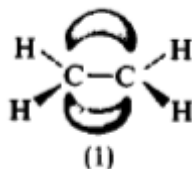


Electrophilic and Nucleophilic addition to C=C

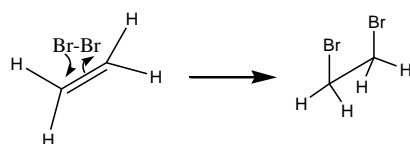
A carbon-carbon double bond consists of a strong sigma bond plus a weaker pi bond differently situated (1):



The pair of electrons in the pi orbital is more diffuse and less firmly held by the carbon nuclei, and so more readily polarizable, than those of the sigma bond, leading to the characteristic reactivity of such unsaturated compounds. As the pi electrons are the most readily accessible by incoming electrophile, the most characteristic reactions of the system are those initiated by electron-deficient species such as X^+ and $X\cdot$ (radicals can be considered electron-deficient species as they are seeking a further electron with which to form a bond), cations inducing heterolytic, and radicals homolytic, fission of the Pi bond. The former is usually found to predominate in polar solvents, the latter in non-polar solvents especially in the presence of light. Radical induced additions are not discussed here.

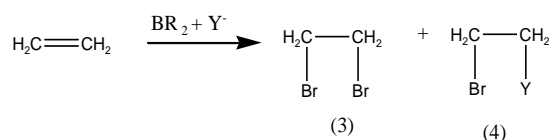
ADDITION OF HALOGENS

The decolorization of bromine, usually in CCl_4 solution, is one of the classical tests for unsaturation, and probably constitutes the most familiar of the addition reactions of alkenes. It normally proceeds readily in the absence of added catalysts, and one is tempted to assume that it proceeds by a simple, one-step pathway:



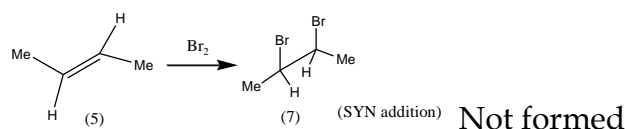
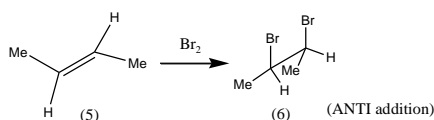
there are, however, two highly significant experimental evidence against this.

1) Firstly, if bromine addition is carried out in the presence of added nucleophiles Y^- or $Y\cdot$ (e.g. Cl^- , NO_3^- , $H_2O\cdot$) then, in addition to the expected 1,2-dibromide (3), products are also obtained in which one bromine atom and one Y atom, or group, have been added to the double bond (4):



This is clearly incompatible with a one-step pathway like the above, in which there would be no opportunity for attack by Y^- .

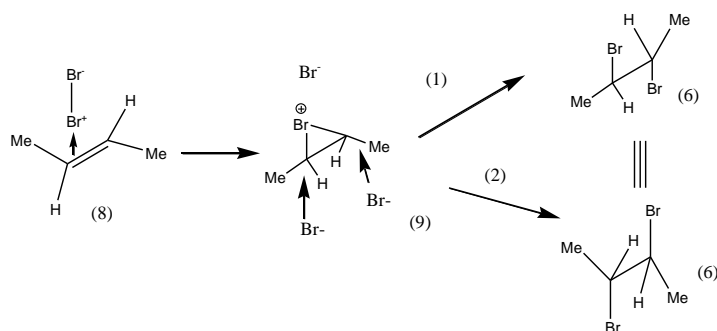
2) Secondly it is found that, in simple alkenes in which it can be detected, e.g. trans 2-butene (5), the two bromine atoms add on from opposite sides of the planar alkene, i.e. ANTI addition.



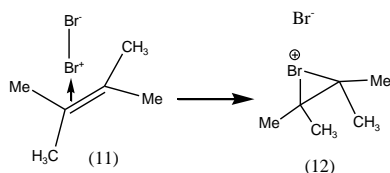
It is found in practice that the addition is almost completely stereoselective, i.e. «100% ANTI addition. This result also is incompatible with a one-step pathway, as the atoms in a bromine molecule are too close to each other to be able to add, simultaneously, ANTI.

