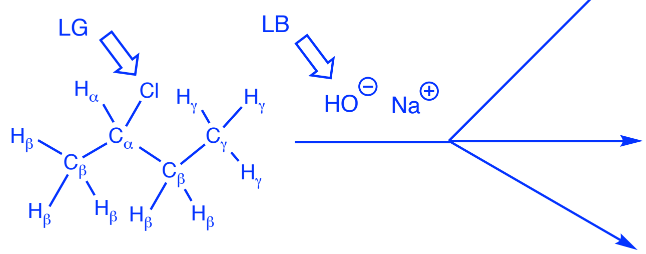
Greek letters are often used to signify the distance that a type of atom is located from a reference functional group, in this case the LG

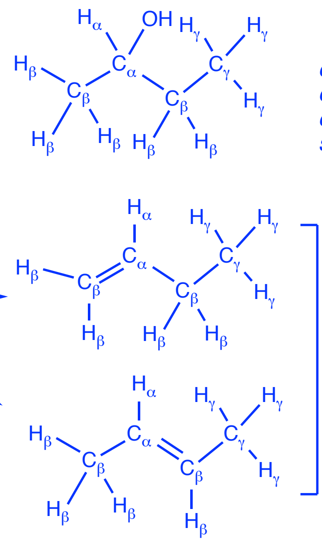
nucleophilic substitution S_N ***elimination E***

Trimethylsilyl cyanide [$(CH_3)_3Si\text{-}CN$] is a source of nucleophilic cyanide ion that, unlike sodium cyanide (NaCN), can dissolve readily in organic solvents. There are five different substitution and elimination products observed in the following reaction with compound W. What are they?

*If you are told that a reaction is one where **substitution** and **elimination** are happening, then possible outcomes can be anticipated:*







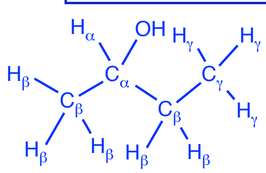
1 nucleophilic substitution outcome (considering connectivity only; ignoring stereochemistry)

2 elimination outcomes (considering connectivity only; ignoring stereochemistry)

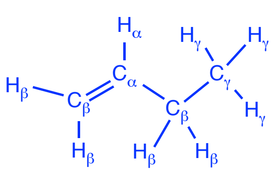
There is one sp^3 C-LG and five β−Hs in two groups, 3 on one of the β−Cs and 2 on the other β−C.

Stereochemical analysis of these connectivities is exactly the same as any prior question, except that now it is assumed that you have this analysis method mastered and in place as a skill.

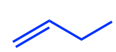
> Every earlier topic will eventually show up in understanding reaction chemistry (which is why they are there in the first place… to build the foundation of ideas): relative acid-base strength and decisions based on pK_a values, relative rates and stabilities and whether the reaction is irreversible (kinetic control) or reversible (thermodynamic control), molecular structure and bonding features such as delocalization, hybridization, geometry, stereochemical analysis, and conformational analysis.

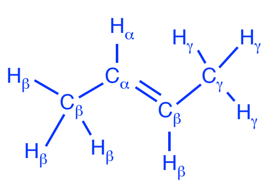


1 stereocenter: 2 stereoisomers R and S enantiomers both chiral



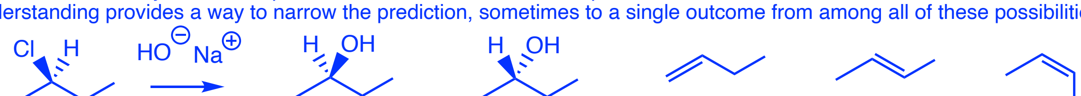
no source of stereoisomers; unique structure for this connectivity





1 double bond capable of providing E and Z diastereomers both achiral

In this example, then, without regard to mechanism, it is possible to use the definition of “substitution” and “elimination” and stereochemical analysis to anticipate all of the POSSIBLE reaction products. This is the maximum number. Mechanistic understanding provides a way to narrow the prediction, sometimes to a single outcome from among all of these possibilities.



S_N with retention of configuration | *S_N with inversion of configuration* | *3 Elimination (E) products (not to be confused with E/Z geometry!)*

