2 The Structures of Organic Molecules

This chapter uses the language of molecular orbital theory developed in Chapter 1 to explain some of the better known structural features of organic molecules. It is concerned with the ground state and with thermodynamic properties, not with how molecules behave in chemical reactions. It is important to realise that conjugation, for example, may, and usually does, make a molecule *thermodynamically more stable* than an unconjugated one, but it does not follow that conjugated systems are less reactive. Indeed, they are often more reactive or, we might say, *kinetically less stable*. Organic chemists use 'stable' and 'stability' without always identifying which meaning they are assuming. In this chapter we shall look at thermodynamic stability, and reserve reactivity for later chapters.

2.1 The Effects of π Conjugation

Much of organic chemistry is explained by making analogies from one compound or reaction to another. We use substituent effects, manifest in one compound or reaction, to inform us about the effects of the same substituents in other compounds or reactions. Substituent effects may be derived by calculation or from experimental measurements like heats of combustion or hydrogenation. But calculations alone do not make immediate *chemical* sense, and an experimental measurement still needs an explanation. The discussion in the following pages shows that we can work out, crudely but usefully, the effects of substituents on π systems in an easy, nonmathematical way, both on the overall energy, and on the energy and polarisation of the frontier orbitals.

2.1.1 A Notation for Substituents

There are three common types of substituents, each of which modifies the orbitals of conjugated systems in a different way (Fig. 2.1). They are: (a) simple conjugated systems, like vinyl or phenyl, which we shall designate with the letter C; (b) π-bonded systems which are also electron withdrawing, like formyl, acetyl,

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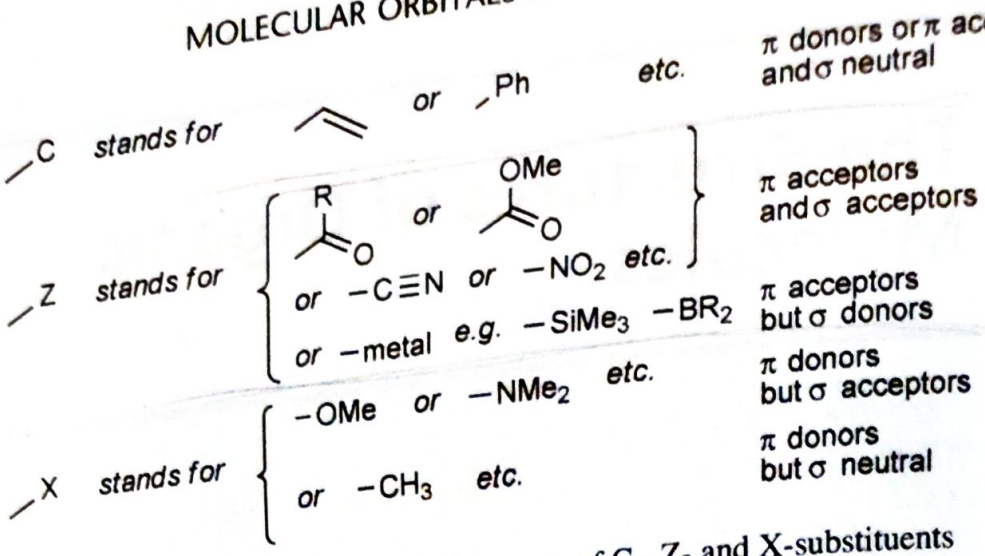


Fig. 2.1 Definitions and character of C-, Z- and X-substituents

cyano, nitro, and carboxy, which we shall designate with the letter Z; and (c) heteroatoms which carry a lone pair of electrons, which we shall designate with the letter X.

The C-substituents can be electron donating or electron withdrawing, depending upon what they are bonded to. They are called π donors or π acceptors, as appropriate, and their effect on the σ framework is small. The Z-substituents withdraw electrons from double bonds that they are conjugated to, and, since most of them have electronegative heteroatoms, they are also weakly electron withdrawing by an inductive effect within the σ framework. Such substituents are therefore strong π acceptors and usually weak, but occasionally, strong σ acceptors, especially for substituents like nitro, where an electronegative heteroatom is the point of attachment. Another group of π electron-withdrawing substituents is slightly different. Metals, and metalloids like the silyl group, are π acceptors [see (Section 2.2.3.2) page 77] but, because metals are more electropositive than carbon, they are σ donors. These substituents do not have a separate symbol, but their effect on the π system is more often than not what we shall be interested in, and they are included among the group labelled Z above. The X-substituents are electronegative heteroatoms with a lone pair of electrons, and they are therefore π donors and σ acceptors. We include simple alkyl groups in the category of X-substituents, because overlap of the C—H (or C—C) bonds [hyperconjugation, see (Section 2.2) page 69] supplies electrons to the π system. The effect is usually in the same direction as that of a lone pair but smaller, but alkyl groups are largely neutral with respect to the σ framework.

2.1.2 The Effect of Substituents on the Stability of Alkenes

2.1.2.1 C-Substituents. A double bond, lowers the π energy when it is conjugated to another double bond (see pages 28–30). The phenyl group is similar— the filled π molecular orbitals in styrene come at 2.14β, 1.41β, 1.00β, 0.66β below the α level, and the LUMO at 0.66β above the α level. The total π stabilisation is $2 \times 5.21\beta$, whereas the total π stabilisation for the separate components benzene and ethylene is $2 \times 5.0\beta$. A C-substituent raises the energy

of the HOMO (from 1β below the α level in ethylene to 0.62β below it in butadiene and 0.66β in styrene), and it lowers the energy of the LUMO (from 1β in ethylene to 0.62β in butadiene and 0.66β in styrene). Similarly with the coefficients—the terminal carbon atom, both in the HOMO and in the LUMO has a larger coefficient than the internal atom, 0.6 and ±0.37 in butadiene and 0.6 and ±0.39 in styrene.

2.1.2.2 Z-Substituents. The simplest Z-substituent is the formyl group in acrolein **2.1**. A simple Hückel calculation gives Fig. 2.2 in which we are looking at the p orbitals from above. This figure gives us what we want, but no insight.

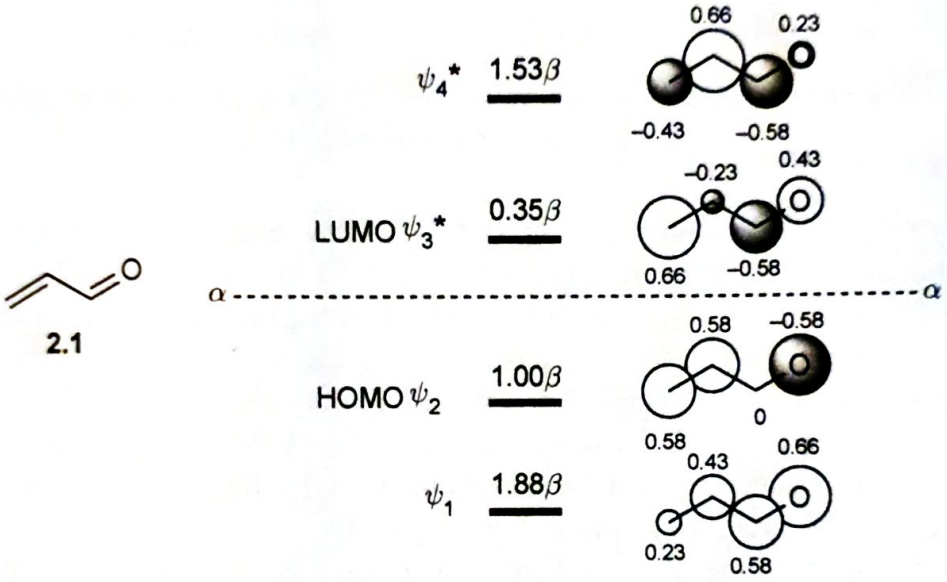


Fig. 2.2 The π molecular orbitals of acrolein. (These energies and coefficients were calculated using $h = 1$ and $k = 1$)

To estimate the π energies, we go to extremes: first we ignore the fact that one of the atoms is an oxygen atom and not a carbon atom, which gives us the orbitals of butadiene **2.3**. Then we go to the other extreme and treat the carbonyl group as a carbocation **2.2**. Normally we do not draw it this way, because such good stabilisation is better expressed by drawing the molecule (as in **2.1**) with a full π bond. The truth is somewhere in between. Organic chemists make the mental reservation about drawings like **2.1** and **2.2** that the butadiene-like system, implied by **2.1**, is only one extreme approximation of the true orbital picture for acrolein, and the other extreme approximation is an allyl cation, substituted by a noninteracting oxy-anion. The truth is somewhere in between—an allyl cation substituted by a strongly interacting oxy-anion.

The energies for the molecular orbitals for these two extremes are shown in Fig. 2.3. The true orbital energy for the orbitals of acrolein must be in between those of the corresponding orbitals of the allyl cation and butadiene. We can perhaps expect the true structure to be more like the butadiene system than the allyl cation system (for the same reason that we prefer to draw it as **2.1** rather than **2.2**). We can see that the effect of having a Z-substituent conjugated with the double bond of

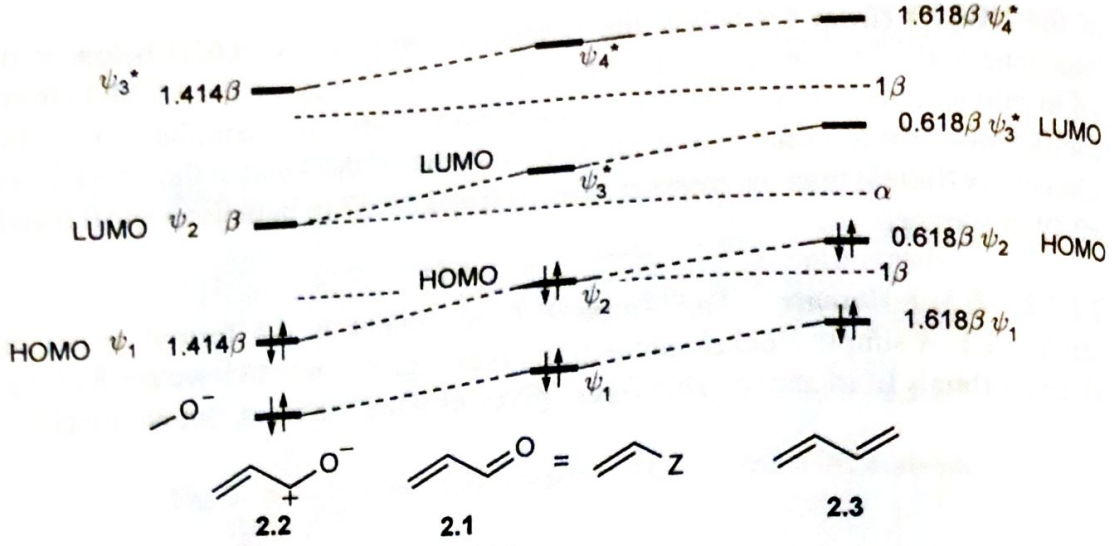


Fig. 2.3 The energies of the π orbitals of acrolein **2.1** as a weighted sum of the π orbitals of an allyl cation **2.2** and butadiene **2.3**

ethylene is to lower the π energy of the system, with ψ_1 and ψ_2 together having more π bonding than the separate orbitals of ethylene and a carbonyl group. The energy of the HOMO of acrolein, ψ_2, is, however, little changed from that of the π orbital of ethylene at the β level. Also, because it is butadiene-like, the HOMO and the LUMO will be closer in energy than they are in ethylene—the LUMO will have been lowered in energy relative to ethylene's and the HOMO will be very similar in energy. We have superimposed the orbitals of an allyl cation on those of butadiene, and, with suitable weighting, added them together.

We can use the same ideas to deduce the pattern of the coefficients. We have again contributions from the allyl-cation-like nature of acrolein and from its butadiene-like nature in Fig. 2.4. The coefficients for acrolein on the right can

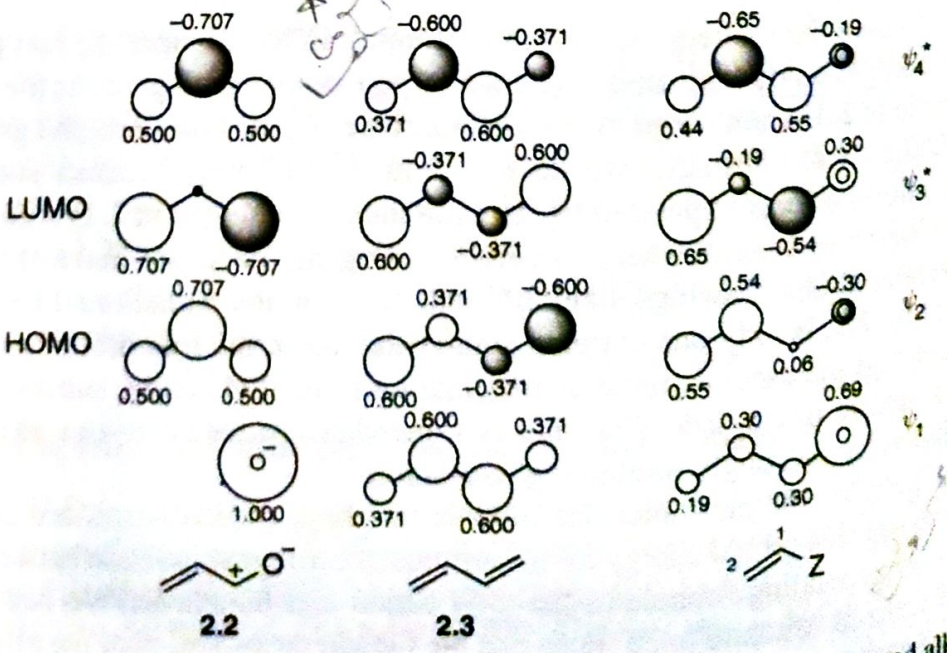


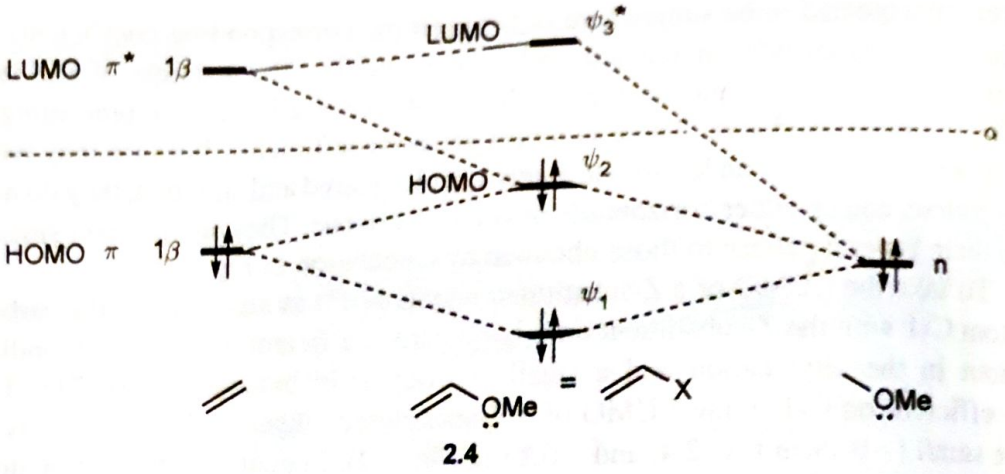
Fig. 2.4 Crude estimates of the coefficients of the π orbitals of a Z-substituted alkene as an unweighted average of the coefficients of an allyl cation **2.2** and butadiene **2.3**

then be expected to be somewhere in between the corresponding coefficients in the two components on the left and in the middle. The average of the two components is given on the right in Fig. 2.4, these arbitrarily representing a simple unweighted sum. These numbers are not coefficients, because they have not been arrived at with legitimate algebra, and, squared and summed, they do not, of course, add up either horizontally or vertically to one. They are however similar in their general pattern to those obtained by calculation in Fig. 2.2.