To explain these two observations, a new type of pathway in which one end of a bromine molecule becomes positively polarized through electron repulsion by the π electrons of the alkene, there by forming a π complex with it. This then breaks down to form a cyclic bromonium ion (9)—an alternative canonical form of the carbocation (10). Addition is completed through nucleophilic attack by the residual Br-(or added Y^-) on either of the original double bond carbon atoms, from the side opposite to the large bromonium ion Br^+ , to yield the meso dibromide (6):

It has become possible to detect such intermediates with the help of a number of different fields: for example by n.m.r. spectroscopy.



Thus reaction of the 1,2-dibromide (11) with SbF_5 in liquid SO_2 at -60° led to the formation of an ion pair, but this exhibited not the two signal (one from each of two different groups of six equivalent protons) n.m.r. spectrum expected of (12). Instead one signal only (62-9) was observed, indicating that all twelve protons were equivalent, i.e. what is being observed is almost certainly the bromonium ion (12):

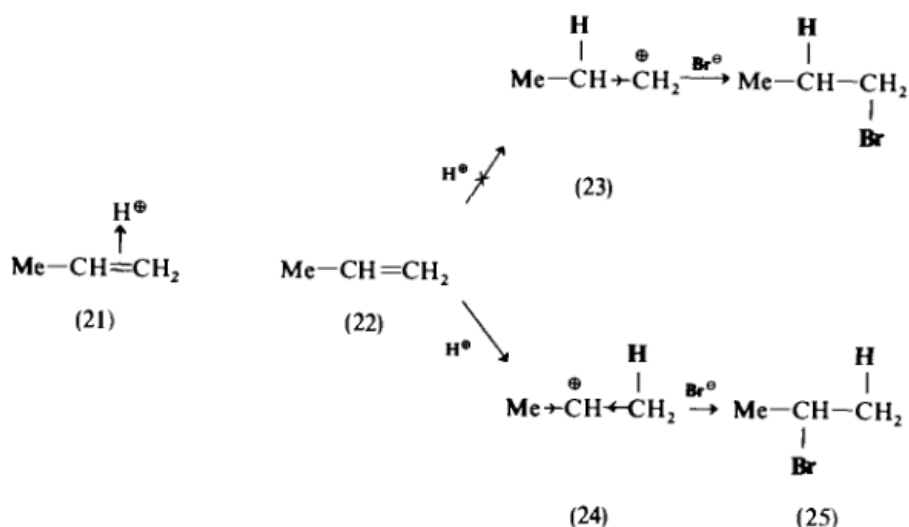


ORIENTATION OF ADDITION

When an unsymmetrical electrophile is added to an unsymmetrical alkene, e.g. propene, the problem of orientation of addition arises: this will be the case with the hydrogen halides. These are found to add to a given alkene in the rate order: $\text{HI} > \text{HBr} > \text{HCl} \gg \text{HF}$, i.e. in order of their acid strengths. This suggests rate-limiting addition of proton to the alkene, followed by rapid nucleophilic attack by Hal to complete the addition.

The addition in this case takes place according to the Markownikov Rule. In this case, first step is the addition of Electrophile (mostly a proton) to give the carbo cation. In the second step the nucleophile (e.g., halidde) is added to complete the addition.

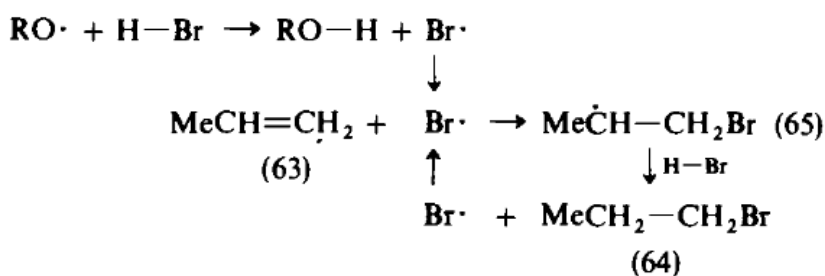
For example consider the addition of HBr to Propene under polar conditions:



As we know already that secondary carbocations are more stable than primary, (24) will be formed in preference to (23). In fact it appears to be formed exclusively, as the only addition product obtained is 2-bromopropane (25). Addition in which halogen (or the more negative moiety of any other unsymmetrical adduct) becomes attached to the more highly substituted of the two alkene carbon atoms is known as Markownikov addition.