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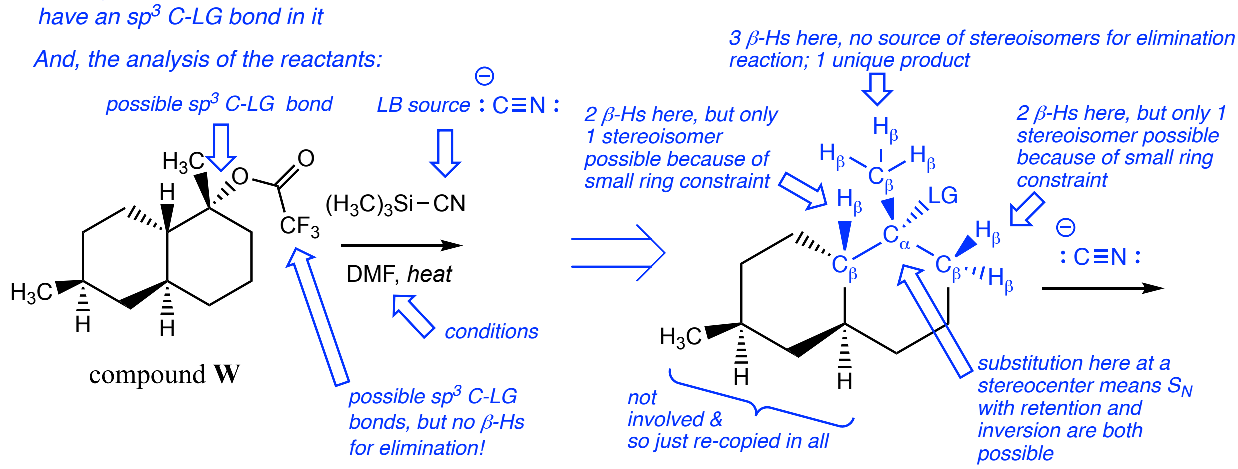
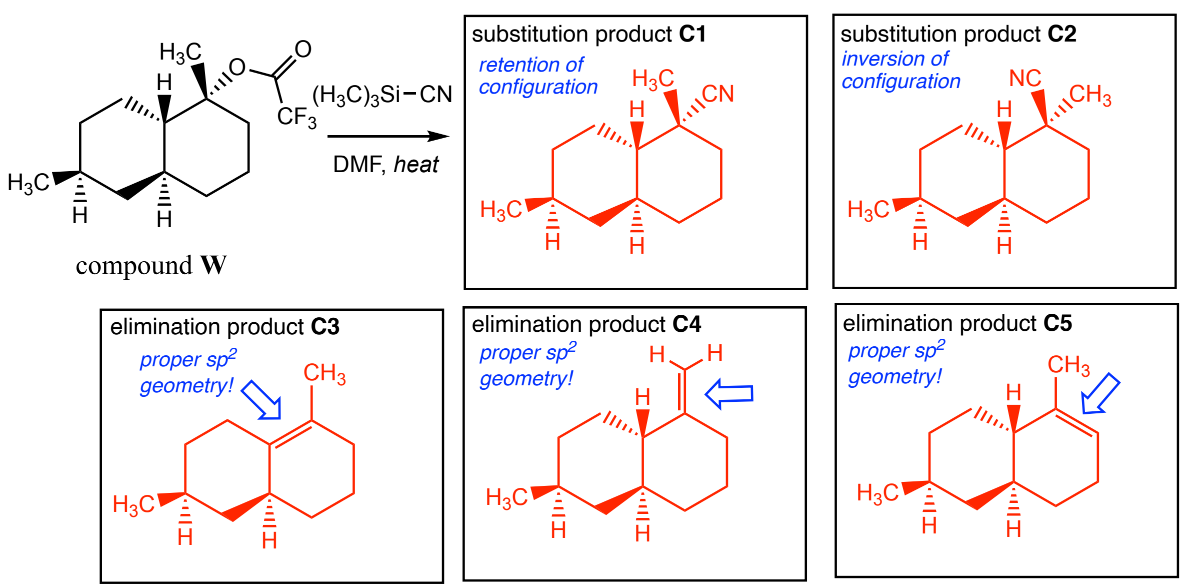
Before you even look at the problem, the text of the problem allows you to anticipate:
(a) substitution and elimination reaction outcomes are observed (so you need to have understood what those mean, as on the previous pages)
(b) there are five outcomes, so stereochemical analysis is likely
(c) the Lewis base (nucleophile) is the cyanide ion, which if you do not understand how to interpret the trimethylsilyl cyanide, the analogy of sodium cyanide is provided (so cyanide is CN^-)
*(d) if cyanide is the nucleophile, and this is a substitution and elimination reaction, then compound **W** is anticipated to have an sp^3 C-LG bond in it*

And, the analysis of the reactants:



Before you write ANYTHING, a visual analysis of the problem identifies exactly what is explicitly asked for in the problem: 5 different substitution and elimination products; and the answer spaces affirm that there are 2 substitution products and 3 elimination products

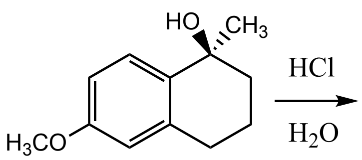


The following reaction produces two pairs of isomeric products derived from substitution and elimination pathways. Draw these pairs and indicate the stereochemical or structural relationship between them.

Although the text of this question is phrased in an open-ended way, at this point you still have a quite-limited number of possible chemical reactions to consider:

I. Lewis Acid-Base complexation/decomplexation
II. Brønsted Acid-Base proton transfer reactions
III. Substitution and Elimination reactions at sp^3 C-LG bonds

The text also says that pairs of isomeric products are formed (two and two only, and they are either stereoisomers or structural isomers).



In this example, it states that two pairs are formed. Stepping through the possible reactions:

I. Lewis Acid-Base complexation/decomplexation - not possible as there are no open shell Lewis acids present

II. Bronsted Acid-Base proton transfer reactions - in principle, there are two protonations, but there are not four

III. Substitution and Elimination reactions at sp^3 C-LG bonds - there is one sp^3 C-electronegative atom bond which is a stereocenter, and it has 5 β-Hs in two groups (from the group of 3, no E/Z diastereomers; from the group of 2, you cannot produce both of the E/Z diastereomers because of the small ring constraint), so there are the two pairs