To take the LUMO of a Z-substituted alkene (ψ_3*) as an example, the carbon atom C-1 with the Z-substituent on it has a zero coefficient on the corresponding atom in the allyl cation and a small coefficient in butadiene (−0.371). The coefficient on C-1 in the LUMO of a Z-substituted alkene is therefore likely to be small (−0.19 in Fig. 2.4, and −0.23 in Fig. 2.2). In contrast, the carbon atom C-2 has large coefficients both in the allyl cation (0.707) and in butadiene (0.60). The coefficient on C-2 in the LUMO of a Z-substituted alkene is therefore large (0.65 in Fig. 2.4, and 0.66 in Fig. 2.2).

Turning now to the HOMO of acrolein (ψ_2) and C-1, the allyl cation has a large coefficient (0.707) on the central atom, but butadiene has a small coefficient on the corresponding atom (0.371). The two effects act in opposite directions—the conjugation causing a reduction in the coefficient on the carbon atom carrying the formyl group, and the allyl-cation-like character causing an increase in this coefficient. The result is a medium-sized coefficient (0.54 in Fig. 2.4, and 0.58 in Fig. 2.2). For C-2, it is the allyl cation that has the smaller coefficient (0.500) and the butadiene the larger (0.600). The combination is again a medium-sized coefficient (0.55 in Fig. 2.4 and 0.58 in Fig. 2.2). We have already said that acrolein is probably better represented by the drawing **2.1** than by the drawing **2.2**, from which we may guess that it is the butadiene-like character which makes the greater contribution to the HOMO, in which case acrolein will have its HOMO coefficients polarised in the same way as those of butadiene, but less so (as they are in Fig. 2.4).

2.1.2.3 X-Substituents. In an X-substituted alkene like methyl vinyl ether **2.4**, we have a lone pair of electrons brought into conjugation with the double bond. We can deduce the pattern of molecular orbitals by an interaction diagram, Fig. 2.5, resembling that for the allyl anion in Fig. 1.28. The difference is that the lone pair on oxygen, being on an electronegative element, is lower in energy than the p orbital on carbon. This lowers the energy of all the orbitals ψ_1–ψ_3* relative to their counterparts in the allyl system. However the orbital ψ_1 is created by the interaction of the lone-pair orbital on the oxygen atom, labelled n, in a bonding sense with both π and π*, strongly with the former and weakly with the latter, because of the greater separation of energy of the interacting orbitals. In contrast, ψ_2 is derived by the weak interaction of n with π* in a bonding sense, and strongly with π in an antibonding sense. As a result ψ_1 is lowered in energy more than ψ_2 is raised, and the overall energy is lowered relative to the energy of the separate orbitals of the π bond and the lone pair. As usual, conjugation has lowered the overall energy. The net π stabilisation has been measured crudely by comparing the heats of hydrogenation of ethylene and ethyl vinyl ether as



2.4

Fig. 2.5 Energies of the π orbitals of an X-substituted alkene

25 kJ mol^{-1} (6 kcal mol^{-1}). We should also note that both the HOMO and the LUMO of an X-substituted alkene are raised in energy relative to the HOMO and LUMO of ethylene, with the HOMO raised more than the LUMO.

In order to deduce the coefficients for an X-substituted alkene, we adopt the idea that at one extreme, the lone pair on the oxygen atom is fully and equally involved in the overlap with the π bond, so that the orbitals will be those of an allyl anion **2.5**. At the other extreme, to make allowance for the fact that the lone pair on an electronegative atom like oxygen is not as effective a donor as a filled p orbital on carbon, it is an alkene with no participation from the lone pair on the oxygen atom. Thus we add a bit of allyl anion-like character, on the left in Fig. 2.6, to the unperturbed alkene, in the centre of Fig. 2.6. The average of the two components is given on the right in Fig. 2.6, these representing a simple unweighted sum. As with the Z-substituted alkene, these numbers are not coefficients, but they match the *pattern* of large, medium and small coefficients

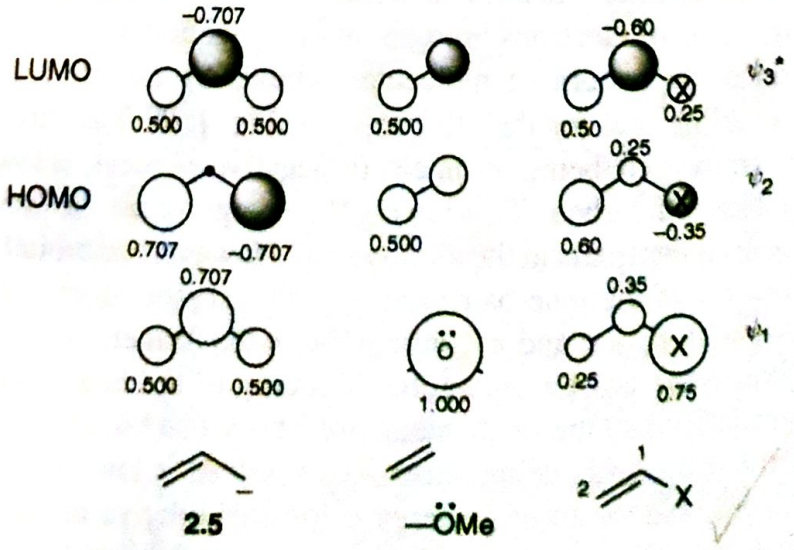


Fig. 2.6 Crude estimates of the coefficients of the π orbitals of an X-substituted alkene as an unweighted sum of the coefficients of an allyl anion **2.5** and an alkene

obtained from a simple Hückel calculation. The lowest-energy orbital ψ_1 has a large contribution from the lone pair added to the lowest-energy orbital of the allyl anion, creating an orbital strongly polarised towards the X-substituent. For the HOMO, the unperturbed alkene has (necessarily) equal coefficients on each atom, and the allyl anion has a zero coefficient on the atom bearing the X-substituent. The result of mixing these two is ψ_2, a strongly polarised orbital as far as the coefficients on C-1 and C-2 are concerned. For the LUMO, the unperturbed alkene again has equal coefficients, but the allyl anion has a larger coefficient on the carbon atom carrying the X-substituent than on the other one. The result is ψ_3*, an orbital mildly polarised in the opposite direction.

2.1.3 The Effect of Substituents on the Stability of Carbocations

2.1.3.1 C- and X-substituents. A molecule having an empty p orbital on carbon, and therefore carrying a positive charge, will be lowered overall in energy by π conjugation with a C-substituent. We have seen this already, from the opposite direction, when we moved from the orbitals of an alkene to those of an allyl cation in Fig. 1.28. Similarly, the effect of an X-substituent is even more stabilising, as we saw in considering the orbitals of a carbonyl group in Fig. 1.51, which could equally well have been drawn with two electrons in the p_O orbital and none in the p_C. The weakest kind of X-substituent is an alkyl group to which we shall return while discussing hyperconjugation [see (Section 2.2) page 69] .

2.1.3.2 Z-substituents. The effect of a Z-substituent is not so straightforward. Fig. 2.7 shows the interaction between the orbitals of a carbonyl group and an empty p orbital on carbon. The set of π orbitals in the middle is essentially the same as the set of orbitals in the middle of Fig. 2.5, but with two fewer electrons in the π system. We deduce that there is an overall lowering of π energy, because ψ_1 is lower in energy than the $\pi_{C=O}$ orbital as a result of the interaction with the empty p orbital, p_C. However, this lowering is not large, because this interaction is

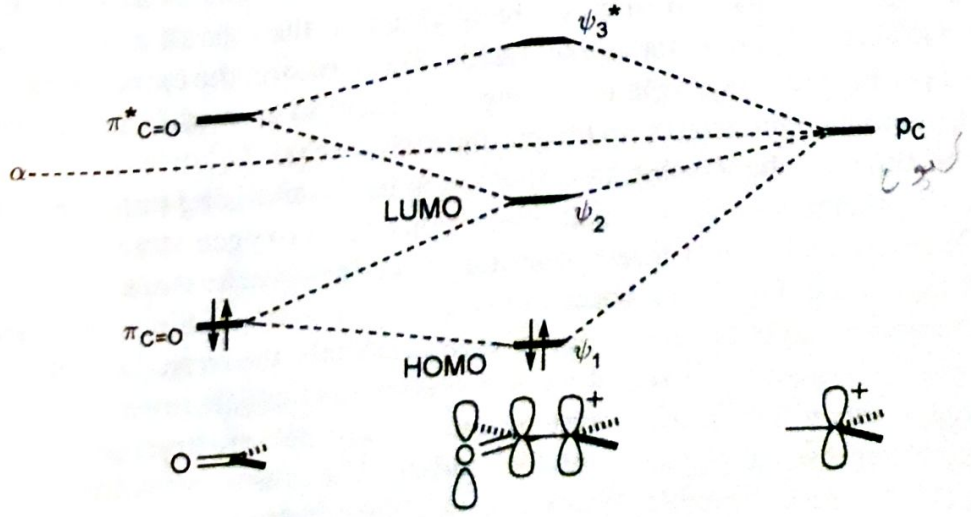


Fig. 2.7 The π orbitals of a carbocation conjugated to a Z-substituent

between an orbital at the α level and a π orbital, $\pi_{C=O}$, low in energy (Fig. 1.51). The overall lowering in π energy is not therefore as great as the corresponding lowering in energy in ψ_1 of the allyl cation (E in Fig. 1.28). We might notice at this stage that ψ_2 is lowered in energy, whereas it was not lowered at all in the allyl cation. This orbital is made up by interaction of the p orbital with the π orbital of the carbonyl group in an antibonding sense and with the π^* orbital in a bonding sense, as with the allyl cation, but, since both the π and π^* orbitals are lower in energy in a carbonyl group than in an alkene, the antibonding contribution to ψ_2 is weaker and the bonding contribution stronger.

It is well known, however, that a carbonyl group does not appear to be a stabilising influence on a carbocation, and yet we have just deduced that it is stabilised in the π system. The most obvious factor that we have left out in the argument above is the Coulombic effect of the partially ionic character of both the σ and the π bond of a carbonyl group. The polarisation of both bonds towards the oxygen atom (Fig. 1.51) places a significant positive charge on the carbonyl carbon atom, immediately adjacent to the full positive charge on the nucleus of the carbon atom carrying the empty p orbital. This is energy-raising, because the now relatively exposed nuclei repel each other. We thus have a small energy-lowering contribution from the π overlap, but an energy-raising contribution from an adverse Coulombic effect. Evidently the latter wins. For the first time, we see that conjugation cannot always be relied upon to lower the overall energy.

2.1.4 *The Effect of Substituents on the Stability of Carbanions*

The orbitals for the interactions of C-, Z- and X-substituents with a filled p orbital on carbon are the same as those we have just used for their interaction with an empty p orbital, but with two more electrons to feed into the π orbitals. The interaction of a C-substituent with a filled p orbital gives us the allyl anion orbitals, and these are just as π stabilised as the allyl cation (Fig. 1.28).

Even better, conjugation of a filled p orbital with a Z-substituent gives us the same orbitals as in Fig. 2.7, but now ψ_2 is filled, and, since it is lowered in energy by the interaction more than ψ_2 of the allyl anion, the overall π energy is lower still. This is the π system for an enolate ion. Furthermore, the extra electrons mean that a partial positive charge is no longer adjacent to an unshielded nucleus, and the Coulombic repulsion is no longer unusually large.

This time it is the X-substituent that might be destabilising rather than stabilising. The interaction of a lone pair of electrons on an oxygen atom, as a model for an X-substituent, and a filled p orbital on carbon create the π orbitals of the carbonyl group (Fig. 1.51), but with two electrons in π^*_{CO}. Since this interaction is straightforwardly the interaction of atomic orbitals, the overall effect is a rise in energy, because π^*_{CO} is raised more in energy than π_{CO} is lowered. In practice, although this effect in the π system must be present, electronegative elements usually stabilise an adjacent 'anionic' carbon. The reason is twofold. In the first place, there is a Coulombic effect working in the σ framework against the effect in the π system. In the second place, we do not usually have an anion—what we have is a carbon-metal (C—M) bond. A C—M bond is polarised, with the filled σ orbital

having a large coefficient on the electronegative element, which in this case is the carbon atom (Fig. 1.48). Thus, the C—M bond has many of the properties of a genuine carbanion, the repulsive interaction of the lone pair on the X-substituent and the σ_{CM} orbital will be energy-raising, just as it would be for a carbanion. But the presence of a metal changes the story, because it has empty orbitals that can accept coordination from the lone pairs of the electronegative heteroatom. This coordination may be directly within the molecule, but is more often present in an aggregate, and it is always powerfully energy-lowering, making any effect on the π overlap less important.

The one X-substituent that probably does destabilise an anion is an alkyl group. An alkyl group, although classified as an X-substituent, is not a σ acceptor, nor does it have coordination sites. Its destabilising effect is by σ conjugation [see (Section 2.2.1) page 69]. In contrast, sulfur- and phosphorus-based groups like phenylthio or diphenylphosphinyl are X-substituents that are well known to be anion-stabilising. This phenomenon, and the even less expected effect of an electropositive element like silicon stabilising an adjacent anion, has most simply been accounted for by invoking overlap of an empty d orbital on sulfur, phosphorus or silicon with the filled p orbital of the anion. This is unmistakably stabilising, as usual with the overlap of a filled with an unfilled orbital, but the contribution it makes is unlikely to be significant, because the 3d orbitals on these second-row elements and a 2p orbital on carbon are too far apart in energy and too ill-matched in size to have a significant interaction. Anion stabilisation by sulfur, phosphorus and silicon appears to be best accounted for by σ conjugation [see (Section 2.2.3.2) page 77].

2.1.5 The Effect of Substituents on the Stability of Radicals

2.1.5.1 C-, Z- and X-Substituents. All three kinds of substituent stabilise radicals. A C-substituent gives the orbitals of the allyl radical, which is just as stabilised as it was for the cation and anion (Fig. 1.28). A Z-substituent gives us the same orbitals as those in Fig. 2.7, but with one electron in ψ_2, leading to an overall drop in π energy and a reduction in the amount of Coulombic repulsion that destabilised cations. Finally an X-substituent gives us the orbitals of the carbonyl group (Fig. 1.51) but with one electron in π^*_{CO}. With two drops in energy from the doubly filled orbital π_{CO} matched by only one rise in energy from the singly occupied π^*_{CO}, the overall effect is a drop in energy.