Anti Markownikov addition:

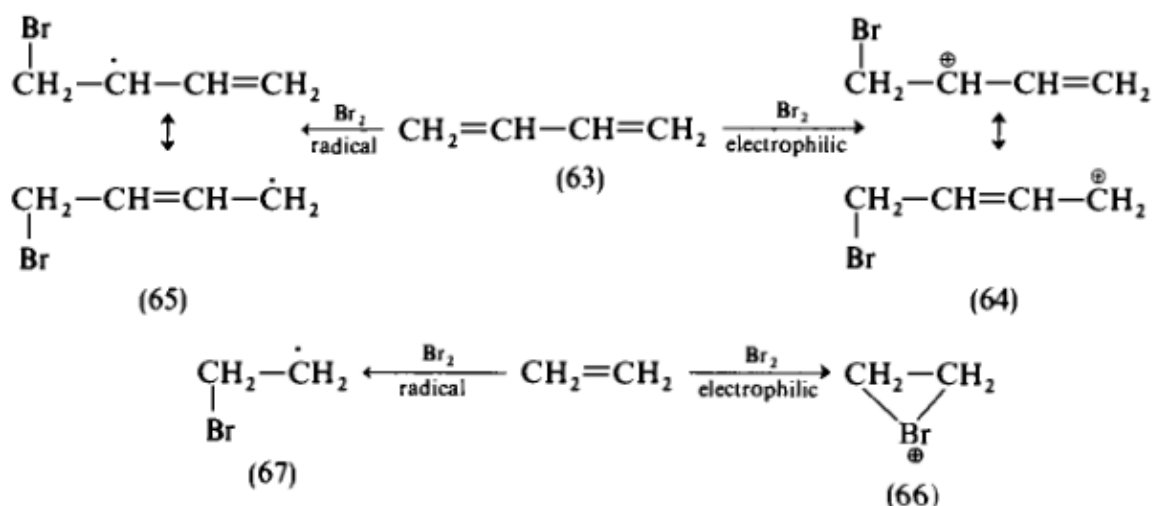
However when the reaction is carried out in free radical conditions e.g., in presence of H_2O_2 , Anti-Markownikov addition will take place to give 1-bromopropane ($\text{MeCH}_2\text{CH}_2\text{Br}$), via the preferentially formed radical intermediate, MeCHCH_2Br . As given below.



ADDITION TO CONJUGATED DIENES

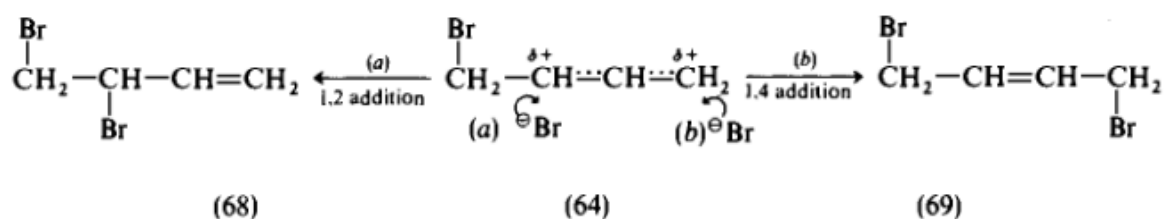
Conjugated dienes, e.g. butadiene (63) are more stable than their corresponding dienes in which the double bonds are not conjugated. This is reflected in their respective heats of hydrogenation. However, conjugated dienes undergo addition reactions more rapidly than non-conjugated dienes. This is due to the reason

because the intermediates (and, more importantly, the transition states that precede them) arising from initial attack by either electrophiles (64) or radicals (65) are of the allylic type, and are stabilized by delocalization to a considerably greater extent than was the initial diene. They are also stabilized with respect to the corresponding intermediates (66 and 67) obtained on similar addition to a simple alkene:



