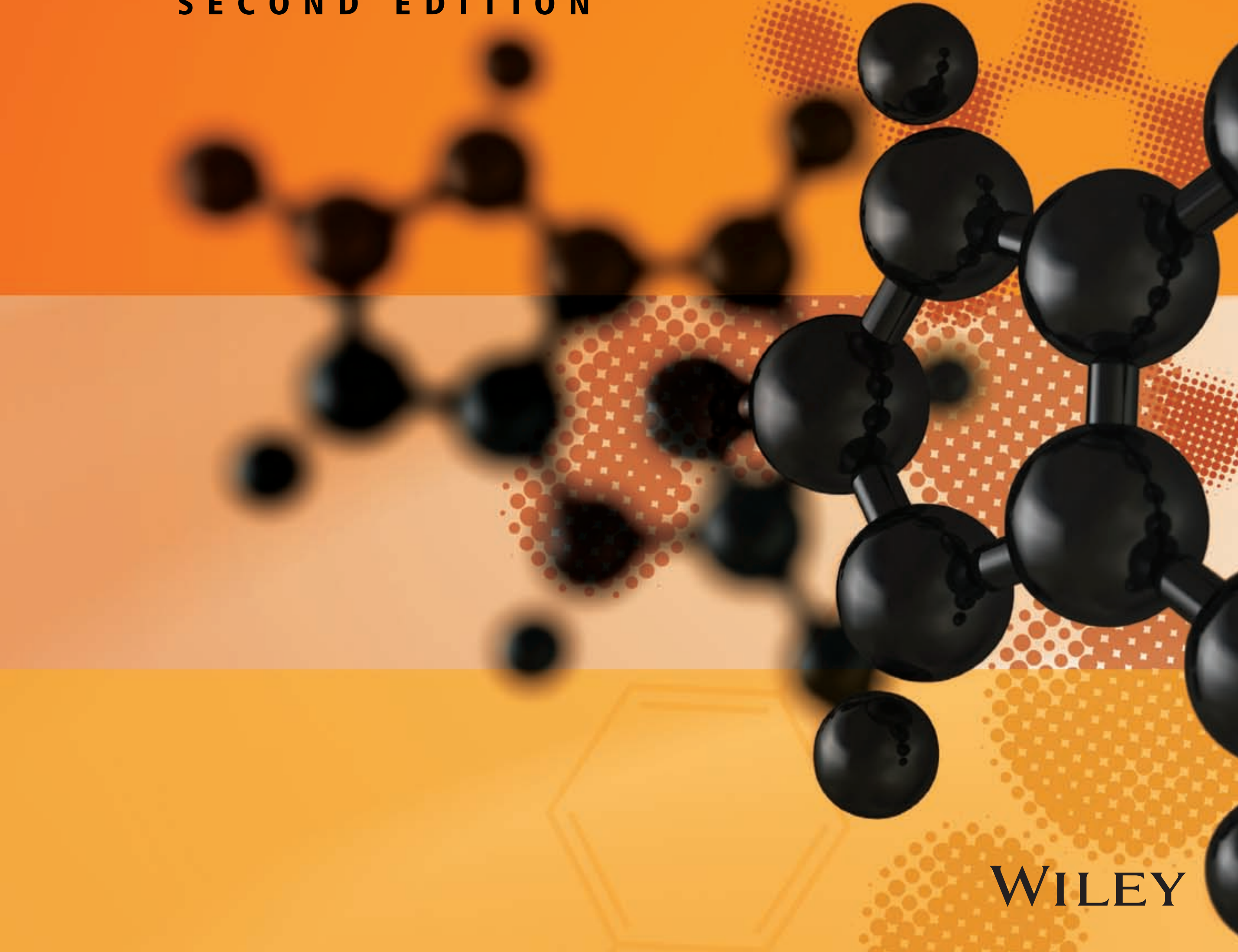
Andrew F. Parsons

KEYNOTES IN Organic Chemistry

SECOND EDITION



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Keynotes in Organic Chemistry

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Second Edition

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Contents

Preface

With the advent of modularisation and an ever-increasing number of examinations, there is a growing need for concise revision notes that encapsulate the key points of a subject in a meaningful fashion. This keynote revision guide provides concise organic chemistry notes for first year students studying chemistry and related courses (including biochemistry) in the UK. The text will also be appropriate for students on similar courses in other countries.

An emphasis is placed on presenting the material pictorially (pictures speak louder than words); hence, there are relatively few paragraphs of text but numerous diagrams. These are annotated with key phrases that summarise important concepts/key information and bullet points are included to concisely highlight key principles and definitions.