2.1.5.2 Captodative Stabilisation.[9] A particularly telling case is a radical that has both an X- and a Z-substituent, either directly attached to a radical centre or conjugated to it through a π system, as in the long-lived radicals **2.6–2.10**. Radicals like this are called captodative or merostabilised, and have been claimed to be more stabilised than the sum of each component would suggest. Since both types of substituent can stabilise a radical, it is reasonable that both together can continue to stabilise a radical. We can see how this might be in Fig. 2.8. The interaction of an X-substituent and a Z-substituent creates the set of orbitals in the centre. There is a rise in energy in creating ψ_3, but there is only one electron in this

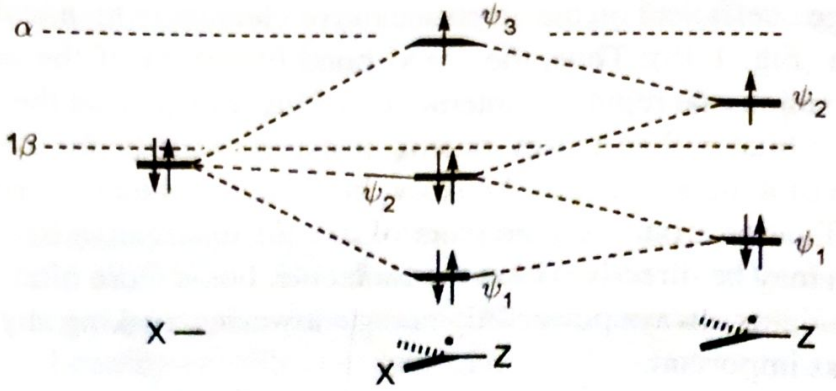
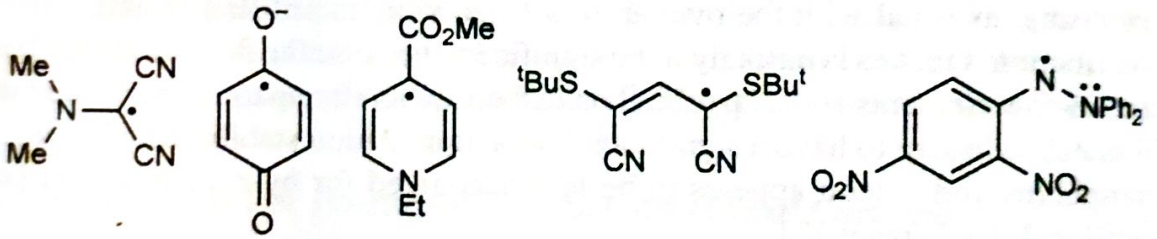


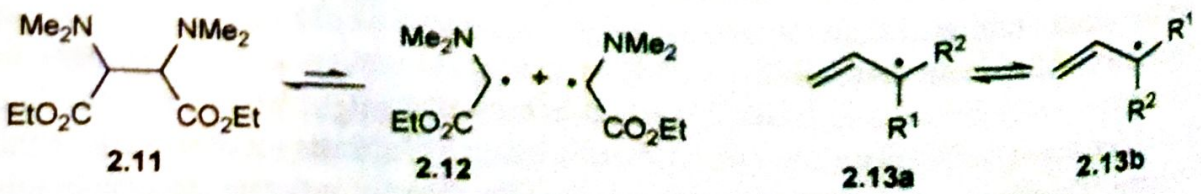
Fig. 2.8 The effect of bringing an X-substituent into conjugation with a Z-substituted radical

orbital. There is a small drop in energy in creating ψ_2 and a more significant drop in energy in creating ψ_1, both of which have two electrons in them. Overall the energy may have dropped and the radical as a whole is lower in π energy than the separate components.



2.6 **2.7** **2.8** **2.9** **2.10**

However, it is not obvious whether captodative substitution is better at lowering the overall energy than having two Z-substituents or two X-substituents. It is clear experimentally that, if there is a specific captodative effect, it is small, never more than about 25 kJ mol^{-1} (6 kcal mol^{-1}). Experimental evidence that seems to imply special stabilisation to captodative radicals is the ease of the reversible C—C fragmentation of the diaminosuccinate **2.11**, in which the rate implies that the captodative radical **2.12** is some 17 kJ mol^{-1} (4 kcal mol^{-1}) lower in energy than might be expected by adding the stabilising effects of each of the substituents. More evidence comes from measurements of the rate of rotation about the C-2 to C-3 bond of a range of allyl radicals **2.13**. At the point of highest energy in the rotation, the radical will lose its allylic character, and be stabilised only by the substituents R^1 and R^2. The captodative radical with $R^1 = OMe$ and $R^2 = CN$ has the lowest activation energy, some 12 kJ mol^{-1} (2.9 kcal mol^{-1}) lower than the sum of the substituent effects would have suggested, but for the radicals with

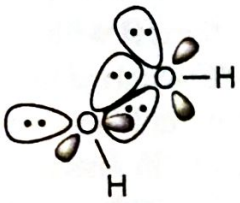


2.11 **2.12** **2.13a** **2.13b**

$R^1 = R^2 = OMe$ and $R^1 = R^2 = CN$ the activation energies are some 24 kJ mol^{-1} (5.7 kcal mol^{-1}) higher in energy. It seems that neither two X- nor two Z-substituents have twice the stabilising effect of one, but one of each does have an additive effect. In this formulation at least, the captodative effect does appear to be real.

2.1.6 *Energy-Raising Conjugation*

Not all conjugation is energy-lowering, especially when a filled p orbital is conjugated with an X-substituent, in which the repulsive effect of two filled atomic orbitals inherently destabilises the π system. Examples of the repulsive interaction of two filled p orbitals where there are no mitigating factors are the conformations adopted by hydrogen peroxide **2.14** and hydrazine **2.15**. The overlap is avoided by twisting about the X—X bond, so that the two lone pairs are as little in conjugation as possible.



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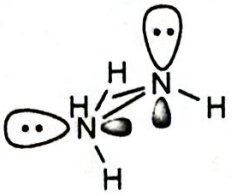
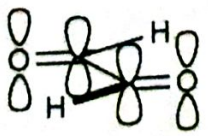


2.15

Another energy-raising conjugation can be found when two carbonyl groups are adjacent. There may be some π stabilisation, but Coulombic repulsion between the two carbon atoms, both of which bear a partial positive charge, is substantially destabilising. Evidence for destabilisation comes from the extent to which α-diketones like 1,2-cyclohexanedione **2.16** enolise, and evidence for the π stabilisation can be found in such molecules as glyoxal **2.17**, where the carbonyl groups stay in conjugation rather than twisting. Twisting would do nothing to relieve the Coulombic repulsion between the charges on the carbon atoms, but it would remove the π conjugation. The s-*trans* conformation is favoured, because the relatively large partial negative charges on the oxygen atoms repel each other. With two more electrons—the enediolate ion **2.18** has π molecular orbitals like those of butadiene, but with two electrons in ψ_3*. It is a conjugated system higher in energy than the sum of the separated components.

2.16



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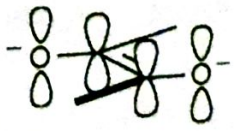


2.18

2.2 σ Conjugation—Hyperconjugation

Conjugation has been discussed so far only as something taking place between p orbitals in a π system. However, it is possible to consider the conjugation of

σ bonds constructed from hybridised orbitals with p orbitals. The major interactions will be between the C—H orbitals σ and σ^* of a C—H or C—C bond with a p orbital. The overlap of σ bonds with p orbitals is called hyperconjugation, a serious misnomer, because hyperconjugation, far from being especially strong, as the prefix hyper implies, is a feeble level of conjugation compared with the kind of π-conjugation that we have seen so far. Another term that is sometimes used is σ conjugation, on the grounds that it is conjugation of a σ bond with something else, but this is not satisfactory either, since the overlap is π in nature not σ. Yet another term that is used is vertical stabilisation, which is not a misnomer, but is not usefully specific about its nature.

2.2.1 C—H and C—C Hyperconjugation

2.2.1.1 Stabilisation of Alkyl Cations. Hyperconjugation is most evident in the stabilisation given to an empty p orbital on carbon by a neighbouring alkyl group, explaining how alkyl substituents stabilise carbocations. Fig. 2.9 shows the interaction of the σ orbitals of the C—H bond on the left with the empty p orbital on the right. The interaction in Fig. 2.9 is similar to that shown in Fig. 1.28 for the allyl cation, except that it is a σ bond instead of a π bond interacting with the empty p orbital. Because the σ_{CH} orbital in Fig. 2.9 is lower in energy than the π orbital in Fig. 1.28, the hyperconjugative interaction with the empty p orbital is less effective, and the overall drop in energy $2E$ is less than it was for simple π-conjugation.

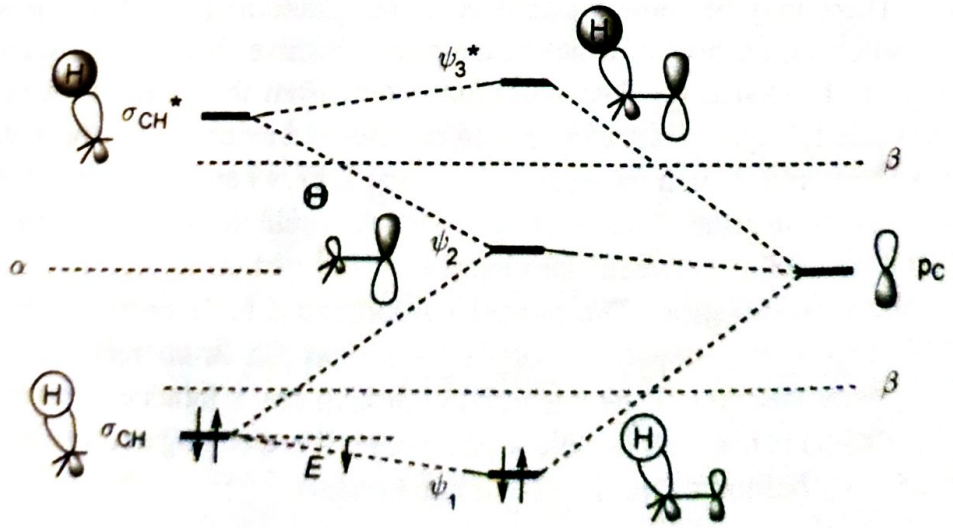


Fig. 2.9 Interaction of the orbitals of a σ C—H bond with an empty p orbital on carbon

As usual, hybridisation, although a convenient device, is unnecessary—the energy lowering could equally well have been explained using the p_z orbital on carbon, with the most significant interaction illustrated on the left in Fig. 2.10. Indeed, this provides a more simple way to appreciate that the lowest-energy conformation of the cation is not overwhelmingly that in which one of the σ bonds is aligned to overlap with the empty p orbital. Because the two π-type orbitals, π_z and π_y have the same energy, the interactions in the two conformations shown in

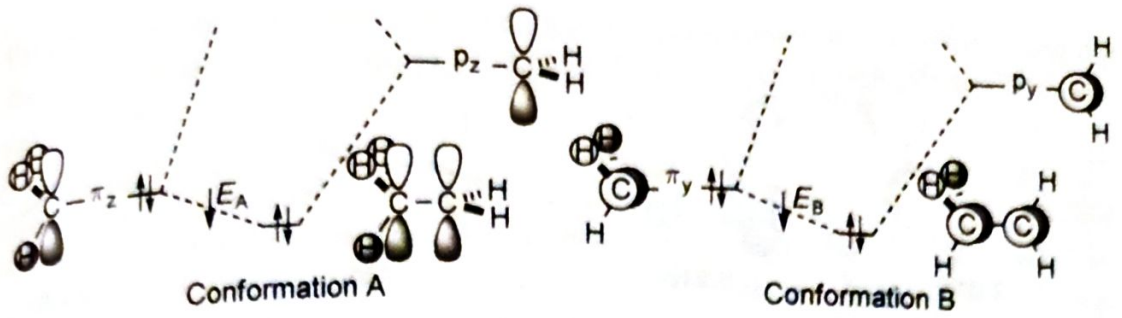
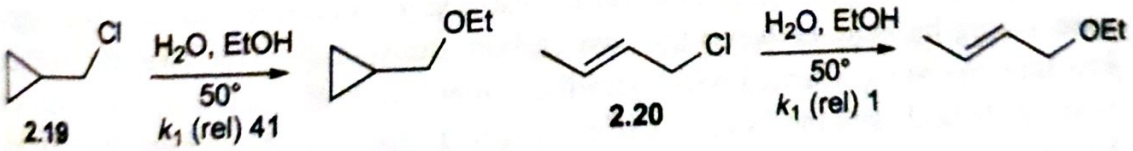


Fig. 2.10 Orbital interactions stabilising two conformations of the ethyl cation

Fig. 2.10 are, to a first approximation, equal ($E_A = E_B$). We can expect that the barrier to rotation about the C—C bond of the ethyl cation will be small. Although intuitively reasonable, it is not so easy to set up an interaction diagram using hybridisation to show that the energy-lowering effect of *imperfectly* lined up overlap of *two* C—H σ orbitals with the empty p orbital is the same as *perfectly* lined up overlap of *one*.

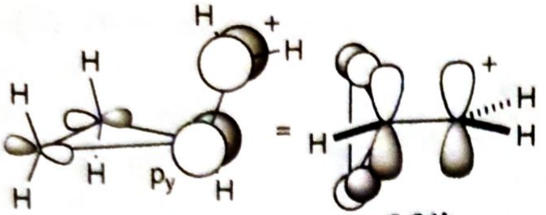
The overlap and its consequences, as illustrated in Fig. 2.9, could equally well have been drawn with C—C bonds in place of the C—H bonds. The energies of C—C and C—H orbitals are similar to each other, and the value of E will be similar. Alkyl groups in general are effectively π electron donors, in much the same way as, but to a lesser extent than, a double bond or a lone pair and we classify alkyl groups as X-substituents.

One case where C—C bonds are exceptionally effective in hyperconjugation is in the stabilisation provided by a cyclopropyl substituent to an empty p orbital. The cyclopropylmethyl cation is actually better stabilised than an allyl cation, as judged by the more rapid ionisation of cyclopropylmethyl chloride **2.19** than of crotyl chloride **2.20**. In this case, hyperconjugation appears, unusually, to be better than π conjugation.

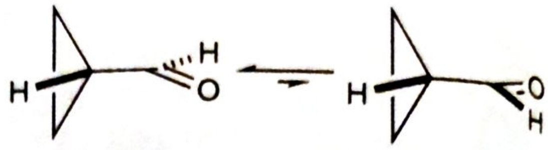


2.19 k_1 (rel) 41 **2.20** k_1 (rel) 1

It can be explained using the Walsh orbitals of a cyclopropane (Fig. 1.42), where one of the degenerate pair of highest occupied orbitals π_{CC} has a large p_y coefficient on carbon which can orient itself in such a way as to stabilise an empty p orbital on a neighbouring atom **2.21a**, seen from a different perspective in **2.21b**. This is like conjugation with a full p orbital, and is more effective in lowering the π energy than conjugation with a π bond is in the allyl cation (Fig. 1.28). The other high-energy filled orbital in the Walsh diagram has the wrong symmetry for overlap with the neighbouring p orbital, and has no effect on its energy one way or the other. This picture is supported experimentally by the preferred conformation in many systems matching that in **2.21**, as can be seen in the two main conformations adopted by cyclopropane carboxaldehyde **2.22a** and **2.22b**, if the carbonyl group is thought of as a highly stabilised carbocation.