Electrophilic addition

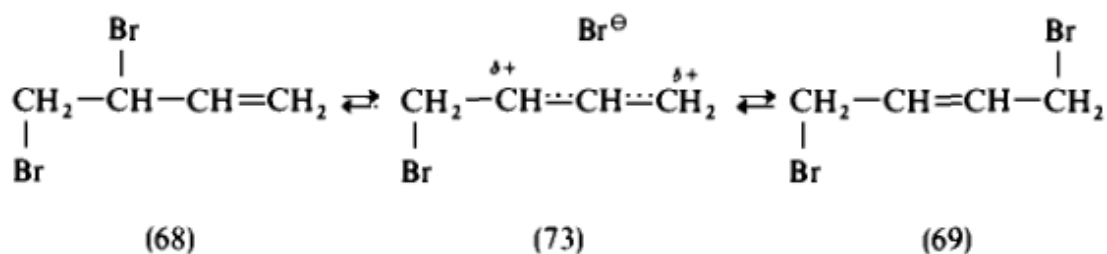
Initial attack will always take place on a terminal carbon atom of the conjugated system, otherwise the carbocationic intermediate (64), that is stabilised by delocalisation, would not be obtained. It is because of this stabilisation that a carbocation intermediate is formed rather than a cyclic bromonium ion. Completion of overall addition by nucleophilic attack of Br⁻ ion (64) can then take place at C2 [1,2-addition, (68)] or C4 [1,4-addition, (69)].



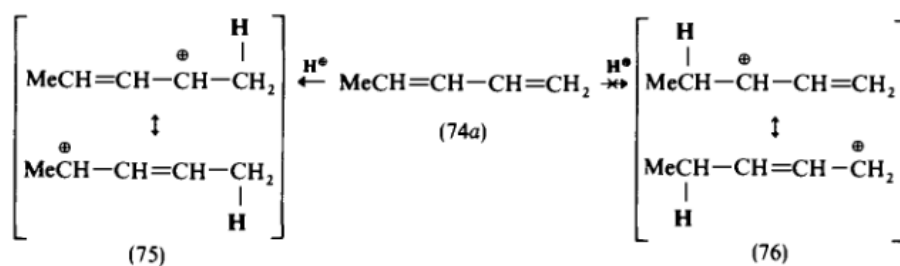
Both products are commonly obtained, but their relative proportions depend very much on the reaction conditions, e.g. temperature. Thus HCl with butadiene (63) at -60° yields only 20-25% of the 1,4-adduct (the rest being the 1,2-adduct), while at higher temperatures almost 75% of the 1,4-adduct was obtained. It is believed that with bromination at lower temperature the control is kinetic, the 1,2-adduct being

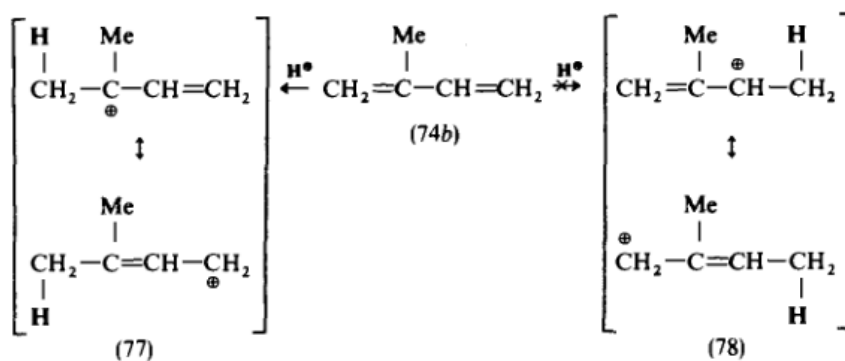
formed more rapidly from 64) than is the 1,4-adduct; while at higher temperatures, and/or with longer reaction times, equilibrium or thermodynamic control operates, and the thermodynamically more stable 1,4-adduct is then the major product. This is borne out by the fact that at higher temperatures pure 1,2- or 1,4-adduct can each be converted into the same equilibrium mixture of 1,2- +1,4- under the conditions of the reaction, 1,4-Addition is also favored by increasing solvent polarity.

It seems likely that the common intermediate is the ion pair 73) involving a delocalised carbocation; interconversion of 1,2- and 1,4-adducts, 68) and 69) respectively, could also proceed via such an intermediate:



With unsymmetrical dienes 74a and 74b) and unsymmetrical adducts, the problem of orientation of addition arises. Initial attack will still be on a terminal carbon atom of the conjugated system so that a delocalised allylic intermediate is obtained, but preferential attack will be on the terminal carbon that will yield the more stable of the two possible cations; i.e. 75) rather than 76), and 77) rather than 78)