The material is organised to provide a structured programme of revision. Fundamental concepts, such as structure and bonding, functional group identification and stereochemistry are introduced in the first three chapters. An important chapter on reactivity and mechanism is included to provide a short overview of the basic principles of organic reactions. The aim here is to provide the reader with a summary of the 'key tools' which are necessary for understanding the following chapters and an important emphasis is placed on organisation of material based on reaction mechanism. Thus, an overview of general reaction pathways/mechanisms (such as substitution and addition) is included and these mechanisms are revisited in more detail in the following chapters. Chapters 5–10 are treated essentially as 'case studies', reviewing the chemistry of the most important functional groups. Halogenoalkanes are discussed first and as these compounds undergo elimination reactions this is followed by the (electrophilic addition) reactions of alkenes and alkynes. This leads on to the contrasting (electrophilic substitution) reactivity of benzene and derivatives in Chapter 7, while the rich chemistry of carbonyl compounds is divided into Chapters 8 and 9. This division is made on the basis of the different reactivity (addition versus substitution) of aldehydes/ketones and carboxylic acid derivatives to nucleophiles. A chapter is included to revise the importance of spectroscopy in structure elucidation and, finally, the structure and reactivity of a number of important natural products and synthetic polymers is highlighted in Chapter 11. Worked examples and questions are included at the end of each chapter to test the reader's understanding, and outline answers are provided for all of the questions. Tables of useful physical data, reaction summaries and a glossary are included in appendices at the back of the book.

New to this edition

A number of additions have been made to this edition to reflect the feedback from students and lecturers:

- A second colour is used to clarify some of the diagrams, particularly the mechanistic aspects
- Reference notes are added in the margin to help the reader find information and to emphasise links between different topics
- Diagrams are included in the introductory key point sections for each chapter
- Additional end-of-chapter problems (with outline answers) are included
- A worked example is included at the end of each chapter
- The information in the appendices has been expanded, including reaction summaries and a glossary

Acknowledgements

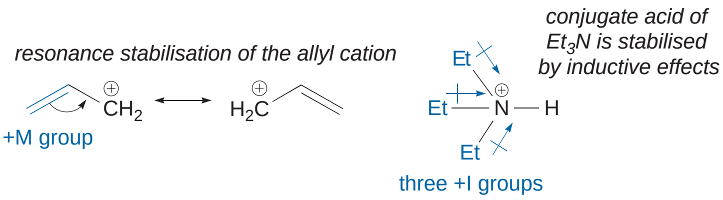
There are numerous people I would like to thank for their help with this project. This includes many students and colleagues at York. Their constructive comments were invaluable. I would also like to thank my family for their support and patience throughout this project. Finally, I would like to thank Paul Deards and Sarah Tilley from Wiley, for all their help in progressing the second edition.

Dr Andrew F. Parsons
2013

1

Structure and bonding

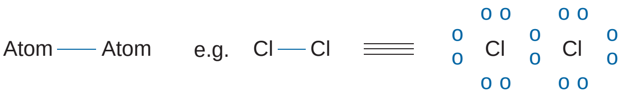
Key point. Organic chemistry is the study of carbon compounds. *Ionic* bonds involve elements gaining or losing electrons but the carbon atom is able to form four *covalent* bonds by sharing the four electrons in its outer shell. Single (C–C), double (C=C) or triple bonds (C≡C) to carbon are possible. When carbon is bonded to a different element, the electrons are not shared equally, as *electronegative* atoms (or groups) attract the electron density whereas *electropositive* atoms (or groups) repel the electron density. An understanding of the electron-withdrawing or -donating ability of atoms, or a group of atoms, can be used to predict whether an organic compound is a good *acid* or *base*.



1.1 Ionic versus covalent bonds

- *Ionic bonds* are formed between molecules with opposite charges. The negatively charged anion will electrostatically attract the positively charged cation. This is present in (inorganic) salts.

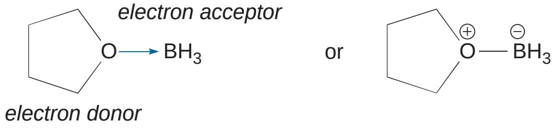
- *Covalent bonds* are formed when a pair of electrons is shared between two atoms. A single line represents the two-electron bond.



Keynotes in Organic Chemistry, Second Edition. Andrew F. Parsons.

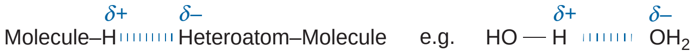
- *Coordinate (or dative) bonds* are formed when a pair of electrons is shared between two atoms. *One* atom donates both electrons and a single line or an arrow represents the two-electron bond.

