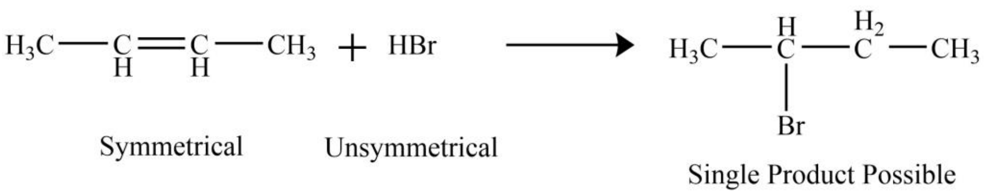
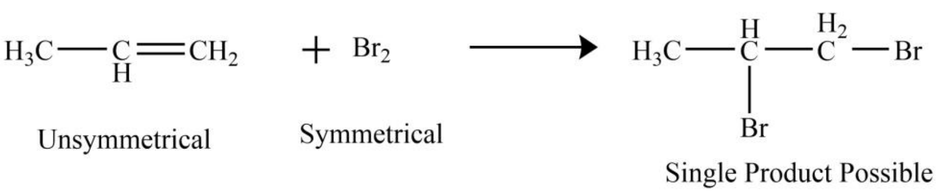
## ❖ Regio- and Chemoselectivity: Orientation and Reactivity

In this section, we will study the orientation (or regio-selectivity) and reactivity (chemo-selectivity) of addition to carbon-carbon multiple bonds.

### ➢ *Orientation of Addition to Carbon-Carbon Multiple Bonds*

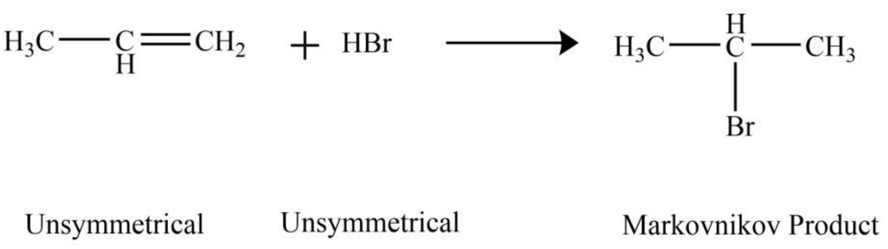
The structural orientation will not affect the final product if either the regent or the alkene is symmetrical in nature. On the other hand, if the alkene and attacking reagent both are unsymmetrical, two different products can be obtained as shown below.




In such a case, one of the products will be major and the other one will be minor depending upon their relative yield. In other words, the structural orientation is nothing but the preference that the double gives during its shift to decide which carbon to bind electrophile and which one to the nucleophile. The regioselectivity of electrophilic addition can be rationalized via two different rules as given below.

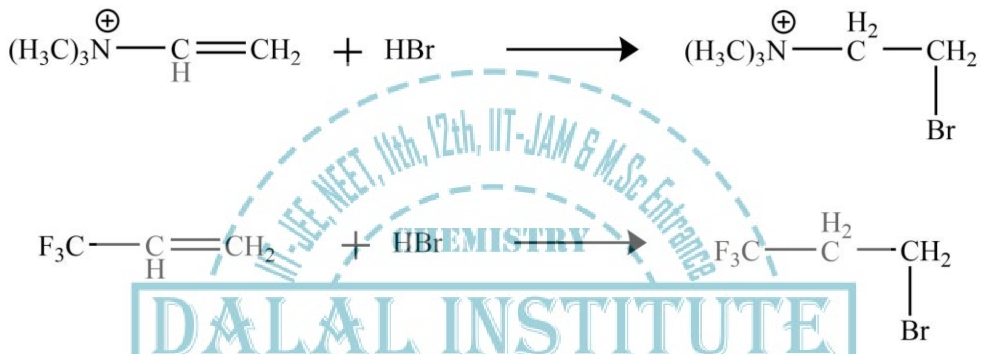
**1. Markovnikov's Rule:** The problem of structural orientation or regioselectivity in electrophilic addition was solved by a Russian chemist, Vladimir Markovnikov, in 1870 by giving an empirical rule called Markovnikov's rule. This rule states that when a polar reagent (like protic acid HX) is added to unsymmetrical alkenes, the electronegative part (i.e., halide) binds to the carbon with more alkyl groups; whereas the electropositive part (i.e., hydrogen) binds to the carbon with more hydrogens.




The theoretical basis for Markovnikov's Rule is the creation of a stable carbocation in the course of addition. The addition of the $H^+$ to one of the carbons in alkene gives rise to a positive charge on another carbon, yielding an intermediate carbocation.

If the carbocation is highly substituted, its stability will increase due to hyperconjugation and induction. The addition reaction's major product will be the one that is formed from the intermediate with the highest stability. So, the major product of the HX-addition (X is atom greater electronegativity than H) to an alkene has the H atom in the less substituted site and X in the more substituted site. Nonetheless, the other substituted product from less stable carbocation will still be yielded as minor having the opposite conjugate attachment of X.

**2. Anti-Markovnikov's Rule:** If the addition pathway carbon-carbon double bond doesn't involve an intermediatory carbocation, the regioselectivity will not be dictated by Markovnikov's rule; for instance, the free radical addition. Such additions are labeled as anti-Markovnikov additions because the halogen binds to the less substituted carbon (i.e., the reverse of Markovnikov addition).



The anti-Markovnikov rule can be demonstrated via the addition of HBr to isobutylene in the presence of hydrogen peroxide or benzoyl peroxide. The addition of hydrogen bromide to substituted alkenes was archetypal in the study of free-radical addition. Chemists in the early era found that the reason for the inconsistency in the ratio of Markovnikov to anti-Markovnikov products was because of the presence of peroxides (which are free radical ionizing substances). They thought that the O−O bond in the peroxide is comparatively weak; and therefore, light or heat, or sometimes even acting on its own, this bond gets broken to give two radicals species. These radicals can then interact with hydrogen bromide to give a Br radical, which in turn, reacts with the C−C double bond.