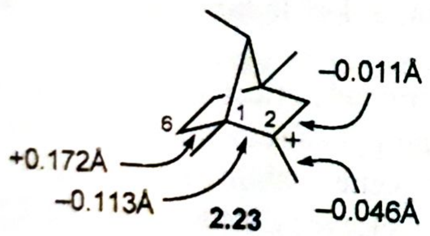


2.21a 2.21b



2.22a 2.22b

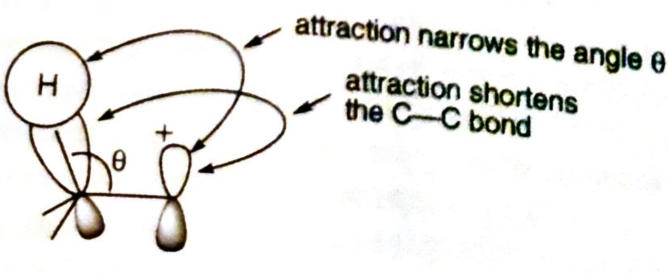
2.2.1.2 Bridging in Carbocations. As usually defined, hyperconjugation implies no change in the shape of the molecule caused by the extra overlap. However, the extra bonding in ψ_1 between the σ C—H bond and the p orbital ought to have the effect of shortening the C—C bond and lengthening the C—H bond (or C—C bond if that is involved), and there is experimental evidence from X-ray crystal structures that this does indeed happen. Thus the bicyclo[2.2.1]heptyl cation **2.23** shows shortening of the three C—C bonds to the cationic centre relative to a typical bond between a tetrahedral and a trigonal carbon (1.522 Å), and lengthening of the bond between C-1 and C-6 relative to a typical bond between two tetrahedral carbons (1.538 Å). This shows the effects expected from the hyperconjugative interactions shown with bold lines on the drawing **2.24**.



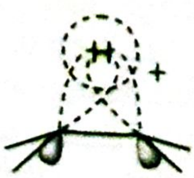
2.23

2.24

Hyperconjugative overlap will also reduce the H—C—C angle θ, because there is now extra bonding between the hydrogen atom and the empty p orbital **2.25**. There is even the possibility that the lowest energy structure has the hydrogen atom sitting halfway between the two carbon atoms **2.26**. The bonding in this structure can be represented with hybridisation as two half filled orbitals made up from sp^3 hybrids and the 1s orbital of hydrogen **2.26a**, or without hybridisation as largely made up by the interaction of the empty 1s orbital of an isolated proton with both lobes of the π bond of ethylene **2.26b**. The bonding, however it is described, is the same, and similar in nature to that of other two-electron, two-bond bridged systems, such as those in diborane. This structure may be the minimum in



2.25



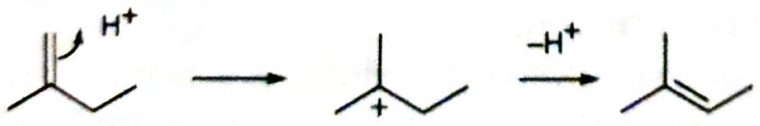
2.26a

2.26b

the energy profile, as it is in diborane, or it may be a maximum, in which case it is the transition structure for the [1,2]-shift of the hydrogen or carbon atom from one carbon to the next.

Although tertiary cations like **2.23** are well established not to have bridged structures, it is not easy to discover whether a localised structure with hyperconjugation, with the minimum movement of the atoms, or the fully bridged structure is the lower in energy for primary and secondary cations. In the 1960s, a large amount of effort went into trying to solve experimentally and computationally the problem of the nonclassical ion, as it was called. Both experiment and calculations gave conflicting or ambiguous answers, one of many problems being that calculations on ions in the gas phase, however high in level, inherently favour bridged structures, because bridged structures spread the charge more effectively. The present state of opinion probably favours structures like **2.25** *without bridging* for almost every alkyl cation except the most simple, the ethyl cation itself, which is only found in the gas phase. A bridged structure like **2.26** is therefore a low-energy transition structure for a 1,2-hydride shift, and, with carbon in the bridge, the transition structure for the Wagner-Meerwein type of cationic rearrangement.

2.2.1.3 ***Stabilisation of a π Bond.*** Hyperconjugation has also been used to explain another well-known thermodynamic property—that having alkyl substituents stabilises alkenes. An alkene like 2-methyl-1-butene **2.27** undergoes easy protonation in acid to give the t-amyl cation **2.28**, which can lose a proton again to give 2-methyl-2-butene **2.29**. The ease of the reaction is explained by the hyperconjugative stabilisation given to the intermediate tertiary cation **2.28**. What is not so obvious is why the more-substituted alkene **2.29** is lower in energy then the less-substituted alkene **2.27**, which it certainly is, because the equilibrium lies well to the right. Heats of hydrogenation of alkenes provide quantitative evidence of the greater thermodynamic stability of the more substituted alkenes, with the attachment of one or more alkyl group more or less additively increasing the heat of hydrogenation of an alkene by about 10 kJ mol^{-1} (2.4 kcal mol^{-1}).



2.27 **2.28** **2.29**

One factor is the hyperconjugative stabilisation of the C=C π bond by the alkyl groups. Fig. 2.11 shows the interaction of the orbitals of a σ bond with the orbitals of a π bond, which is similar to the interaction of two π bonds in butadiene (Fig. 1.32). Although the σ-bonding orbital and the π*-antibonding orbital are further apart than ψ_2 and ψ_3^* in butadiene, they are just close enough to mix in a bonding sense effectively to lower the energies of ψ_1 and ψ_2 in Fig. 2.11, making the drop in energy E_1 a little greater than the rise in energy E_2.

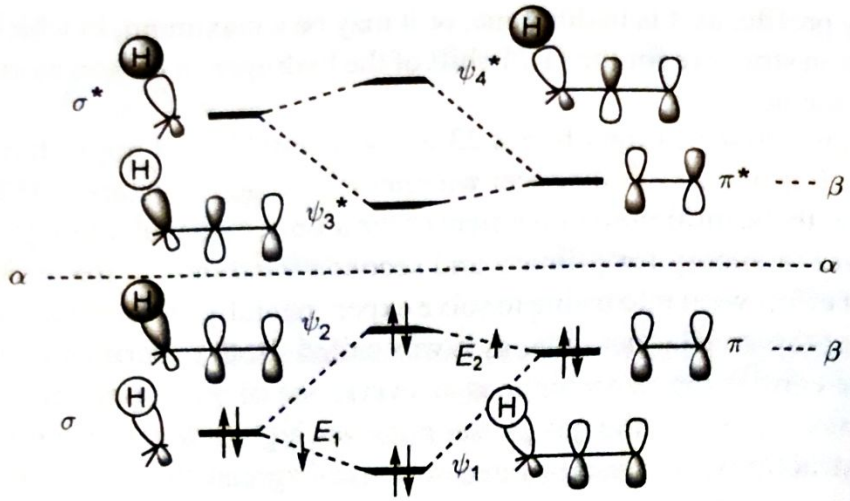


Fig. 2.11 Hyperconjugative stabilisation of a C=C π bond

2.2.2 C—M Hyperconjugation

In Fig. 2.9, the stabilising effect of the hyperconjugation was small, because the energy gap between the σ-bonding orbital and the empty p orbital on carbon was large. A σ bond closer in energy to the empty p orbital should have a larger interaction and be more stabilising. This is the case when the σ bond is between a metal and carbon, because a metal is inherently more electropositive than carbon. Fig. 2.12 shows the energies of the bonding and antibonding orbitals to carbon both to a generic electropositive element M and to a generic electronegative element X. The σ_{CM}-bonding and antibonding orbitals will be higher in energy than the corresponding σ_{CH} or σ_{CC} orbitals, and the σ_{CX} orbitals will be lower in energy than the σ_{CH} or σ_{CC} orbitals.

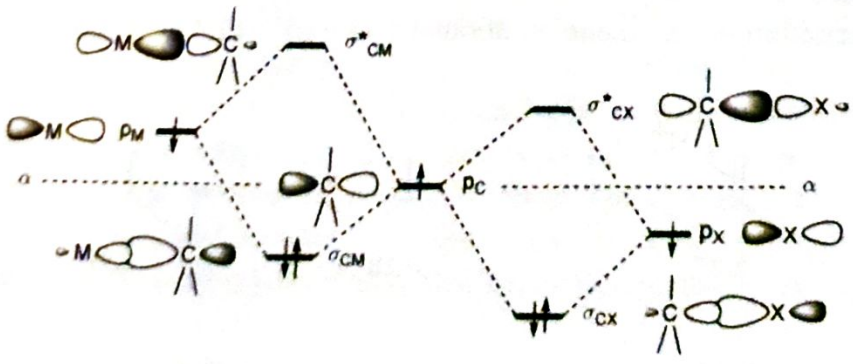


Fig. 2.12 σ-Bonding and antibonding orbitals from carbon to an electropositive element M and to an electronegative element X

Transferring the energy levels for a C—M bond on the left in Fig. 2.12 to an interaction diagram leads to Fig. 2.13 as a description of a β-metalloethyl cation **2.30**. With the σ_{CM}-bonding orbital higher in energy than the bonding σ_{CH} orbital,

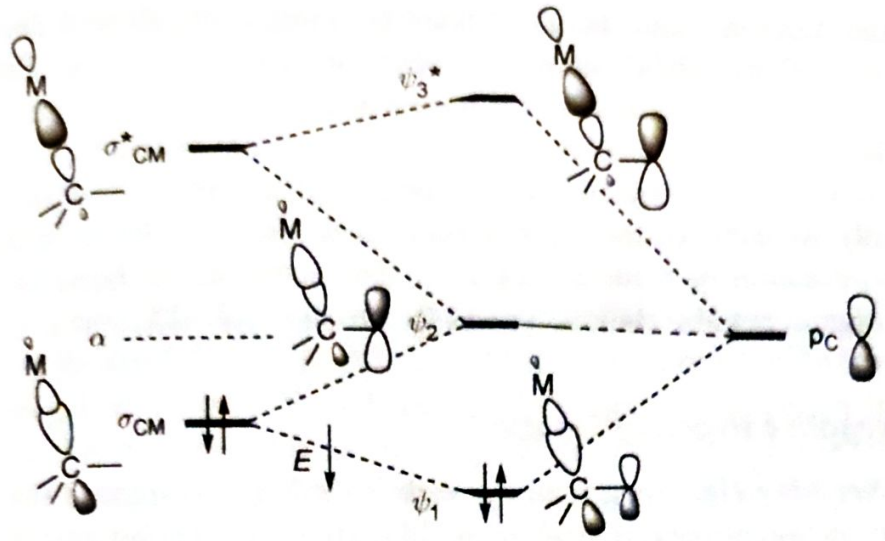
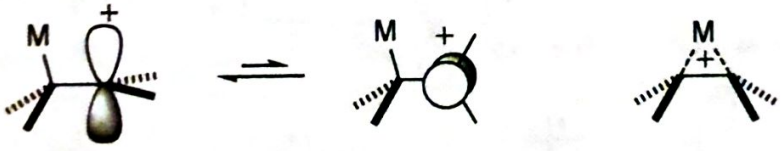


Fig. 2.13 Interaction of the orbitals of a carbon-metal bond with an empty p orbital on carbon

the interaction with the empty p orbital on carbon will be stronger than it was for C—H, and the drop in energy E will be greater. Such cations are well stabilised by hyperconjugation.



2.30 **2.31** **2.32**

The alternative conformation **2.31**, with the empty p orbital at right angles to the M—C bond, is not stabilised any better than it is by an alkyl group, because the M—C bond is in the node of the empty p orbital and there will be no interaction between them. Thus metal-stabilised cations can be expected to adopt and retain the configuration **2.30**. The stabilisation seen in Fig. 2.13 is enhanced by the polarisation of the M—C bond. The coefficients in the σ_{CM} orbital are large on the carbon and small on the metal, just as the coefficients of the C—X-bonding orbital are large on the X atom and small on the carbon. The bonding interaction of the σ_{CM} orbital with the empty p orbital will therefore be greater than it was for the corresponding overlap of the σ_{CH} orbital, where the coefficient on the carbon atom is smaller. Thus we have a more favourable energy match and a more favourable coefficient for the overlap of the M—C bond than for the H—C bond.

The degree of this stabilisation is of course dependent upon what the metal is. In practice, cations with this general structure have been investigated using barely metallic metals, like silicon. Even a trimethylsilyl group as the atom M in a cation of general structure **2.30** is lost too easily for the cation itself to be studied directly with any ease. It is clear from much evidence that silyl groups are substantially stabilising of β cations. The Si—C bond is oriented in the plane of the empty p

orbital, and rotation about the C—C bond is dramatically slowed down so that cations like **2.30** are configurationally stable during most reactions. The question of bridging also arises here, since the lowest energy structure may be the bridged cation **2.32**. Calculations in simple systems indicate that only the least substituted β-silyl cation, the trimethylsilylethyl cation itself, might be bridged. The more substantially metallic elements, however, very probably have bridged structures—coordination of a metal cation to the centre of a π bond is a familiar theme in organometallic chemistry, and the structure is **2.32**.

2.2.3 Negative Hyperconjugation

2.2.3.1 Negative Hyperconjugation with a Cation. If instead the carbon is bonded to an electronegative element like fluorine, the interaction diagram corresponding to Fig. 2.13 changes. The orbitals of the X—C bond, taken from

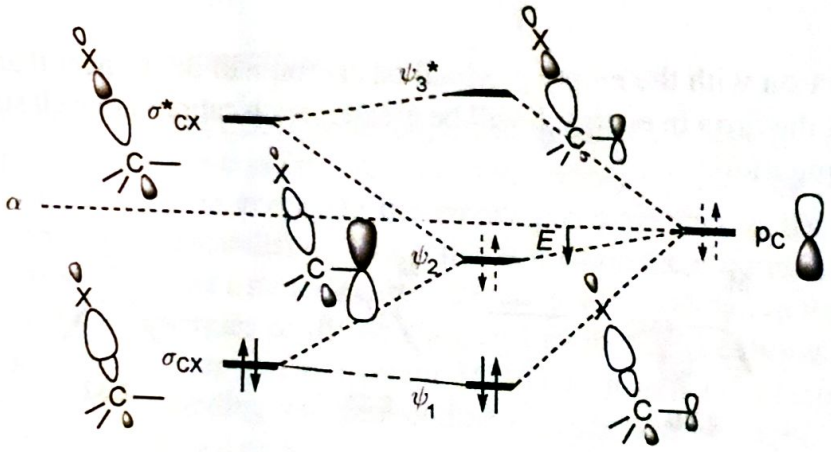


Fig. 2.14 Interaction of the orbitals of a bond between carbon and an electronegative element X with a p orbital on carbon

Fig. 2.12 and moved into Fig. 2.14, are lower in energy than the corresponding C—H orbitals. The interaction of σ_{CX} with the p orbital will now have little energy-lowering effect on ψ_1, because the orbitals are so far apart in energy. There is therefore little π stabilisation afforded to a cation in the conformation **2.33**, and in addition there will be the usual strong inductive electron withdrawal destabilising it in the σ framework. The alternative conformation **2.34** possesses the greater degree of hyperconjugative stabilisation, as long as the other substituents on the carbon atom are not as electronegative as X, and will be preferred, but the inductive withdrawal will still make it a relatively high-energy cation.