The cyclic ether is tetrahydrofuran (THF) and BH_3 is called borane (Section 6.2.2.5)



- *Hydrogen bonds* are formed when the partially positive ($\delta+$) hydrogen of one molecule interacts with the partially negative ($\delta-$) heteroatom (e.g. oxygen or nitrogen) of another molecule.

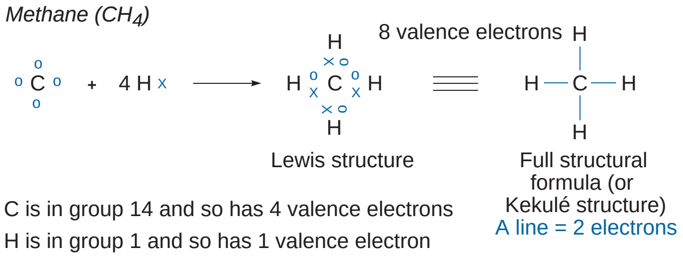
Intramolecular hydrogen bonding in carbonyl compounds is discussed in Section 8.4.1



1.2 The octet rule

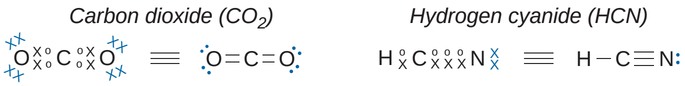
To form organic compounds, the carbon atom shares electrons to give a stable ‘full shell’ electron configuration of eight valence electrons.

Methane is the smallest alkane – alkanes are a family of compounds that contain only C and H atoms linked by single bonds (Section 2.4)



Drawing organic compounds using full structural formulae and other conventions is discussed in Section 2.5

A single bond contains two electrons, a double bond contains four electrons and a triple bond contains six electrons. A lone (or non-bonding) pair of electrons is represented by two dots (• •).



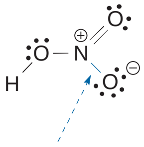
1.3 Formal charge

Formal positive or negative charges are assigned to atoms, which have an apparent ‘abnormal’ number of bonds.

Atom(s)	**C**	**N, P**	**O, S**	**F, Cl, Br, I**
Group number	14	15	16	17
Normal number of 2 electron bonds	4	3	2	1

Formal charge = group number in periodic table – number of bonds to atom – number of unshared electrons – 10

Example: Nitric acid (HNO_3)



Nitrogen with 4 covalent bonds has a formal charge of +1

Formal charge: 15 – 4 – 0 – 10 = +1

The nitrogen atom donates a pair of electrons to make this bond

Nitric acid is used in synthesis to nitrate aromatic compounds such as benzene (Section 7.2.2)

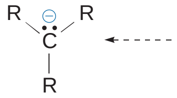
Carbon forms four covalent bonds. When only three covalent bonds are present, the carbon atom can have either a formal negative charge or a formal positive charge.

The stability of carbocations and carbanions is discussed in Section 4.3

- *Carbanions*–three covalent bonds to carbon and a formal negative charge.

Formal charge on C:

14 – 3 – 2 – 10 = –1



8 outer electrons:
3 two-electron bonds
and 2 non-bonding
electrons

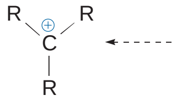
The negative charge is used to show the 2 non-bonding electrons

Carbanions are formed on deprotonation of organic compounds. Deprotonation of a carbonyl compound, at the α-position, forms a carbanion called an enolate ion (Section 8.4.3)

- *Carbocations*–three covalent bonds to carbon and a formal positive charge.

Formal charge on C:

14 – 3 – 0 – 10 = +1



6 outer electrons:
3 two-electron bonds

The positive charge is used to show the absence of 2 electrons

Carbocations are intermediates in a number of reactions, including S_N1 reactions (Section 5.3.1.2)

1.4 Sigma (σ–) and pi (π–) bonds

The electrons shared in a covalent bond result from overlap of atomic orbitals to give a new molecular orbital. Electrons in 1s and 2s orbitals combine to give sigma (σ–) bonds.

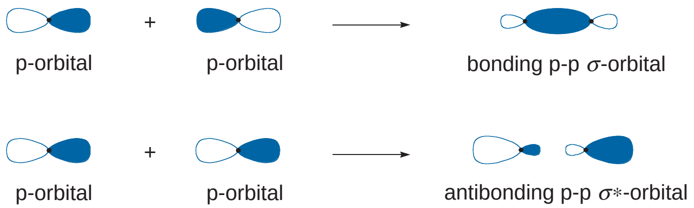
When two 1s orbitals combine *in-phase*, this produces a *bonding molecular orbital*.