NUCLEOPHILIC ADDITION

As in aromatic rings, the electron withdrawing group makes possible the attack of nucleophile, same is true for addition to alkenes. Thus the introduction of electron-withdrawing groups inhibit the addition initiated by electrophiles; the same groups are also found to promote addition initiated by nucleophiles. A partial order of effectiveness is found to be,

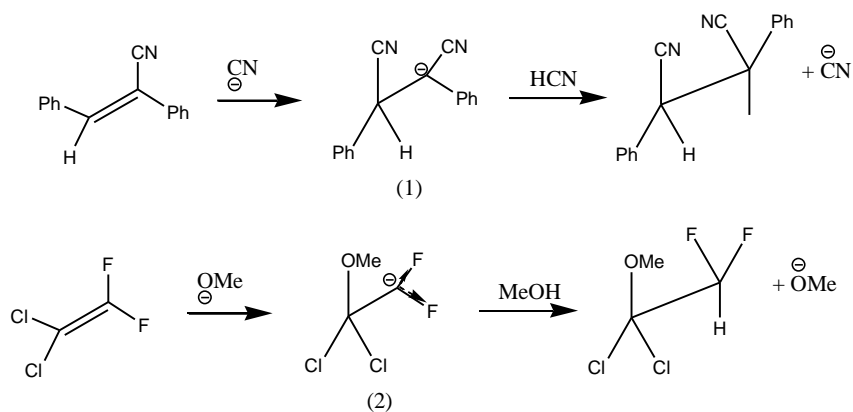


but SOR, SO₂R and F also act in the same way.

Such substituents operate by reducing π electron density at the alkene carbon atoms, thereby facilitating the approach of a nucleophile, Y⁻ but more particularly by delocalizing the negative charge in the resultant carban ion intermediate, e.g. (1) and (2). This delocalization is generally more effective when it involves mesomeric delocalization (1), rather than only inductive electron-withdrawal (2).

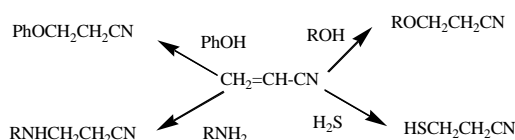
Cyanoethylation

One of the most important examples of Nucleophilic addition is one in which ethene carries a cyano-substituent (acrylonitrile).



Attack of Y⁻ or Y: on the unsubstituted carbon, followed by abstraction of a proton from the solvent, leads overall to the attachment of a 2-cyanoethyl group to the original nucleophile; the procedure is thus referred to as cyano ethylation. It is often carried out in the presence of base in order to convert HY into the more powerfully nucleophilic Y⁻.

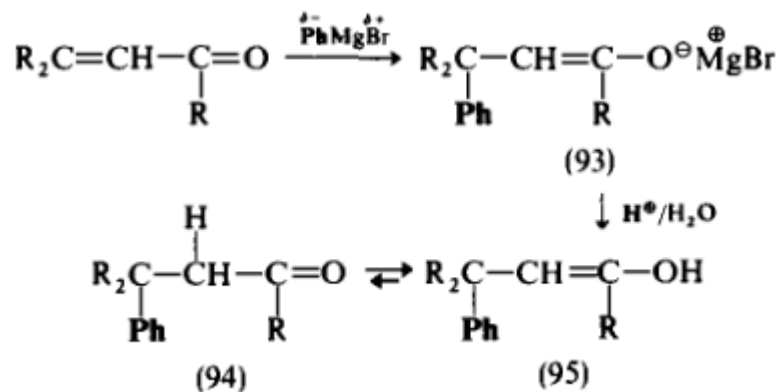
Addition of Y⁻, e.g. ⁻NH₂ will of course, form a carbanion, YCH₂–⁻CHCN, and, in the absence of a proton donor, this can add to a further molecule of CH₂=CHCN resulting, on subsequent repetition, in anionic polymerization.