2.33 **2.34**

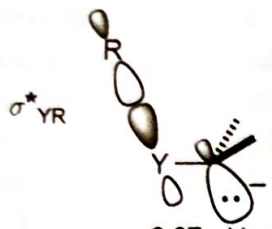
2.2.3.2 ***Negative Hyperconjugation with an Anion.*** However, if it is a carbanion that is conjugated to the X—C bond, the p orbital is filled. The orbital ψ_2 in Fig. 2.14 is lowered in energy significantly by an amount E as a consequence of the orbital σ^*_{CX} being so much closer in energy to the p orbital than either of the orbitals σ^*_{CM} in Fig. 2.13 or σ^*_{CH} in Fig. 2.9. Since this orbital is filled, there is a drop in overall energy $2E$, which the cation does not benefit from. As a consequence of the hyperconjugation, the conformation **2.35** is now stabilised more than the alternative **2.36**. Furthermore, the large coefficient on carbon in the σ^*_{CX} orbital makes its overlap with the filled p orbital even more bonding than without the electronegative element X, and the small coefficient on carbon in the σ_{CX} orbital makes its overlap with the filled p orbital even less antibonding, both factors further contributing to E, the lowering in energy of the ψ_2 orbital. This type of hyperconjugation is sometimes called 'negative' hyperconjugation, because it is conjugation with a negative charge, but it is another misnomer, since energy-lowering is usually regarded as a positive outcome.

2.35 **2.36**

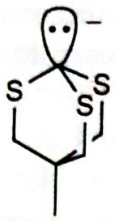
In practice, this phenomenon is not usually seen with carbanions themselves. Even if it were, simple carbanions would not be trigonal as they are shown in Fig. 2.14 and in **2.35**. Organic chemists use the word carbanion loosely, but most often they refer either to compounds with trigonal carbons carrying substantial excess negative charge, as with enolate ions [see (Section 2.1.4) page 66], or to compounds with C—M bonds. In enolate ions, the orbital p_C used in Fig. 2.14 would correspond to the p orbital on the terminal carbon in ψ_2 of an X-substituted alkene [see (Section 2.1.2.3) page 63], which has a large coefficient on C-2 (Fig. 2.6). In compounds containing a C—M bond, the orbital p_C used in Fig. 2.14 would correspond to the orbital σ_{CM} in Fig. 2.13, which also has a large coefficient on carbon. The origins of the π stabilisation would be seen to be similar to those identified above, but made a little more complicated by having to bring in more orbitals. Fig. 2.14 is therefore the paradigm for the general case. The well-known electron-withdrawing power of a trifluoromethyl group is explained by negative hyperconjugation substantially supporting the inductive effect.

The same explanation applies to the well-known stabilisation of carbanions by a neighbouring sulfur, phosphorus or silicon group. The main stabilisation comes from overlap of the filled orbital on carbon with the σ^*_{YR} orbital **2.37**, and is at a maximum when the orbitals are anti-periplanar, accounting for the exceptional ease with which the anion **2.38** can be prepared by removing the bridgehead proton. The interaction diagram is essentially the same as that in Fig. 2.14, except that the energy of the σ^*_{YR} orbital, when Y is one of Si, P or S, is lower than it is when Y is the corresponding first-row element. The bonding interaction between a hydrogen atom or a first-row atom and a second-row atom is inherently less

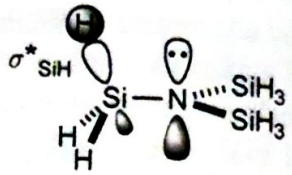
energy-lowering. The sulfur and the phosphorus have the added advantage of being (mild) σ-withdrawing groups, but silicon has the advantage of having the Si—R bonds polarised from silicon towards the R group, if R is hydrogen or a carbon group, making them electronegative elements in this context. This explanation has largely replaced that using overlap with empty d orbitals.



2.37 Y = Si, P or S



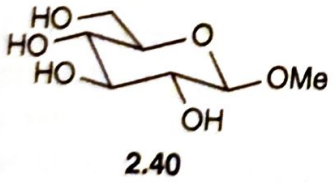
2.38



2.39

A lone pair on an electronegative element can take the place of the carbanion in the arguments above, and overlap with an appropriately electron-withdrawing σ bond can be π-stabilising. Trisilylamine **2.39**, unlike trimethylamine, is planar, with a trigonal nitrogen atom, probably largely as a result of the overlap of the nitrogen lone pair with the antibonding Si—H orbitals, which are polarised from silicon towards the hydrogen.

2.2.3.3 The Anomeric Effect.[10] A lone pair conjugated to a C—X bond, in which X is an electronegative element, is a special category of negative hyperconjugation. The best-known illustration of this *anomeric effect*, as it is called, is in the equilibrium for the glucosides **2.40** and **2.41**, where the diastereoisomer with the axial methoxy group **2.41** is favoured, in spite of the usual equatorial preference for substituents in six-membered rings.



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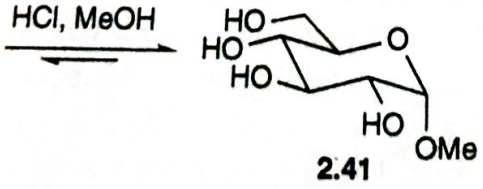
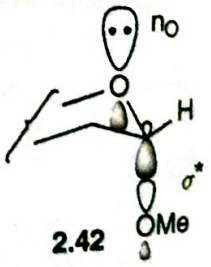


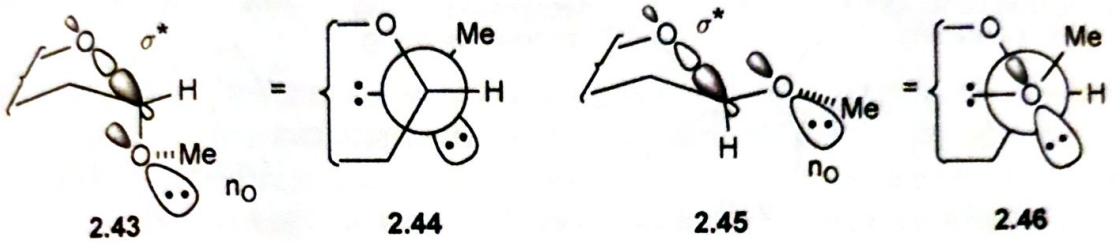
2.41



2.42

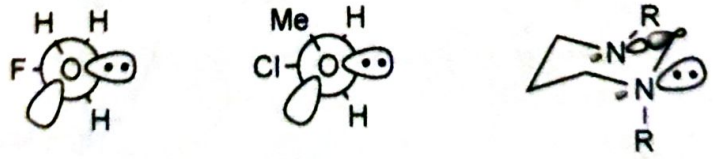
The generally accepted explanation for this phenomenon is associated with negative hyperconjugation, similar to the stabilisation of a carbanion discussed in the preceding section, but with the lone pair on the ring oxygen atom taking the place of the filled p orbital on carbon. Lone pairs are often given the letter n as a distinctive label. The anomeric effect is a consequence of the overlap of the nonbonding lone pair n_O with the low-lying σ^* orbitals of the exocyclic C—O bond **2.42**, superimposed, of course, on all the usual interactions of filled orbitals with filled orbitals. Only when the exocyclic C—O bond is axial are its orbitals able to overlap well with the axial sp^3 hybrid lone pair on the ring oxygen. Alternatively, without using hybridisation, it is the nonbonding p_z lone pair that overlaps better with an axial C—O bond.

At the same time, the methyl group on the exocyclic oxygen adopts a conformation in which it sits gauche to the ring oxygen atom, as a consequence of the lone pair on the exocyclic oxygen atom being conjugated anti-periplanar with the endocyclic C—O bond **2.43**. This is perhaps a little clearer in the Newman projection from above **2.44**. The preference for the gauche orientation is called the exo anomeric effect. The exo anomeric effect operates even with those tetrahydropyrans that have equatorial substituents at the anomeric centre—although the endocyclic oxygen cannot indulge in an anomeric interaction, the exocyclic oxygen can **2.45** (= **2.46**).



2.43 **2.44** **2.45** **2.46**

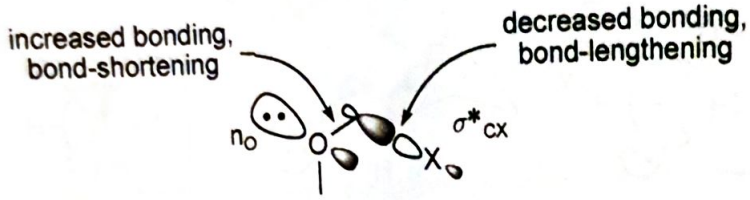
The anomeric effect can be seen to affect the conformation of many systems with the features RO—C—X, most of which adopt a conformation with the R group gauche to the X group rather than anti, as one might have expected. This is the generalised anomeric effect, and it has many manifestations, such as the preferred conformations for fluoromethanol **2.47** and methoxymethyl chloride **2.48**. Nor, of course, is it confined to oxygen lone pairs. The preferred conformation **2.49** for *N,N*-dialkyl-1,3-diazacyclohexanes has one of the alkyl groups axial in order that the lone pair on that nitrogen can be conjugated with the C—N bond. The optimum anomeric effect in this system would have both alkyl groups axial, so that both lone pairs could be involved in an anomeric interaction, but this conformation would have a 1,3-diaxial interaction between the alkyl groups, and this steric repulsion, not surprisingly, overrides the anomeric effect.



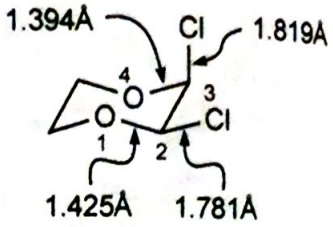
2.47 **2.48** **2.49**

Bond lengths are also affected. When the two heteroatoms are different **2.50**, with one lone pair on a less electronegative atom like oxygen and the other on a more electronegative element like halogen, bond shortening is more noticeable in the O—C bond, and the C—X bond is increased in length. The anomeric effect between n_O and σ^*_{CX} increases the π bonding in the C—O bond but, because it mixes in an antibonding orbital between the C atom and the halogen, that bond is weakened and made longer. The anomeric effect of n_X with σ^*_{CO} is lower, because σ^*_{CX} is lower in energy than σ^*_{CO} and n_O is higher in energy than n_X, making the energy match better between n_O and σ^*_{CX}. Thus the consequence of a lop-sided anomeric effect is overall to weaken the C—X bond—as the electron

population is increased on the carbon atom, the X atom moves away. This is dependent upon the geometry, as seen in the structure of *cis*-2,3-dichlorodioxan **2.51**. The equatorial C—Cl bond is the same length as that in methyl chloride, because it is oriented at an angle giving little conjugation with the lone pairs on the neighbouring O-1. In contrast, the axial C—Cl bond is lined up for an anomeric effect with the axial lone pair on O-4, and it is longer. At the same time, the bond between O-4 and C-3 is shortened, whereas the bond between O-1 and C-2 is close to that for a normal ether link.

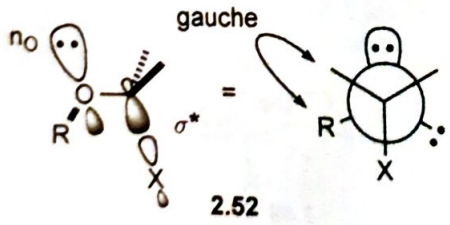


2.50

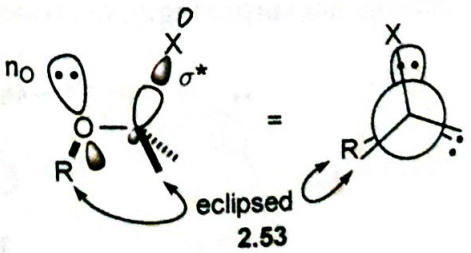


2.51

2.2.3.4 Syn-coplanar and Anti-Periplanar Overlap. In the discussion about the anomeric effect, the lone pair has been oriented, without comment, anti to the C—X bond. The lone pair and the C—X bond are able to overlap in this orientation **2.52** because they are coplanar, but at first sight they could equally easily have overlapped had they been syn **2.53**. Undoubtedly, coplanarity is the single most important constraint for good overlap, but what about the choice between syn and anti? One answer is that the syn arrangement **2.53** carries with it at least one eclipsing interaction with the substituent R, whereas the anti arrangement **2.52** has all substituents and lone pairs staggered. The eclipsed arrangement is not even a minimum, but a transition structure for rotation about the O—C bond.



2.52

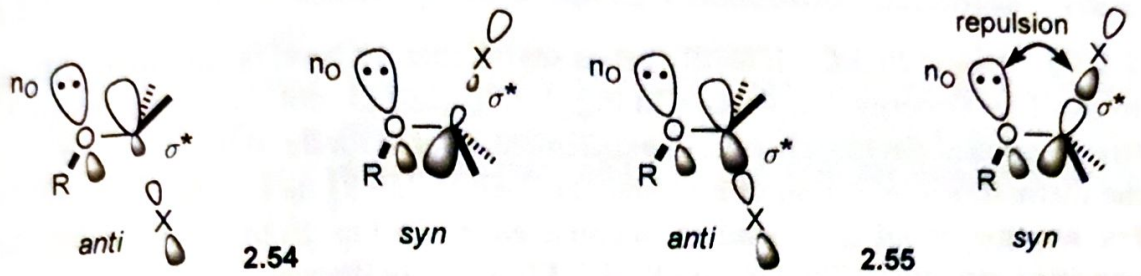


2.53

This simple difference alone seems to account for why anti arrangements, both in anomeric effects and in β-eliminations (to be discussed in Chapter 4) are so common, but it is not the whole story, because there are systems where this factor is not present, and yet there is still a preference for anti anomeric effects [and anti eliminations, see (Section 5.1.2.1) page 156].

A tempting way to explain the inherent preference for anti over syn arrangements is to picture the antibonding hybridised orbitals with the large lobes outside the bond instead of between the atoms. Thus we might redraw the σ^*_{CX} orbital in **2.52** as **2.54**. This seems to make sense—the atomic orbitals of opposite sign will repel each other. Many organic chemists succumb to this temptation, for we

immediately see that there is better overlap with the n_O orbital in the anti arrangement—the large lobes are close. In the corresponding syn arrangement, the large lobes are on opposite sides and the overlap is 'obviously' less.



Unfortunately it is illegitimate. When we mix two atomic orbitals, the bonding orbital with an attendant drop in energy is paired with an antibonding orbital with its corresponding rise in energy. If we establish σ overlap for two p orbitals in the usual way, the antibonding orbital σ^* must match it. Although the lobes may be compressed by the repulsion, one cannot arbitrarily move them in and out, however commonly you may come across this device in your reading. A better picture can be seen in the wire-mesh drawing for methyl chloride in Fig. 1.47, where the σ^*_{CCl} orbital shows that both the inside lobe and the outside are large, and not like those in the drawing **2.54**. We are left therefore with the problem of accounting for the preference for anti overlap. Perhaps the simplest explanation is a more careful use of pictures like those drawn in **2.55** with a somewhat more realistic hybrid orbital. The anti arrangement still has good bonding overlap, but in the syn arrangement, there are both attractions and repulsions between the n_O orbital and σ^*_{CX} orbital. Furthermore, and perhaps more important still, the anti arrangement keeps the centres of negative charge as far apart as they can be.