Molecular orbitals and chemical reactions are discussed in Section 4.10

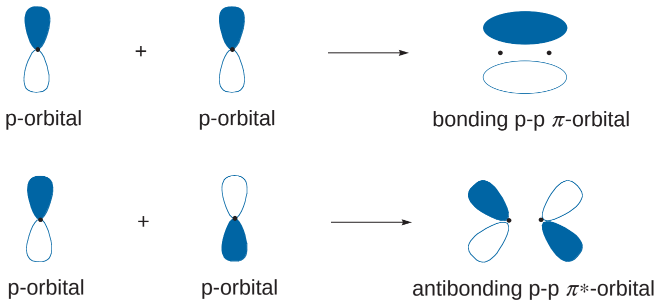
When two 1s orbitals combine *out-of-phase*, this produces an *antibonding molecular orbital*.

Electrons in p orbitals can combine to give sigma (σ) or pi (π) bonds.

- *Sigma (σ−) bonds* are strong bonds formed by head-on overlap of two atomic orbitals.



- *Pi (π−) bonds* are weaker bonds formed by side-on overlap of two p-orbitals.



Alkenes have a C=C bond containing one strong σ-bond and one weaker π-bond (Section 6.1)

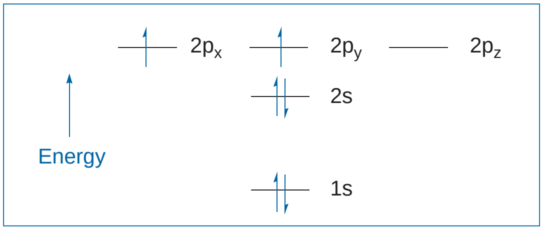
All carbonyl compounds have a C=O bond, which contains one strong σ-bond and one weaker π-bond (Section 8.1)

Only σ- or π-bonds are present in organic compounds. All single bonds are σ-bonds while all multiple (double or triple) bonds are composed of one σ-bond and one or two π-bonds.

1.5 Hybridisation

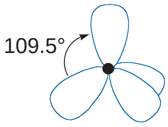
- The ground-state electronic configuration of carbon is $1s^2 2s^2 2p_x{}^1 2p_y{}^1$.
- The six electrons fill up lower energy orbitals before entering higher energy orbitals (Aufbau principle).
- Each orbital is allowed a maximum of two electrons (Pauli exclusion principle).
- The two 2p electrons occupy separate orbitals before pairing up (Hund's rule).

Hund's rule states that when filling up a set of orbitals of the same energy, electrons are added with parallel spins to different orbitals rather than pairing two electrons in one orbital

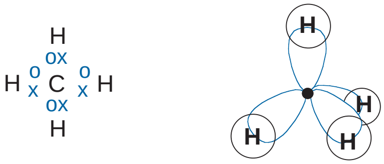


The carbon atom can mix the 2s and 2p atomic orbitals to form four new hybrid orbitals in a process known as *hybridisation*.

- *sp^3 Hybridisation*. For four single σ-bonds – carbon is sp^3 hybridised (e.g. in methane, CH_4). The orbitals move as far apart as possible, and the lobes point to the corners of a tetrahedron (109.5° bond angle).



sp^3 hybridisation

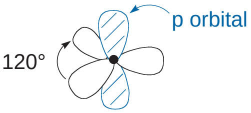


methane: 4 × C–H σ-bonds

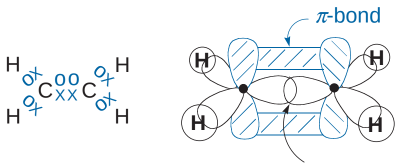
- *sp^2 Hybridisation*. For three single σ-bonds and one π-bond – the π-bond requires one p-orbital, and hence the carbon is sp^2 hybridised (e.g. in ethene, $H_2C{=}CH_2$). The three sp^2-orbitals point to the corners of a triangle (120° bond angle), and the remaining p-orbital is perpendicular to the sp^2 plane.

Alkenes have a C=C bond containing one strong σ-bond and one weaker π-bond (Section 6.1)

All carbonyl compounds have a C=O bond, which contains one strong σ-bond and one weaker π-bond (Section 8.1)



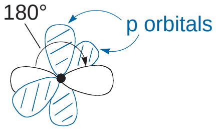
sp^2 hybridisation



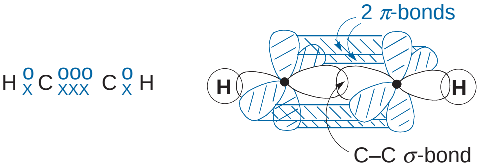
ethene: 4 × C–H σ-bonds, 1 × C–C σ-bond, 1 × C–C π-bond

- *sp Hybridisation*. For two single σ-bonds and two π-bonds – the two π-bonds require two p-orbitals, and hence the carbon is sp hybridised (e.g. in ethyne, HC≡CH). The two sp-orbitals point in the opposite directions (180° bond angle), and the two p-orbitals are perpendicular to the sp plane.