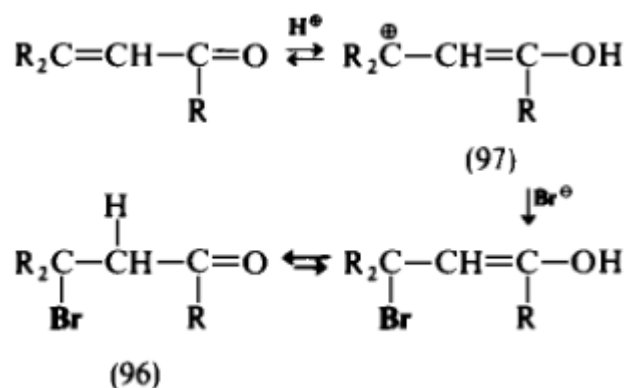
Addition to C=C–C=O

Among the commonest substituents 'activating' an alkene to nucleophilic attack is the C=O group, in such alpha, beta-unsaturated compounds as RCH=CHCHO, RCH=CHCOR', RCH=CHCO₂Et, etc. As the carbonyl group in such compounds can itself undergo nucleophilic attack, the question arises as to whether addition is pre- predominantly to C=C, to C=O, or conjugate (1,4-) to the overall C=C–C=O system.

In fact, the last type of addition (93) normally yields the same product (94) as would be obtained from addition to C=C, owing to tautomerisation of the first formed enol (95), e.g. with the Grignard reagent PhMgBr followed by acidification:



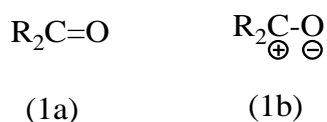
Incidentally, 1,4-electrophilic addition (e.g. HBr) also yields the C=C adduct (96) for the same reason, and can be looked upon formally as acid-catalysed (97) addition of the nucleophile Br⁻:



Less powerful nucleophiles such as ROH can also be made to add 1,4- under acid catalysis.

Nucleophilic addition to C=O

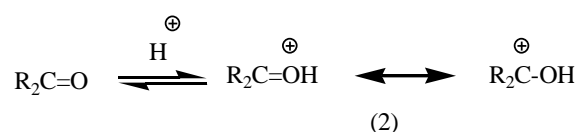
Carbonyl compounds exhibit dipole moments (μ) because the oxygen atom of the C=O group is more electronegative than the carbon. As well as the C=O inductive effect in the sigma bond joining the two atoms, the more readily polarizable pi electrons are also affected so that the carbonyl group is best represented by a hybrid structure (1).



As the C=O linkage looks similar with C=C, so it can also undergo addition reactions. However the difference is that the addition to alkene is normally initiated only by electrophiles. But attack in C=O, because of its bipolar nature, could be initiated either by electrophilic attack of X^+ or X on oxygen or by nucleophilic attack of Y^- or Y on carbon (radical-induced addition reactions of carbonyl compounds are rare).

In practice, initial electrophilic attack on oxygen is of little significance except where the electrophile is an acid (or a Lewis acid), when rapid, reversible protonation may be followed by slow, rate limiting attack by a nucleophile on carbon, to complete the addition, i.e. the **addition is then acid-catalyzed**.

Protonation will clearly increase the positive character of the carbonyl carbon atom (2): And so facilitate the Nucleophilic attack upon it.



In the absence of such activation, weak nucleophiles, e.g. H_2O :, may react only very slowly, but strong ones, e.g. $^- \text{CN}$, do not require such aid. Additions may also be **base-catalyzed**, the base acting by converting the weak nucleophile HY into the stronger one, Y^- , e.g.



Further, while acids may activate the carbonyl carbon atom to nucleophilic attack, they may simultaneously reduce the effective concentration of the nucleophile, e.g. $^- \text{CN} + \text{HA} \rightleftharpoons \text{HCN} + \text{A}^-$, $\text{RNH}_2 + \text{HA} \rightleftharpoons \text{RNH}_3^+ + \text{A}^-$

Many simple addition reactions of carbonyl compounds are thus found to have an optimum pH; this can be of great importance for preparative purposes.

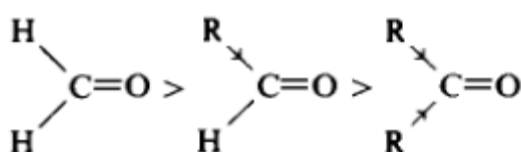
STRUCTURE AND REACTIVITY

In general, there are two factors, Electronic and steric, which effects the rate of addition reactions to C=O. Nucleophile structure also effects the rate.