Now because the Br atom is comparatively bigger, more likely it will encounter and react with the least substituted carbon which can be attributed to less static interactions between the two. Additionally, just like a positively charged species, the radical will be more stable if the unpaired electron is in the more substituted site. The intermediary radical is then stabilized by the hyperconjugation effect. In the more substituted sites, a greater number of carbon-hydrogen bonds are aligned with the electron-deficient molecular orbital of the radical. All this implies that there are superior hyperconjugation effects, so that site will be more favorable. In such a case, the terminal carbon of the substrate will give rise to the primary addition product rather than the secondary one.

➢ ***Reactivity of Addition to Carbon-Carbon Multiple Bonds***

The double bond's reactivity towards the electrophilic addition increases with electron-donating groups and decreases with electron-withdrawing groups. For instance, consider the following order of reactivity.

$$CH_3CH{=}CH_2 > ClCH_2CH{=}CH_2 > Cl_2CHCH{=}CH_2 > CCl_3CH{=}CH_2$$

The above-given order gets revered if addition type becomes nucleophilic it will be supported by electron-withdrawing groups rather than electron-donating i.e.

$$CH_3CH{=}CH_2 < ClCH_2CH{=}CH_2 < Cl_2CHCH{=}CH_2 < CCl_3CH{=}CH_2$$

Also, the favourability of nucleophilic addition becomes significant only if three or four strongly electron-withdrawing groups like $F_2C{-}CF_2$ and $(NC)_2C{-}C(CN)_2$ are present. The substituents' effect is so dominant that polyhalo (or polycyano) alkenes almost always react via the nucleophilic pathway, whereas simple alkenes prefer to go via the electrophilic-addition route. Many reagents like ammonia which can only act as nucleophiles attack only react substrates vulnerable for such attacks. Conversely, the 'electrophilic only' type reagents simply refuse to add to the substrate like $F_2C{=}CF_2$. Furthermore, there are some reagents that add via electrophilic pathway if the substrate is simple alkene, but changes their mode of addition to nucleophilic if the substrate a polyhalo-alkene. For instance, HF and $Cl_2$ normally add via electrophilic attack, but it has been shown that $Cl_2$ and HF add to $(N{\equiv}C)_2C{=}CHC{\equiv}N$ and $F_2C{=}CClF$ via $Cl^-$ and $F^-$, respectively.




Reactivity Toward Bromine in Acetic Acid

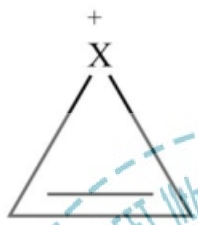
Substrates like the form −C=C−Z− (Z = CHO, COR, etc.), where the substituent is conjugated with the double bond, almost always react via nucleophilic addition. The order of activation by the substituent Z is given below.

$$NO_2 > COAr > CHO > COR > SO_2Ar > CN > CO_2R > SOAr > CONH_2 > CONHR$$

The nucleophilic attack on substituted alkenes can be attributed to the reduced electron density which attracts the electron-rich species. Nevertheless, some alkenes do react via an electrophilic pathway even after substituted with electron-withdrawing groups.

The rationale given above isn't totally suitable when comparing addition to carbon-carbon double vs triple bonds. For instance, even though the triple bond is richer in electron density than the double bond, it is less susceptible to electrophilic attack, and usually prefers to react via nucleophilic addition. It has been observed that reagents that form bridged intermediate prefer to add to double bond the triple one. Also, the rate ratio of alkenes to alkyne is reduced when electron-withdrawing groups are attached.

The higher susceptibility of triple bonds to nucleophilic attack can be attributed to the firm attachment of electrons in the triple bond due to smaller carbon-carbon bond length, which in turn make the electron density less available for any such attack. Alternatively, the lower susceptibility of triple bonds to electrophilic attack can be explained in terms of the accessibility of the empty orbital in the alkyne. In other words, it has been shown theoretically that bent alkynes have a $\pi^*$ orbital of lower energy than the $\pi^*$ orbital of simple alkenes; and therefore, linear alkynes can get a bent during transition states (electrophile addition) but alkene cannot. Also, bridged-ion intermediates arising from electrophilic addition to triple bonds will be more strained than their double bond counterparts; and therefore, slowing the rate of electrophilic addition. Nevertheless, triple bonds conjugated to the Z group favor the nucleophilic addition more aggressively.



More Strain

Less Strain



As expected, the attachment of alkyl groups typically increases the electrophilic addition's rates because of increased electron density; thought the order might change depending upon whether the intermediate formed is an open carbocation or a cyclic cation. If the first step is slowest (rate-determining) in electrophilic additions, like in the case of brominations, the rates for different substituted alkenes are dictated by the corresponding ionization potentials only and steric effects play little to no role.

No special types of substrates are required for free radical additions and the presence of a reactive free radical species predominantly dictates the overall rate. In the absence of initiator, reagents HBr or RSH) prefer to attack via ionic pathway; however, the mechanism changes to free radical addition as the in the radical initiator is mixed. Nucleophilic and electrophilic radicals behave more or less like nucleophiles and electrophiles, respectively; and the rate is affected accordingly. Nevertheless, it isn't expected but The rate of reaction of nucleophilic radical attack is faster with alkenes than with alkynes. Finally, it is also worthy to note that the steric effect might get an important role in some particular cases like catalytic hydrogenation where substitution decreases the reaction rate due to adsorption on the catalyst surface.

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