Alkynes have a C≡C bond containing one strong σ-bond and two weaker π-bonds (Section 6.1)



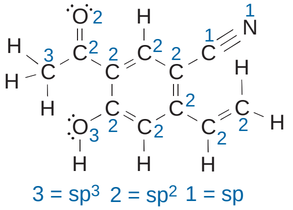
sp hybridisation

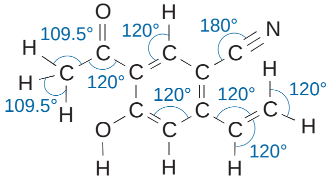


ethyne: 2 × C–H σ-bonds, 1 × C–C σ-bond, 2 x C–C π-bonds

- For a single C–C or C–O bond, the atoms are sp^3 hybridised and the carbon atom(s) is *tetrahedral*.
- For a double C=C or C=O bond, the atoms are sp^2 hybridised and the carbon atom(s) is *trigonal planar*.
- For a triple C≡C or C≡N bond, the atoms are sp hybridised and the carbon atom(s) is *linear*.

This compound contains four functional groups, including a phenol. Functional groups are introduced in Section 2.1





The shape of organic molecules is therefore determined by the hybridisation of the atoms.

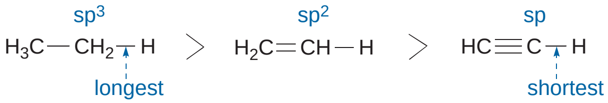
Functional groups (Section 2.1) that contain π-bonds are generally more reactive as a π-bond is weaker than a σ-bond. The π-bond in an alkene or alkyne is around $+250\,\text{kJ mol}^{-1}$, while the σ-bond is around $+350\,\text{kJ mol}^{-1}$.

Bond	Mean bond enthalpies (kJ mol^{-1})	Mean bond lengths (pm)
C—C	+347	153
C=C	+612	134
C≡C	+838	120

A hydrogen atom attached to a C≡C bond is more acidic than a hydrogen atom attached to a C=C bond or a C–C bond; this is explained by the change in hybridisation of the carbon atom that is bonded to the hydrogen atom (Section 1.7.4)

Rotation about C–C bonds is discussed in Section 3.2

The shorter the bond length, the stronger the bond. For C–H bonds, the greater the ‘s’ character of the carbon orbitals, the shorter the bond length. This is because the electrons are held closer to the nucleus.



$$\underset{\text{longest}}{\overset{sp^3}{H_3C{-}CH_2{-}H}} \;>\; \overset{sp^2}{H_2C{=}CH{-}H} \;>\; \underset{\text{shortest}}{\overset{sp}{HC{\equiv}C{-}H}}$$

A single C–C σ-bond can undergo free rotation at room temperature, but a π-bond prevents free rotation around a C=C bond. For maximum orbital overlap in a π-bond, the two p-orbitals need to be parallel to one another. Any rotation around the C=C bond will break the π-bond.

1.6 Inductive effects, hyperconjugation and mesomeric effects

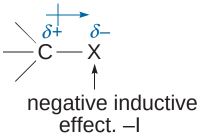
1.6.1 Inductive effects

In a covalent bond between two different atoms, the electrons in the σ-bond are not shared equally. The electrons are attracted towards the most electronegative atom. An arrow drawn above the line representing the covalent bond can show this. (Sometimes an arrow is drawn on the line.) Electrons are pulled in the direction of the arrow.

An inductive effect is the polarisation of electrons through σ-bonds

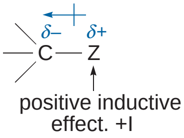
When the atom (X) is more electronegative than carbon

electrons **attracted to X**



When the atom (Z) is less electronegative than carbon

electrons **attracted to C**



–I groups

X = Br, Cl, NO_2, OH, OR, SH, SR, NH_2, NHR, NR_2, CN, CO_2H, CHO, C(O)R

The more electronegative the atom (X), the stronger the –I effect

+I groups

Z = R (alkyl or aryl), metals (e.g. Li or Mg)

The more electropositive the atom (Z), the stronger the +I effect

An alkyl group (R) is formed by removing a hydrogen atom from an alkane (Section 2.2).