2.3 The Configurations and Conformations of Molecules

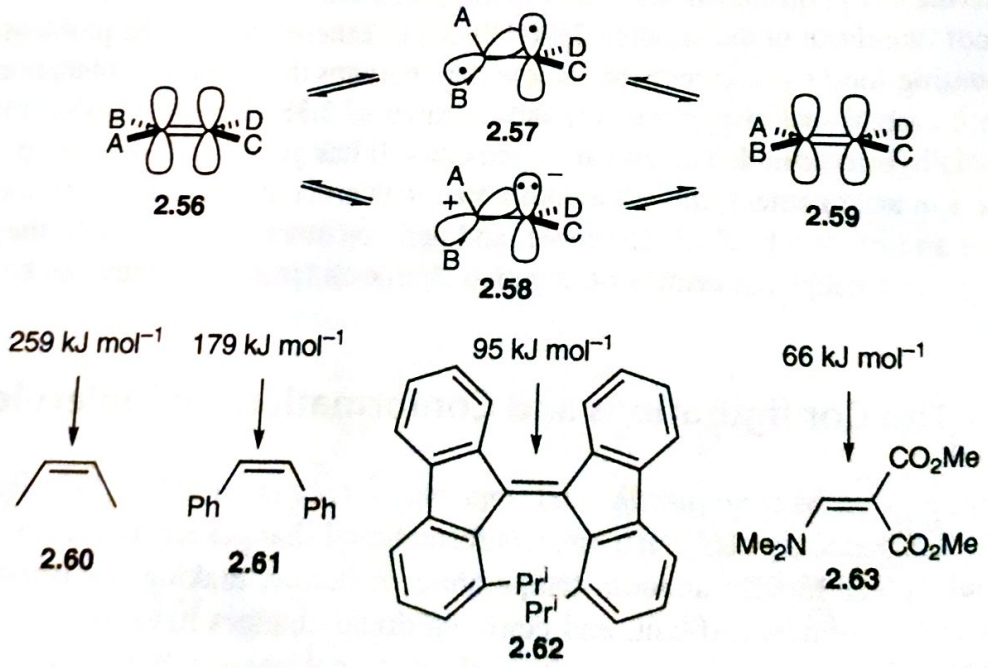
Defining the terms *configuration* and *conformation* poses a problem, because there is no sharp boundary between them. Conformational changes are usually those that can take place rapidly at room temperature or below, making the isolation of separate conformers difficult, and configurational changes have energy barriers high enough to make it easy to isolate configurational isomers. But conformational barriers can rise above those that can be crossed at room temperature, and configurational barriers, like double bond geometries, can become so low that they are easily crossed, but the ambiguity is usually not a problem.

Conjugation, whether it is in the π system or in the σ system, is one of the factors responsible both for the configurations and the conformations that molecules adopt. The energy-lowering induced by π conjugation usually has the effect of making the planar arrangement with the maximum π overlap the lowest in energy, and imparting a barrier to rotation about any single bonds separating the elements of conjugation. At one extreme, strong π overlap fixes the *configuration* of benzene as a perfectly flat hexagonal ring. At the other extreme, weak π overlap

in the anomeric effect controls the *conformation* of methoxymethyl chloride **2.48**, but with a low barrier to rotation.

2.3.1 Restricted Rotation in π-Conjugated Systems

2.3.1.1 One π Bond. It hardly needs saying that a π bond is not usually free to rotate. The π energy $2E_\pi$ we saw in Fig. 1.22 (~280 kJ mol^{-1}) is high enough to stop rotation about the π bond. An experimental value for the activation barrier for the thermal isomerisation of *cis*-2-butene **2.60** is 259 kJ mol^{-1} (62 kcal mol^{-1}). For rotation about a π bond to become easier in the ground state either the transition structures like the diradical **2.57** or the zwitterion **2.58** must be stabilised or the planar structure **2.56** must be destabilised. Phenyl groups stabilise radical centres, and the barrier to rotation in stilbenes **2.61** is lower than that in 2-butene. Steric interaction between the *cis*-vicinal substituents, raising the energy of the planar structure, contributes to lowering the barrier to rotation, as in the bifluorenylidene **2.62**, which benefits from both effects. Alternatively, the substituents A and B may stabilise a cationic centre on one side and the substituents C and D an anionic centre on the other **2.58**. Alkenes having donor



substituents (X) at one end and acceptors (Z) at the other are called 'push-pull' alkenes, and the barriers to rotation are indeed lowered, with the enamine system of the alkene **2.63** having a strikingly low barrier.

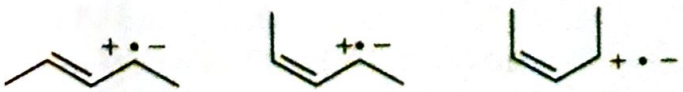
Photochemical excitation, however, takes one electron from the π orbital and promotes it to the π*. The π energy now is $(E_\pi - E_{\pi^*})$, which is negative, removing the energetic benefit of conjugation altogether, and making the conformation **2.57**, with the two p orbitals orthogonal, the lowest in energy. Initially, the excited state must be in the high energy, planar conformation **2.56**, but if the photochemically excited molecule has a long enough lifetime the conformation will change

to that with the lower energy **2.57**. Later, when the electron in the π^* orbital returns to the π orbital, the molecule will return to the planar arrangement **2.56** or **2.59**.

2.3.1.2 ***Allyl and Related Systems.*** The allyl conjugated system is also more or less configurationally stable, whether it is the cation, the radical or the anion. The drawing of a σ bond in the localised structure **2.64a** disguises the π bonding still present between C-1 and C-2. The alternative and exactly equivalent drawing **2.64b** reveals that this is not the case, and C-1 and C-2 are just as strongly π-bonded as C-2 and C-3.

2.64a **2.64b**

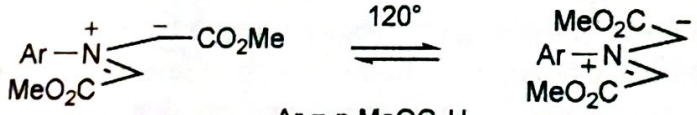
The molecular orbitals of the allyl system (Fig. 1.28) demonstrate the configurational stability more powerfully—the lowest filled orbital, ψ_1, has π bonding across the whole conjugated system, and the nonbonding ψ_2, makes no contribution to π bonding whether it is empty or filled. The total π-bonding energy for all three allyl systems (Fig. 1.26) is $2 \times 1.414\beta$. If rotation were to take place about the bond between C-1 and C-2, the transition structure would have a full π bond between C-2 and C-3 and an orthogonal p orbital on C-1. The difference in π energy between the conjugated allyl system ($2 \times 1.414\beta$) and this transition structure with a full π bond (2β) is therefore $2 \times 0.414\beta$, or about 116 kJ mol^{-1} (28 kcal mol^{-1}), making the π bond strength between C-1 and C-2 nearly half that of a simple π bond, quite large enough to restrict rotation under normal conditions. Higher levels of calculation confirm that a substantial barrier is present, but reveal that the cation, radical and anion are not in detail the same—the unsubstituted cation is calculated to have a rotation barrier in the gas phase of 140 kJ mol^{-1} (33.5 kcal mol^{-1}), the radical a barrier of 63 kJ mol^{-1} (15 kcal mol^{-1}) and the anion a barrier of 85 kJ mol^{-1} (20 kcal mol^{-1}). In solution, solvation by a notional polar solvent lowers the numbers for the cation and anion to 115 and 70 kJ mol^{-1} (27.5 and 17 kcal mol^{-1}), still large enough to retain configurational identity under normal conditions. 1,3-Disubstituted allyl systems therefore have three configurations, usually called W-shaped **2.65**, sickle-shaped **2.66**, and U-shaped **2.67**, which do not easily interconvert by rotation about the C—C bonds. Interconversion between the stereoisomeric allyl cations can take place by capture of a nucleophile, followed by rotation about the single bond, and regeneration of the cation by ionisation. Possibly because of the availability of these pathways, experimental measurements of the rotational barrier are lower for the cation than the theoretical value of 140 kJ mol^{-1}.



W-shaped **2.65** sickle-shaped **2.66** U-shaped **2.67**

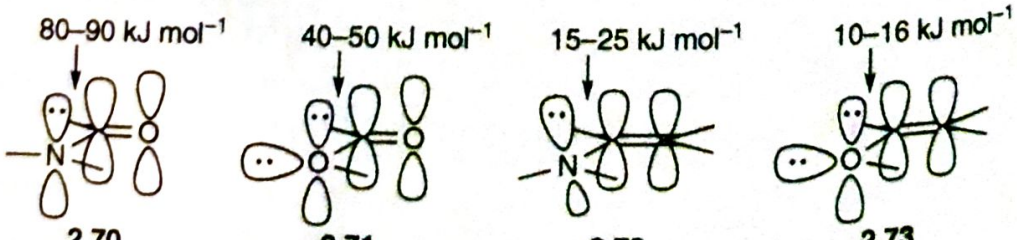
Allyl radicals also retain their configuration before being trapped by a reagent. Free energies of activation for a change from sickle-shaped to W-shaped of 66 kJ mol^{-1} (16 kcal mol^{-1}) and 60 kJ mol^{-1} (14 kcal mol^{-1}) have been measured for this process with substituents D and Me, respectively. The lower barrier in the radical, relative to that for the cation and anion, may be associated with the difficulty of localising charge on a carbon atom in the transition structure.

For the allyl anion itself, a good measurement is not really possible, because the free anion is not an accessible intermediate in solution. What we usually have is allyl-metal species, and interconversion between the corresponding geometries can take place by σ coordination. If the coordination to the metal is η^1, it will weaken the π bonding relative to the free anion, but if it is η^3 it will greatly strengthen it. Values of 45, 70, and 76 kJ mol^{-1} (11, 17, and 18 kcal mol^{-1}) have been measured for allyl-lithium, potassium and caesium, respectively, with the last of these presumably a lower limit for the true barrier in a free allyl anion. One system free of this complication has been thoroughly studied: the azomethine ylids **2.68** and **2.69** are isoelectronic with an allyl anion, but do not have metal counterions. The free energy barrier to the conversion of the sickle-shaped isomer into the W-shaped isomer is 85 kJ mol^{-1} (20.3 kcal mol^{-1}) and for the reverse reaction it is 84 kJ mol^{-1} (20.1 kcal mol^{-1}), there being little difference in energy between them. Note that the ester groups greatly stabilise the anionic charge at C-1 and C-3, making rotation about the bond between C-1 and C-2 (or between C-2 and C-3) much easier than it would be in a free allyl anion.



2.68 **2.69**

A number of other conjugated systems of three p orbitals show restricted rotation, although not to the same degree. Amides **2.70** typically have a barrier to rotation about the C—N bond of 80–90 kJ mol^{-1} (19–21.5 kcal mol^{-1}), they have nearly trigonal nitrogen atoms, in contrast to amines, which have nearly tetrahedral nitrogen atoms, and the C—N bond is shortened because of the extra bonding provided by the π overlap between the nitrogen lone pair and the π bond. The comparatively rigid and planar conformation present in the amide system has profound consequences on the conformations of peptides and proteins.



2.70 **2.71** **2.72** **2.73**

The other systems, esters **2.71**, enamines **2.72**, and enol ethers **2.73**, similarly have restricted rotation about the bond drawn as a single bond, but the barrier is

successively lower in each as the degree of π bonding becomes less and less, and the degree of π bonding localised at the double bond increases. This localisation also affects the lone pair, so that enamines, unlike amides, do not have a trigonal nitrogen atom, but a somewhat pyramidalised one, with the lone pair tilted slightly away from the vertical, relieving some of the eclipsing suffered by the alkyl substituents on the nitrogen atom.

Whereas the allyl anion, with a plane of symmetry through the central atom, has a node at that atom in ψ_2, amides, esters, enamines, enol ethers and enolate ions do not have a node precisely on the central atom. Taking planar *N*,*N*-dimethylvinylamine and the enolate of acetaldehyde as examples, simple Hückel calculations give the π orbitals in Fig. 2.15, which includes the allyl anion for comparison.

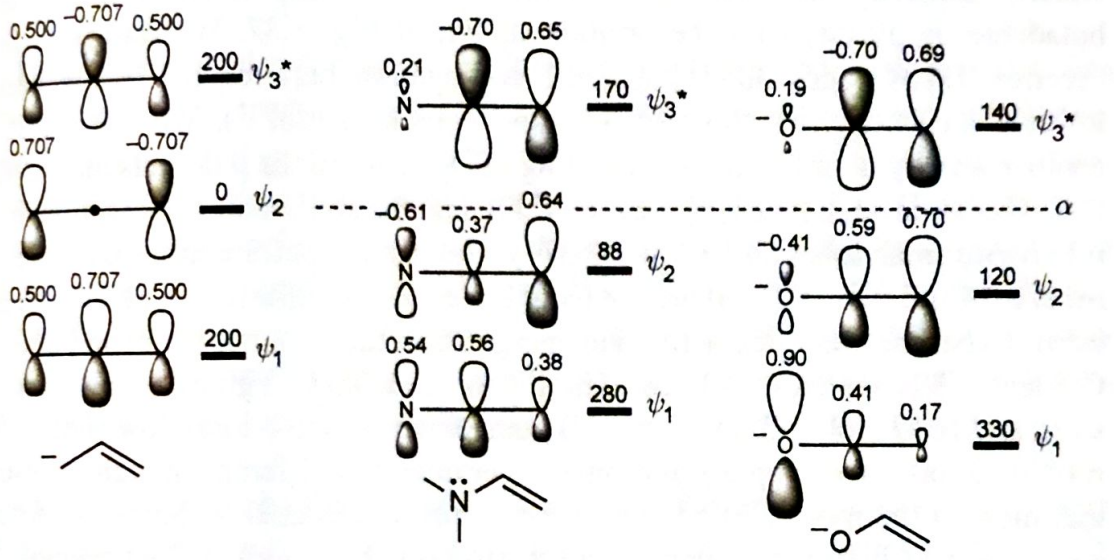
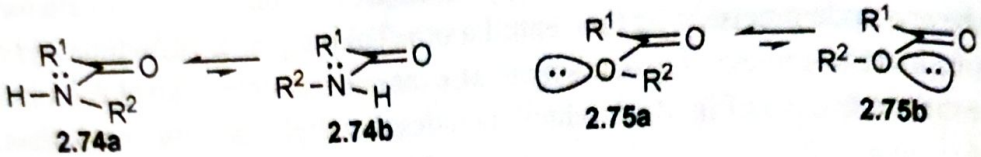


Fig. 2.15 π Orbital energies and coefficients from simple Hückel calculations of the allyl anion, enamine and enolate ion (orbital energies in kJ mol^{-1} relative to α)

While the overlap between the atomic orbitals on the N or the O and the adjacent C are strongly bonding in ψ_1, they are antibonding in ψ_2. However, both ψ_1 and ψ_2 contribute to π bonding between the two carbon atoms, and enamines and enolate ions have restricted rotation there. This is one reason why it is usually wise to draw enolate ions with the charge on oxygen rather than as carbonyl-stabilised carbanions—not only is more of the total charge on oxygen, but the degree of π bonding is better illustrated this way.

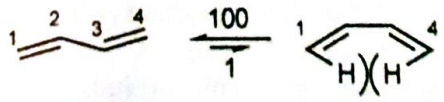
One remaining detail to be explained is the relative energy of the two planar conformations available to amides and esters. Secondary amides adopt the *Z* conformation **2.74a** rather than the *E* **2.74b**, and esters adopt the s-*trans* conformation **2.75a** rather than the s-*cis* **2.75b**. In both the esters and the amides, the conformations **2.74a** and **2.75a** benefit from the anti orientation of the carbon chains R^1 and R^2. In other words, the alkyl chain R^1 is effectively a larger substituent than the carbonyl oxygen, and the amide and ester alkyl groups R^2 prefer to be anti to R^1. However, this is not the whole story, because formate esters, with R^1 only a hydrogen atom, ought to be the other way round, and they are not. There is a

stereoelectronic component as well, at least for the esters, which is identifiable as the generalised anomeric effect [see (Section 2.2.3.3) page 79]. In the s-*trans* conformation **2.75a**, a lone pair on the oxygen atom is favourably oriented anti to the C—O single bond of the carbonyl group, but in the s-*cis* conformation **2.75b** it is syn. This is responsible for the relatively high reactivity of lactones compared with open-chain esters, since lactones are forced to adopt the high-energy s-*cis* conformation.