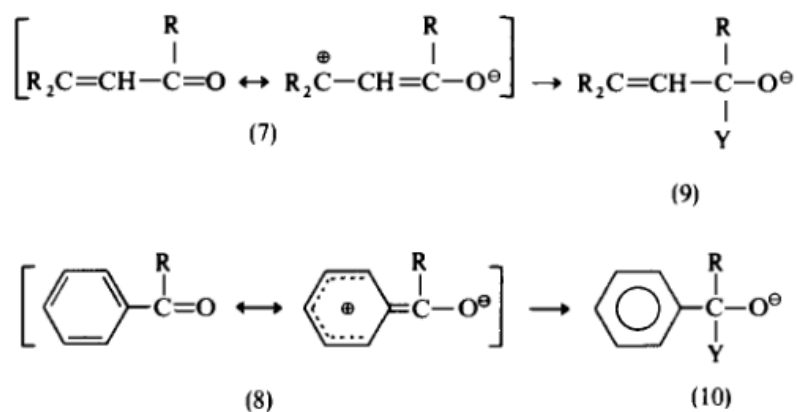
a) Electronic Factors:

All those factors which increase the positive charge on the Carbonyl carbon will increase the rate of reaction while those factors which decrease the positive charge on carbonyl will decrease the rate of reaction. E.g.,

i) Due to this reason the rate of addition to be reduced by electron- donating R groups and enhanced by electron-withdrawing ones; this is borne out by the observed sequence:



ii) R groups in which the C=O group is conjugated with C=C (1, 4- addition can also compete here), or with a benzene ring, also exhibit slower addition reactions than their saturated analogues. This is because the stabilization, through delocalization, in the initial carbonyl compounds (7 and 8) is lost on proceeding to the adducts (9 and 10), and to the transition states that precede them:

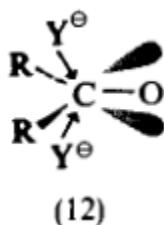


iii) The effect of electron withdrawing and donating groups can also be seen in the following series of compounds (11):



b) Steric Factors:

So far as steric effects are concerned, the least energy-demanding direction of approach by the nucleophile to the carbonyl carbon atom will be from above, or below, the substantially planar carbonyl compound.



Increasing bulk in the R groups will slow the reaction as the sp^2 hybridised carbon atom in the original carbonyl compound ($R-C-R$ bond angle $\ll 120^\circ$) is converted to an sp^3 hybridised carbon atom in the adduct—and in the preceding T.S.—($R-C-R$ bond angle $\ll 109^\circ$). The R groups thus move closer together as the reaction proceeds, i.e. the T.S. becomes more crowded, its energy level therefore increases and the reaction rate drops, as R increases in size. The observed drop in reaction rate, $H_2C=O > RHC=O > R_2C=O$, is thus determined by both electronic and steric effects. Increase in size of the nucleophile, with a given carbonyl compound, may also lead to a drop in reaction rate for the same reason.

c) Size of the nucleophile

For a given carbonyl compound, Rate of the reaction K will be influenced by the size of the nucleophile; thus the value of K for addition of the very bulky bisulphite anion ($S_2O_3^{2-}$, p. 213) to $(MeCH_2)C=O$ is only 4×10^{-4} , compared with $K = 38$ for addition of HCN (above) to the very similar ketone, $MeCH_2COMe$. The value of K is also influenced by the nature of the atom in the nucleophile that attacks the

carbonyl carbon atom, and of the bond that is thereby formed; as is observed in the following sequence for reaction with the same carbonyl compound:

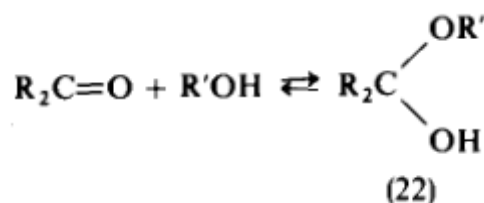


Other additions:

A number of the more characteristic addition reactions will now be studied in greater detail;

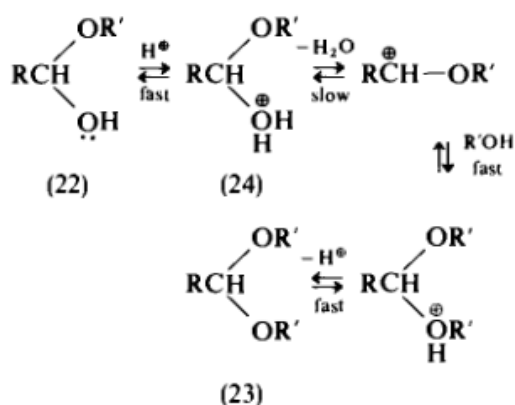
Alcohols (Acetal and hemiacetal formation)