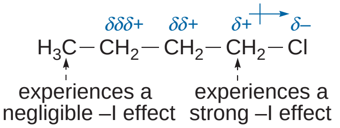
An aryl group (Ar) is benzene (typically called phenyl, Ph) or a substituted benzene group (Section 2.2)

Pauling electronegativity scale

K = 0.82	I = 2.66
C = 2.55	Br = 2.96
N = 3.04	Cl = 3.16
O = 3.44	F = 3.98

The higher the value the more electronegative the atom

The inductive effect of the atom rapidly diminishes as the chain length increases

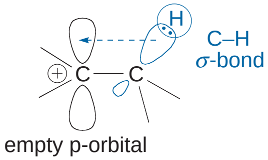


The overall polarity of a molecule is determined by the individual bond polarities, formal charges and lone pair contributions and this can be measured by the dipole moment (μ). The larger the dipole moment (often measured in debyes, D), the more polar the compound.

1.6.2 Hyperconjugation

A σ-bond can stabilise a neighbouring carbocation (or positively charged carbon, e.g. R_3C^+) by donating electrons to the vacant p-orbital. The positive charge is delocalised or ‘spread out’ and this stabilising effect is called *resonance*.

Hyperconjugation is the donation of electrons from nearby C–H or C–C σ-bonds



The electrons in the C–H σ-bond spend some of the time in the empty p-orbital

The stability of carbocations is discussed in Section 4.3.1

1.6.3 Mesomeric effects

Whilst inductive effects pull electrons through the σ-bond framework, electrons can also move through the π-bond network. A π-bond can stabilise a negative charge, a

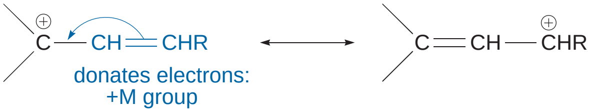
Resonance forms (sometimes called canonical forms) show all possible distributions of electrons in a molecule or an ion

positive charge, a lone pair of electrons or an adjacent bond by *resonance* (i.e. delocalisation or ‘spreading out’ of the electrons). Curly arrows (Section 4.1) are used to represent the movement of π- or non-bonding electrons to give different resonance forms. It is only the electrons, not the nuclei, that move in the resonance forms, and a double-headed arrow is used to show their relationship.

1.6.3.1 Positive mesomeric effect

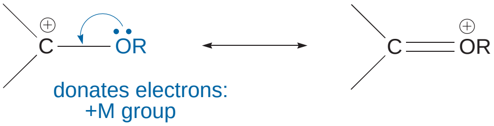
- When a π-system donates electrons, the π-system has a positive mesomeric effect, +M.

This carbocation is called an allylic cation (see Section 5.3.1.2)



- When a lone pair of electrons is donated, the group donating the electrons has a positive mesomeric effect, +M.

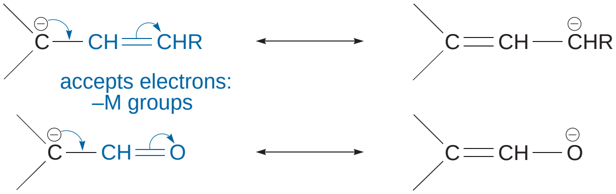
The OR group is called an alkoxy group (see Section 2.4)



1.6.3.2 Negative mesomeric effect

- When a π-system accepts electrons, the π-system has a negative mesomeric effect, −M.

This anion, formed by deprotonating an aldehyde at the α-position, is called an enolate ion (Section 8.4.3)



Functional groups are discussed in Section 2.1

The actual structures of the cations or anions lie somewhere between the two resonance forms. All resonance forms must have the same overall charge and obey the same rules of valency.

–M groups generally contain an electronegative atom(s) and/or a π-bond(s):

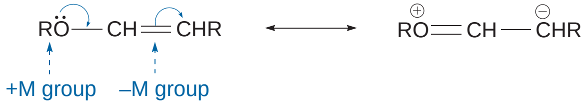
CHO, C(O)R, CO_2H, CO_2Me, NO_2, CN, aromatics, alkenes

+M groups generally contain a lone pair of electrons or a π-bond(s):

$\ddot{\mathrm{Cl}}$, $\ddot{\mathrm{Br}}$, $\ddot{\mathrm{O}}\mathrm{H}$, $\ddot{\mathrm{O}}\mathrm{R}$, $\ddot{\mathrm{S}}\mathrm{H}$, $\ddot{\mathrm{S}}\mathrm{R}$, $\ddot{\mathrm{N}}\mathrm{H}_2$, $\ddot{\mathrm{N}}\mathrm{HR}$, $\ddot{\mathrm{N}}\mathrm{R}_2$, aromatics, alkenes

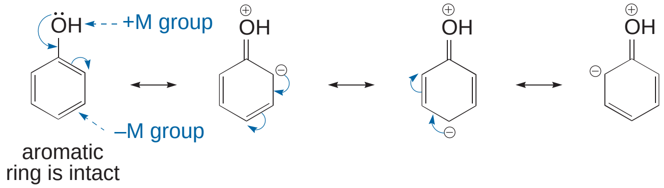
Aromatic (or aryl) groups and alkenes can be *both* +M and –M.