2.74a **2.74b** **2.75a** **2.75b**

2.3.1.3 ***Dienes.*** In order to maintain the maximum level of π bonding, butadiene, is planar, with the orbitals shown in Fig. 1.32. We estimated [see (Section 1.4.3) pages 30–31] that the conjugation between the two π bonds lowered the energy by about 66 kJ mol^{-1} (16 kcal mol^{-1}). We can see it in another way by noting that the π bonding in ψ_1 between the p orbitals on C-2 and C-3 is between large lobes ($c_2 = c_3 = 0.600$), and the antibonding interaction in ψ_2 is between small lobes ($|c_1| = |c_2| = 0.371$). The planar conformations are called s-*trans* **2.76** and s-*cis* **2.77**, where the letter s denotes a conformation about a single bond. Experimentally, the activation energy for rotation about the bond between C-2 and C-3 is approximately 28 kJ mol^{-1} (6.7 kcal mol^{-1}) going from s-*trans* to s-*cis*, and 16 kJ mol^{-1} (3.8 kcal mol^{-1}) going from s-*cis* to s-*trans*, low enough for rotation to take place rapidly at room temperature, but different enough to ensure that most of the molecules will be in the s-*trans* conformation. Since the difference in energy between these two conformations is 12 kJ mol^{-1} (2.9 kcal mol^{-1}), there is about 1% of the s-*cis* conformation at room temperature.



2.76 **2.77**

There are two reasons for the preference for the s-*trans* conformation. The more obvious is that the hydrogen atoms at C-1 and C-4 which are *cis* to the other double bond are sterically quite close in the s-*cis* conformation **2.77**, and repel each other. However, the difference in energy between *cis*- and *trans*-2-butene, which have similar, although not the same, differences in steric compression, is only about 4 kJ mol^{-1} (1 kcal mol^{-1}). Another reason can be found in the π system (exaggerated in Fig. 2.16), where the p orbitals on C-1 and C-4 are closer in space in the s-*cis* conformation than they are in the s-*trans*, and all the other orbital interactions, C-1 with C-2, C-1 with C-3, and their symmetry counterparts, are all equal in the two conformations. The lobes on C-1 and C-4 in ψ_1 are small and bonding, but this attractive overlap is more than offset by the antibonding interaction between the large lobes in ψ_2, making the overall interaction repulsive ($|\Delta E_2| > |\Delta E_1|$).

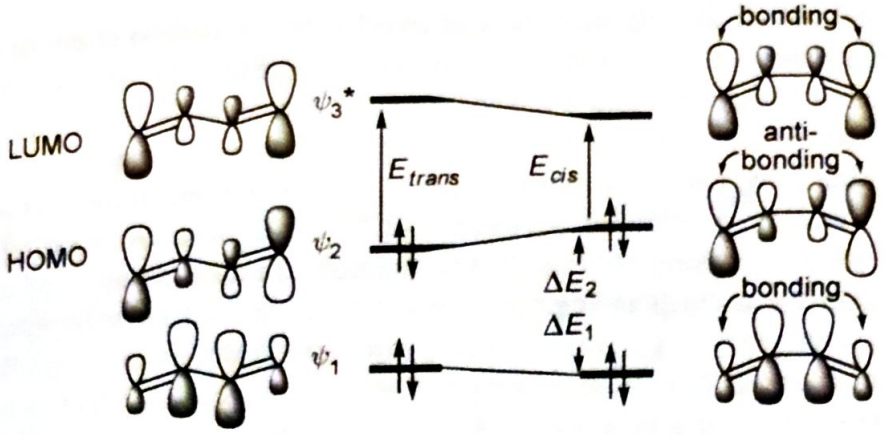


Fig. 2.16 Differences in π orbital energies for s-*trans* and s-*cis* butadiene

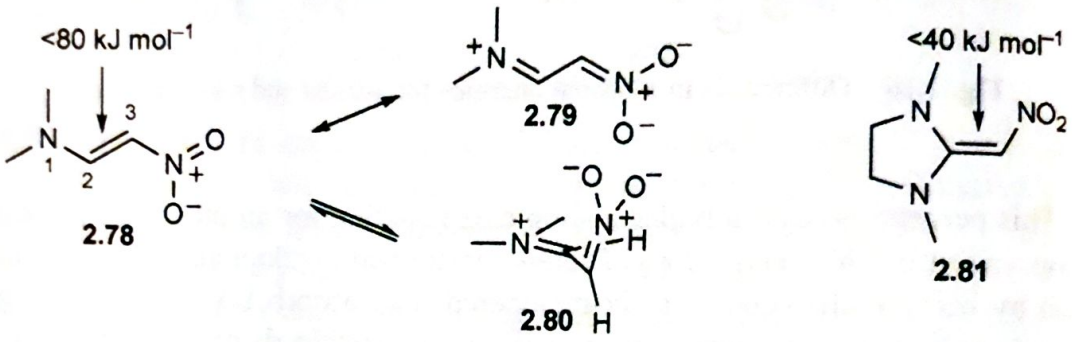
This perception also provides a simple explanation for an otherwise puzzling observation in UV spectroscopy. Dienes constrained to adopt an s-*cis* conformation by being endocyclic in a six-membered ring, absorb UV light at a longer wavelength than open-chain dienes with a comparable degree of substitution. Woodward's rules for UV absorption in dienes give a base value for s-*trans* dienes of 214 nm and for s-*cis* dienes of 253 nm. This absorption is a measure of the gap in energy between ψ_2 and ψ_3^*. In Fig. 2.16, we can see that ψ_2 is raised in energy in the s-*cis* conformation relative to the s-*trans*, and ψ_3^* is lowered in energy, making the energy gap E_{cis} less than E_{trans}.

2.3.1.4 ***Lowering the Energy of the Transition Structure for Rotation.*** With longer conjugated systems the π stabilisation increases in the usual way, but each increment makes a smaller and smaller difference. In the transition structure for rotation, the full π stabilisation is divided into two, with each part having a shorter conjugated system. As a result, the barrier to rotation about the internal double bonds goes down as conjugated systems get longer. Carotenoids, for example, having eleven double bonds conjugated together, are notoriously susceptible to *cis-trans* isomerisation, and it seems likely that some of them are simply thermally induced rotations.

Moving on to the weaker π bonding in allyl systems, we deduced [see (Section 2.3.1.2) page 83] that the simple Hückel barrier to rotation is 0.828β. By the same type of calculation we can estimate the barrier in the pentadienyl system: the full degree of π stabilisation (Fig. 1.35) is $2\beta + (2 \times 1.73\beta) = 5.46\beta$; the π stabilisation of the separate components for rotation between C-2 and C-3 is the sum of the energy of a π bond (2β) and of an allyl system ($2 \times 1.414\beta$), which comes to 4.82β, and so the difference is now only 0.64β. The experimental value in simple allyl systems is only a little above that which can be crossed at the normal temperatures of chemical reactions, and so we can expect that the longer conjugated systems with an odd number of atoms will rarely have stable configurations.

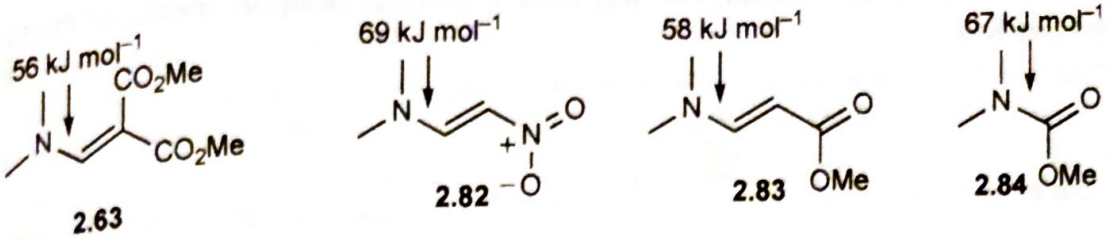
This effect is supplemented by terminal electronegative substituents, which increase the overall electron population at the extremities of the conjugated

system, and reduce the effectiveness of overlap in the carbon chain in between. Thus the system of five conjugated p orbitals present in an alkene with an X-substituent at one end and a Z-substituent at the other (a 'push-pull' alkene), will have molecular orbitals related to the pentadienyl anion (Fig. 1.35). The nitroenamine **2.78**, which has one of the best donors and one of the best acceptors, has much weaker π bonding between C-2 and C-3 than the drawing implies. Rotation about this bond is actually fast enough to make isolation of individual geometrical isomers impossible.



Another way of looking at the ease of rotation between C-2 and C-3 and the restriction between N-1 and C-2 is with the resonance structure **2.79**, which has the effect of expressing the reduction in double bond character. However, it is important to recognise the difference between the resonance structure and the transition structure for rotation **2.80**. The difference is that overlap of orbitals expressed as resonance cannot have any change in the position of the atoms, and it is correctly symbolised with the double-headed arrow. Rotation does have a change in the position of the atoms, and it is a 'reaction', symbolised with conventional reaction arrows. The cation-stabilising group at one end and the anion-stabilising group at the other stabilise the intermediate components, which are no longer conjugated in the transition structure. Such contributions to lowering the energy barrier will come from any stabilisation of the intermediate components in the transition structure—cation-stabilising, radical-stabilising or anion-stabilising, as appropriate—they will all lower the barrier. Increasing the stabilisation of the cationic centre in the transition structure, by having two donor substituents, as in the enediamine **2.81**, causes the two *N*-methyl groups to be coincident in the NMR spectrum even at −63 °C, because rotation about the formal C=C double bond is fast on the NMR timescale.

At the same time, rotation about the formally single bond between N-1 and C-2 in these compounds is more restricted than the drawing of a single bond implies, just as it was with amides. The two *N*-methyl groups in both enamines **2.63** and **2.82** have different chemical shifts and coalescence measurements show that the free energy of activation for rotation is 56 kJ mol^{-1} (13 kcal mol^{-1}) for the former and 69 kJ mol^{-1} (16.5 kcal mol^{-1}) for the latter. Decreasing the stabilisation of the anionic centre in the transition structure with a less powerful acceptor than a nitro group, as in the ester **2.83** reduces the barrier to rotation about the N—C bond to 58 kJ mol^{-1} (14 kcal mol^{-1}).



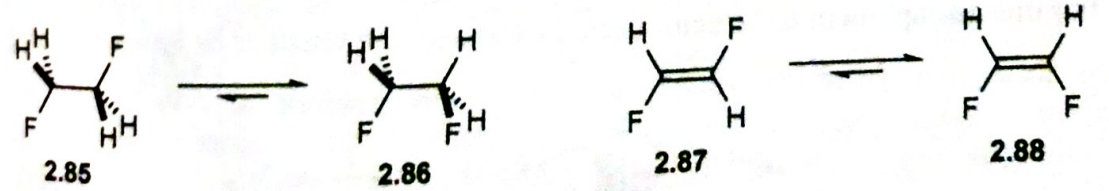
2.63 2.82 2.83 2.84

Extended conjugation through double bonds illustrates the principle of *vinylogy*, a word made up by combining vinyl and analogy. Vinylogous conjugated systems often have similar properties, both in the ground state and in reactivity, to the parent systems. The conjugated system of **2.83**, for example, is that of a vinylogous carbamate, in which the restricted rotation about the N—C bond is similar to but smaller than that of the corresponding carbamate **2.84**.

2.3.2 Preferred Conformations from Conjugation in the σ Framework

We have already seen [see (Section 2.2.3.3) page 79] how the generalised anomeric effect sometimes causes a chain of atoms to adopt a seemingly more hindered gauche conformation **2.47**, **2.48** and **2.49** rather than the more usual zigzag arrangement. Similar hyperconjugative interactions in neutral molecules between two σ bonds can lead them to adopt less obvious conformations in which the effect of conjugation overrides steric and electrostatic effects.

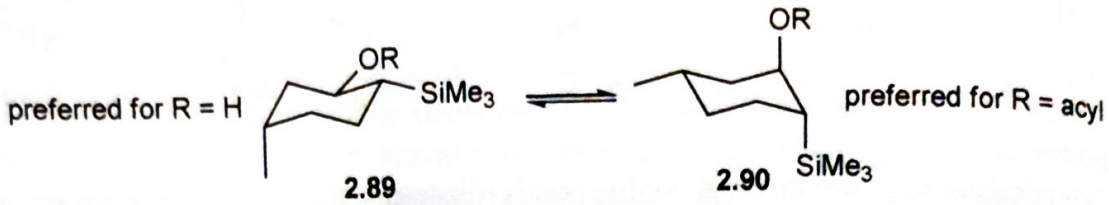
1,2-Difluoroethane might be expected to adopt the zigzag conformation **2.85**, both because the dipoles from the C—F bonds would be opposed, and because the two larger groups would be further apart. However, it does not—it adopts the conformation **2.86**, with an enthalpy advantage of 2.5–3.8 kJ mol^{-1} (0.6–0.9 kcal mol^{-1}) as well as a small favourable entropy factor, since there are two gauche conformations and only one anti. The enthalpy advantage in this conformation stems from the antiperiplanar conjugation of the C—H bonds with the vicinal C—F bonds. Hyperconjugation will be energy-lowering with an interaction diagram like that in Fig. 2.9, but with the low-lying antibonding orbital σ^*_{CF}, with the large coefficient on the carbon atom, taking the place of the empty p_C orbital. A similar explanation accounts for the fact that *cis*-difluoroethene **2.88** is lower in energy than its *trans* isomer **2.87**, in contrast to most other alkenes.



2.85 2.86 2.87 2.88

With a more powerful donor than an H—C bond, cyclohexyl esters carrying a β silyl group demonstrate the preference for the donor and the acceptor bonds to be anti. The equilibrium proportion of the alcohol **2.89** (R = H) is in favour of the diequatorial isomer, but with esters (R = acyl) the equilibrium shifts to favour the diaxial conformation **2.90**. Furthermore, the equilibrium constant correlates

with how good the carboxylate ion is as a leaving group as measured by the pK_a of RO^-.



2.4 Other Noncovalent Interactions

We began in Chapter 1 by considering the strongest forces involved in bonding, the covalent bonds themselves, and worked our way down from strong σ bonds to the weaker π bonds. In this Chapter, we have looked at the weaker π interactions of covalent bonds with each other and with p orbitals, and have come down to a level at which they provide only a delicate balance affecting the shapes that molecules adopt. There are other forces at work, both within a molecule and affecting how one molecule can interact with another, which also stem from the electron distribution. Weak though some of them are, these forces have profound consequences on the degree and sites of solvation, on intermolecular forces affecting the conformations of polymers, protein folding, crystal packing, and molecular recognition between an enzyme and its substrate, and between a receptor and its agonist.

2.4.1 The Hydrogen Bond

2.4.1.1 X—H · · · X Bonds. Strong hydrogen bonds are found when a hydrogen atom bonded to one electronegative atom is close to another electronegative atom. It is found at its strongest and most simple in the HF_2^- ion, which has been estimated to have a gas phase energy below that of the separate components of 167 kJ mol^{-1} (39 kcal mol^{-1}), and at its most famous in the strong AT and GC pairing of bases in the helical structure of DNA.