The reactions of carbonyl compounds with alcohols, R'OH, to yield hemi-acetals (22),

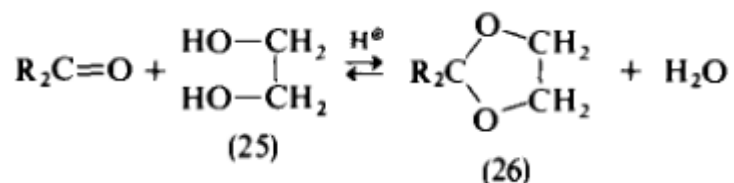


Stable hemi-acetals may, however, be isolated from carbonyl compounds carrying electron-withdrawing groups, e.g. Br₃CCHO with EtOH.

Conversion of the hemi-acetal to the acetal proper (23) requires specific acid catalysis, however i.e. it is loss of H₂O from (24) that is slow and rate limiting,

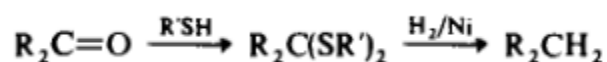


The reaction does not normally take place with ketones under these conditions (i.e. with simple alcohols), but they can often be made to react with 1,2-diols, e.g. (25), to form cyclic acetals (26):



Thiols

Carbonyl compounds react with thiols, RSH, to form hemi-thioacetals and thioacetals, rather more readily than with ROH; this reflects the greater nucleophilicity of sulphur compared with similarly situated oxygen.

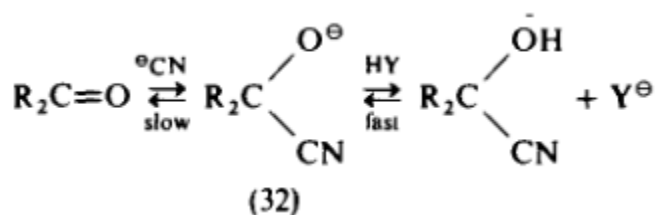


Hydrogen cyanide

Although addition of HCN could be looked upon as a carbanion reaction, it is commonly regarded as involving a simple anion. It is of unusual interest in that it was almost certainly the first organic reaction to have its mechanistic pathway established.

HCN is not itself a powerful enough nucleophile to attack C=O, and the reaction requires base-catalysis in order to convert HCN into the more nucleophilic CN^- ; the reaction then obeys the rate law. The addition of CN^- is reversible, and tends to lie over in favour of starting materials unless a proton donor is present; this pulls the reaction over to the right, as the equilibrium involving the cyanohydrin is more

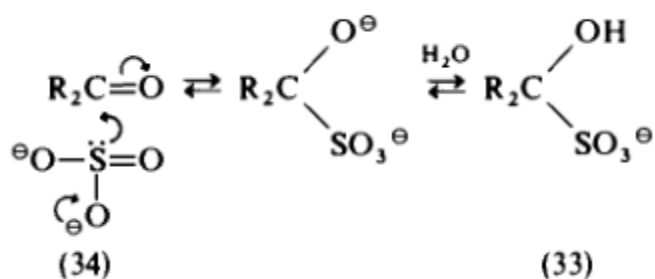
favourable than that involving the intermediate anion (32):



Attack by CN^- is slow (rate-limiting), while proton transfer from HCN or a protic solvent, e.g. H_2O , is rapid.

Bisulphite

Another classic anion reaction is that with bisulphite ion to yield crystalline adducts. The structure of these was long a matter of dispute before it was established that they were indeed salts of sulphonic acids (33), reflecting the greater nucleophilicity of sulphur rather than oxygen in the attacking anion. The effective nucleophile is almost certainly SO_3^{2-} (34) rather than HSO_3^- ($\text{HO}^- + \text{HSO}_3^- \rightleftharpoons \text{H}_2\text{O} + \text{SO}_3^{2-}$), as though the latter will be present in higher relative concentration the former is a much more effective nucleophile:



The attacking anion is already present in solution as such so no base catalysis is required, and SO_3^{2-} is a sufficiently powerful nucleophile not to require activation (by protonation) of the carbonyl group, so no acid catalysis is required either.