In neutral compounds, there will always be a +M *and* −M group(s): one group donates (+M) the electrons, the other group(s) accepts the electrons (−M).



An amide, such as $RCONH_2$, also contains both a +M group (NH_2) and a −M group (C=O). See Sections 1.7.2 and 9.3.1

All resonance forms are *not* of the same energy. Generally, the most stable resonance forms have the greatest number of covalent bonds, atoms with a complete valence shell of electrons, and/or an aromatic ring. In phenol (PhOH), for example, the resonance form with the intact aromatic benzene ring is expected to predominate.



Benzene and other aromatic compounds, including phenol, are discussed in Chapter 7

As a rule of thumb, the more resonance structures an anion, cation or neutral π-system can have, the more stable it is.

1.6.3.3 *Inductive versus mesomeric effects*

Mesomeric effects are generally stronger than inductive effects. A +M group is likely to stabilise a cation more effectively than a +I group.

Mesomeric effects can be effective over much longer distances than inductive effects provided that *conjugation* is present (i.e. alternating single and double bonds). Whereas inductive effects are determined by distance, mesomeric effects are determined by the relative positions of +M and −M groups in a molecule (Section 1.7).

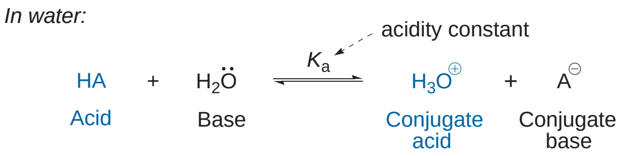
Conjugated enones, containing a C=C–C=O group, are discussed in Section 8.5.1

1.7 Acidity and basicity

1.7.1 Acids

An acid is a substance that donates a proton (Brønsted-Lowry). Acidic compounds have low pK_a values and are good proton donors as the anions (or conjugate bases), formed on deprotonation, are relatively stable.

Equilibria and equilibrium constants are discussed in Section 4.9.1.1



The more stable the conjugate base the stronger the acid

$$K_a \approx \frac{[H_3O^{\oplus}]\,[A^{\ominus}]}{[HA]}$$

As H_2O is in excess

$$pK_a = -\log_{10} K_a$$

The higher the value of K_a, the lower the pK_a value and the more acidic is HA

The pK_a value equals the pH of the acid when it is half ionised. At pH's above the pK_a the acid (HA) exists predominantly as the conjugate base (A^-) in water. At pH's below the pK_a it exists predominantly as HA.

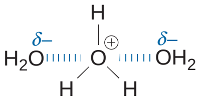
pH = 0, strongly acidic

pH = 7, neutral

pH = 14, strongly basic

The influence of solvent polarity on substitution and elimination reactions is discussed in Sections 5.3.1.3 and 5.3.2.3

The pK_a values are influenced by the solvent. Polar solvents will stabilise cations and/or anions by *solvation* in which the charge is delocalised over the solvent (e.g. by hydrogen-bonding in water).



The more electronegative the atom bearing the negative charge, the more stable the conjugate base (which is negatively charged).

pK_a	3		16		33		48	
most acidic	HF	>	H_2O	>	NH_3	>	CH_4	*least acidic*

decreasing electronegativity on going from F to C

Inductive effects are introduced in Section 1.6.1

Mesomeric effects are introduced in Section 1.6.3

Therefore, F^- is more stable than H_3C^-.

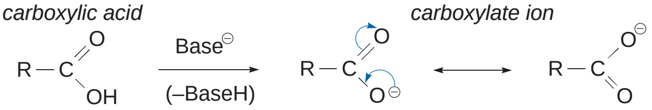
The conjugate base can also be stabilised by −I and −M groups which can delocalise the negative charge. (The more 'spread out' the negative charge, the more stable it is).

–I and –M groups therefore *lower* the pK_a while +I and +M groups *raise* the pK_a

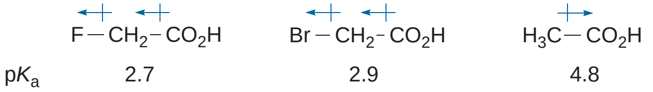
1.7.1.1 Inductive effects and carboxylic acids

The carboxylate ion (RCO_2^-) is formed on deprotonation of a carboxylic acid (RCO_2H). The anion is stabilised by resonance (i.e. the charge is spread over both oxygen atoms) but can also be stabilised by the R group if this has a −I effect.