The molecular orbitals in the HF_2^- system in Fig. 2.17 resemble those of the allyl anion—a low-energy orbital with no nodes, and an orbital with a node at the central atom. The node at the hydrogen atom leaves it with no interactions with the two fluorine atoms, which are far enough apart to be essentially nonbonding. For this arrangement to be stabilised, ψ_1 and ψ_2 must together be lower in energy

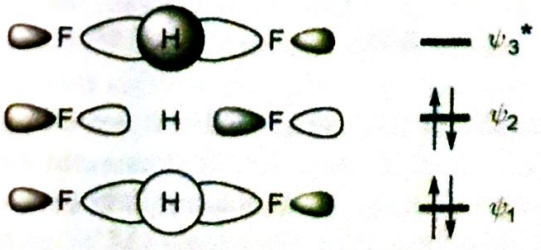
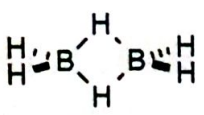


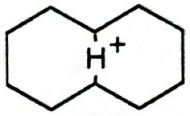
Fig. 2.17 The molecular orbitals of the symmetrical hydrogen bonds in HF_2^-

than the corresponding orbitals in the separate components HF and F^-. Electronegative elements will lead to high electron populations on the atoms at the two ends of the three-atom system, incidentally making it difficult to locate hydrogen atoms by X-ray crystallography, and leading to the low field at which they come into resonance in ^{1}H-NMR spectra. Electronegative elements have compact orbitals in ψ_2, making residual repulsion between them lower. This explains why strong hydrogen bonds are those involving electronegative elements, and why a linear array is best—any bending decreases the bonding in ψ_1 and increases the antibonding in ψ_2.

The same set of orbitals applies to the bridged B—H—B bonds in diborane **2.91** and the bridged C—H—C bond in the cyclodecyl cation **2.92**, except that in these systems there are only two electrons to feed into the orbitals, leaving ψ_2 empty. Since high electronegativity for the two atoms at the ends principally exerts its effect in keeping ψ_2 as nonbonding as possible, high electronegativity is no longer a requirement when ψ_2 is empty.



2.91

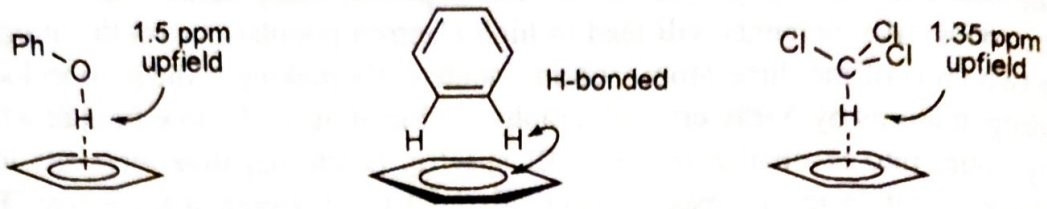


2.92

An alternative perception for the nature of conventional hydrogen bonding, not in conflict with the molecular orbital picture, is that it stems from a Coulombic attraction between the negative charge of the lone pairs of the one electronegative element, and the partial positive charge left on the hydrogen atom by the polarisation of the bond towards the other electronegative element.

2.4.1.2 ***C—H···X Bonds.*** When the hydrogen atom is attached to carbon, the degree of hydrogen bonding is much smaller than with conventional hydrogen bonds, usually much less than 17 kJ mol^{-1} (4 kcal mol^{-1}). These kinds of hydrogen bonds manifest themselves in small shifts in spectroscopic properties, such as a lowering in the C—H stretching frequency in their infrared spectra, in small downfield shifts when ^{1}H-NMR spectra are taken in oxygen-containing solvents, and in preferred conformations seen in solid-state structures.

2.4.1.3 ***X—H···π Bonds.*** Similarly weak hydrogen bonds can also be formed from protons bound to electronegative elements coordinating to the p orbitals of C=C π bonds. The strength has been estimated to be anything up to 17 kJ mol^{-1} (4 kcal mol^{-1}). The effect is seen in lower frequency O—H stretching in the infrared spectra of alcohols, correlating with how closely the hydrogen atom sits to a double bond or an aromatic ring, and most dramatically in the upfield shift of 1.5 ppm for the phenolic OH proton when the spectrum is taken in benzene, as a consequence of the proton sitting in the shielding region of the ring current **2.93**.



2.93 **2.94** **2.95**

2.4.1.4 ***C—H $\cdots$ π Bonds.*** Even weaker hydrogen bonds, never more than 4 kJ mol^{-1} (1 kcal mol^{-1}), can be detected between C—H bonds and C=C π bonds. These interactions are seen in solid-state structures like that of benzene with its edge-to-face arrangement **2.94**, and in some noticeable upfield shifts in the ^{1}H-NMR spectra on changing solvents from carbon tetrachloride to benzene. Larger shifts in the NMR spectra are seen with the more acidic C—H bonds, with chloroform showing an upfield shift of 1.35 ppm at infinite dilution, because of the formation of a bond to the centre of the π system **2.95**.

2.4.2 Hypervalency

There are many molecules which clearly have more than the octet of electrons found in traditional Lewis structures. These include such molecules as PF_5, SF_4, $PhICl_2$, and XeF_2, such ions as SiF_5^- and PCl_6^-, and intermediates like those involved in S_N2 reactions taking place at any of the elements below the first row in the periodic table. Such molecules have been called hypervalent, or to have expanded valence shells. Hypervalent molecules almost always have a high proportion of electronegative elements among their ligands.

The standard method of explaining how such molecules can be stable is to invoke the interactions of filled p or hybrid orbitals on the ligands with an empty d orbital on the central element. Like any interaction of filled with unfilled orbitals, interactions with empty d orbitals are bound to be stabilising, but d orbitals are too high in energy relative to the p orbitals for their interaction to have any significant effect.

It is better to see hypervalent bonding as the consequence of orbital interactions. Essentially, the central atom Y is involved in normal bonding to $n-2$ of its ligands. In addition, orbitals on each of the two remaining ligands X interact with an unused p orbital on the central element Y to create a set of three molecular orbitals (Fig. 2.18). To be overall bonding, ψ_2 must be largely nonbonding, which

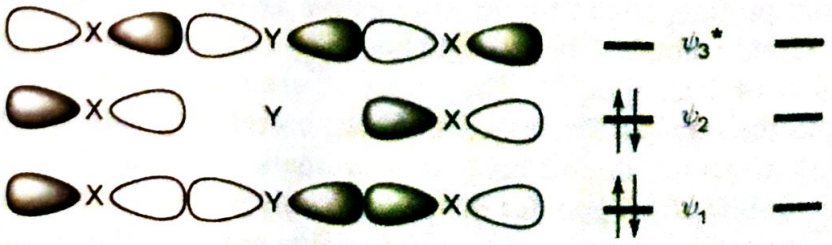
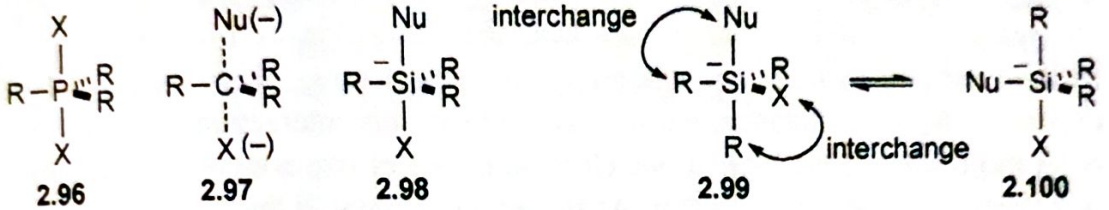


Fig. 2.18 The key molecular orbitals of hypervalent bonding

it will be if the ligands are kept well apart, and are electronegative elements, just as they are in hydrogen bonding.

Thus a pentacovalent phosphorus compound will have the three least electronegative ligands R in the plane of a trigonal bipyramid **2.96**, with bonds formed from the 3s and the $3p_x$ and $3p_y$ orbitals, and the two most electronegative ligands disposed linearly at the apices, with bonds formed from the two lower orbitals in Fig. 2.18. Furthermore, the electronegative ligands X will carry more negative charge, and will repel each other best if they are both apical. In consequence of both orbital and charge effects, the apical bonds are weaker than the basal, and these are the ones that make and break during reactions.



2.96 **2.97** **2.98** **2.99** **2.100**

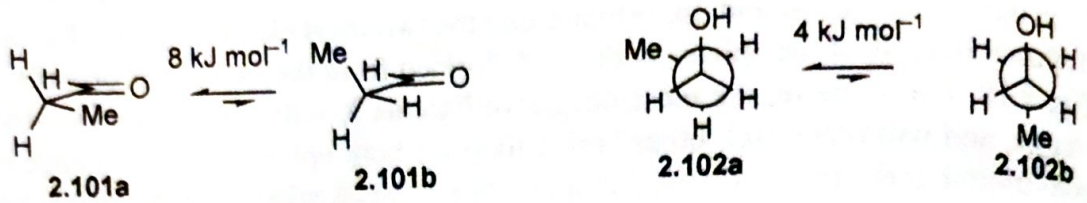
The same pattern is seen in the transition structures for nucleophilic substitution reactions. Apical entry of a nucleophile and apical departure will have the lowest-energy transtition structure **2.97** for the S_N2 reaction at carbon, and can give an intermediate with a lifetime **2.98** at silicon. The preference for electronegative elements to retain their apical positions ensures inversion of configuration when the nucleophile Nu and nucleofugal group X are both electronegative. When they are not both electronegative, apical attack **2.99** may be followed by a *pseudorotation* to give a different intermediate **2.100**, interchanging the positions of the ligands. Apical departure of X then explains the retention of configuration that is often seen in silicon chemistry when the leaving group is not conspicuously electronegative, and hence does not stabilise the arrangement in which it is apical.

2.4.3 Polar Interactions, and van der Waals and other Weak Interactions

2.4.3.1 Coulombic Forces. If two molecules, or two parts of one molecule, have charges or dipoles, the sites of opposite charge attract each other, and sites with the same charge repel each other. These forces can be large and have a conspicuous influence on molecular properties. The same electrostatic forces also come into play in a number of weaker interactions. Furthermore, polar attractions from one polar molecule to another, or from one strongly hydrogen-bonding molecule to another, lead such molecules to aggregate, and to exclude nonpolar molecules. This is the basis for the well-known hydrophobic effect, in which nonpolar molecules stick together to avoid being in water.

2.4.3.2 Dipole-Dipole Attraction. If only one of the molecules is charged or a dipole, it can still respond to weak polar forces in molecules not traditionally thought of as being polar. Two examples of weak dipolar interactions are seen in propanal **2.101** and propanol **2.102**, in which the lower-energy gauche conformations **2.101a** and **2.102a** have the methyl group close to the oxygen atom. The

polarisation of the H—C bonds in the methyl groups leaves a weak positive charge on the outside and this is attracted to the partial negative charge on the oxygen atoms, lowering the energy of these conformations below those of the anti.



2.101a **2.101b** **2.102a** **2.102b**

2.4.3.3 van der Waals Attraction. The interaction of filled orbitals of one reagent with the filled orbitals of another is inherently energy-raising, and this is countered by a small attractive force from the interactions of filled orbitals with unfilled orbitals, which are inherently energy-lowering. Both forces fall off exponentially with distance, but they are not the only interactions between nonpolar molecules. If we look at one electron in one of two nonpolar molecules, it will repel an electron in the other. At any given moment, if the first electron is on the side of the molecule facing the other molecule, it will cause its opposite number to spend more of its time on the far side of the second molecule. The electrons are said to be *correlated*. As the two electrons spend, on average, more of their time far away from each, the two molecules experience a small attractive dipolar electrostatic attraction. This only comes into play at short distances, with the energy falling off as the inverse sixth power of the distance apart. The resultant attractive force is known as a dispersion force, or more commonly as the van der Waals attraction. It is responsible, for example, for the weak force that helps to keep liquid hydrocarbons in the liquid state, and that helps them to aggregate in polar solvents. In liquid helium, at very low temperatures to be sure, the *only* attractions holding the atoms together are the van der Waals forces.

2.4.3.4 π-π Interactions and π Stacking. Aromatic rings show an aptitude to aggregate that is not simply explained by van der Waals attraction. The phenomenon shows up in such important areas of molecular recognition as the stacked interactions between the aromatic rings in the DNA double helix, in intercalation by drugs and carcinogens into the DNA stack, in the aggregation of the chlorin rings in the chloroplast, in the tertiary structure of proteins, and in many host-guest supramolecules. An edge-to-face stacking arrangement is common, because of hydrogen bonding **2.94**, but a face-to-face stacking arrangement is not uncommon. However, a stack of nonpolar aromatic rings perfectly lined up directly on top of each other is straightforwardly repulsive (Fig. 2.19a)—one π system repels the other, and the van der Waals attractions are not powerful enough to stabilise this arrangement. Aromatic rings stacked above one another are stabilised when one π system is offset relative to the other (Fig. 2.19b), because there is an electrostatic attraction from the positively charged σ framework with the negatively charged π cloud, especially since the positive charge is largely on the peripheral and therefore exposed hydrogen atoms. π Stacking is more common

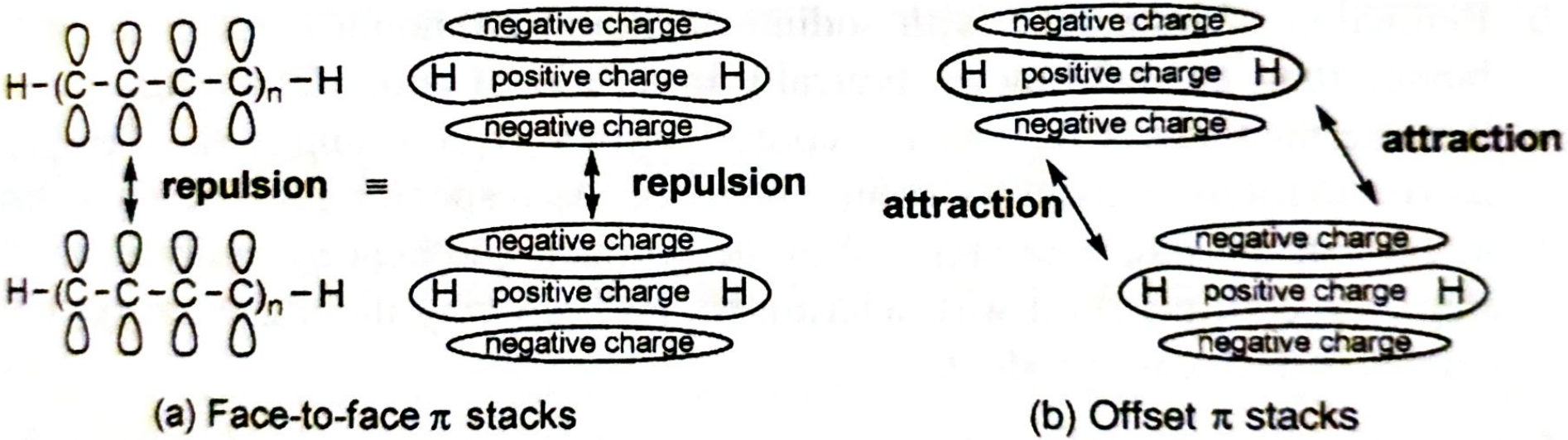


Fig. 2.19 π Stacking

with the larger aromatic systems like porphyrins, probably because of the greater area for the van der Waals forces to work on, than they are with simple benzenes, where the arrangement **2.94** and the offset π stack are close in energy.