The reactions of carboxylic acids are discussed in Chapter 9



The greater the −I effect, the more stable the carboxylate ion (e.g. $FCH_2CO_2^-$ is more stable than $BrCH_2CO_2^-$) and the more acidic the carboxylic acid (e.g. FCH_2CO_2H is more acidic than $BrCH_2CO_2H$).



Most acidic as F is more electronegative than Br and has a greater –I effect

Least acidic as the CH_3 group is a +I group

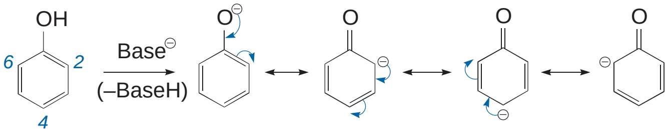
1.7.1.2 Inductive and mesomeric effects and phenols

Mesomeric effects can also stabilise positive and negative charges.

The *negative* charge needs to be on an adjacent carbon atom for a **–M** group to stabilise it

The *positive* charge needs to be on an adjacent carbon atom for a **+M** group to stabilise it

On deprotonation of phenol (PhOH) the phenoxide ion (PhO^-) is formed. This anion is stabilised by the delocalisation of the negative charge on to the 2-, 4- and 6-positions of the benzene ring.



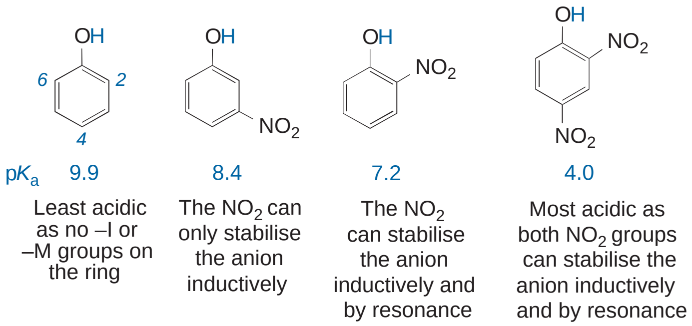
Double-headed curly arrows are introduced in Section 4.1

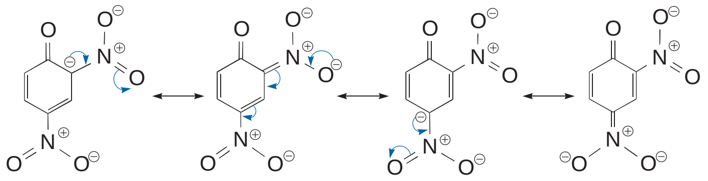
- If −M groups are introduced at the 2-, 4- and/or 6-positions, the anion can be further stabilised by delocalisation through the π-system as the negative charge can be spread onto the −M group. We can use double-headed curly arrows to show this process.
- If −M groups are introduced at the 3- and/or 5-positions, the anion cannot be stabilised by delocalisation, as the negative charge cannot be spread onto the −M group. There is no way of using curly arrows to delocalise the charge on to the −M group.
- If −I groups are introduced on the benzene ring, the effect will depend on their distance from the negative charge. The closer the −I group is to the negative charge, the greater the stabilising effect will be. The order of −I stabilisation is therefore 2-position > 3-position > 4-position.
- The −M effects are much stronger than −I effects (Section 1.6.3).

Examples

The NO_2 group is strongly electron-withdrawing; –I and –M

Naming substituted benzenes is discussed in Section 2.4





1.7.2 Bases

A base is a substance that accepts a proton (Brønsted-Lowry). Basic compounds are good proton acceptors as the conjugate acids, formed on protonation, are relatively stable. Consequently, strong bases (B: or B^-) give conjugate acids (BH^+ or BH) with high pK_a values.

Equilibria and equilibrium constants are discussed in Section 4.9.1.1

In water:

basicity constant

$$\underset{\text{Base}}{\ddot{B}} + \underset{\text{Acid}}{H_2O} \overset{K_b}{\rightleftharpoons} \underset{\text{Conjugate acid}}{\overset{\oplus}{B}H} + \underset{\text{Conjugate base}}{HO^{\ominus}}$$

For the use of bases in elimination reactions of halogenoalkanes, see Section 5.3.2

The strength of bases is usually described by the K_a and pK_a values of the conjugate acid.

$$\overset{\oplus}{B}H + H_2O \overset{K_a}{\rightleftharpoons} \ddot{B} + H_3O^{\oplus}$$

For reactions of bases with carbonyl compounds see Sections 8.4.3 and 9.11

$$K_a \approx \frac{[B]\,[H_3O^{\oplus}]}{[\overset{\oplus}{B}H]}$$

As H_2O is in excess

Inductive effects are introduced in Section 1.6.1

- If B is a *strong* base then BH^+ will be relatively stable and not easily deprotonated. BH^+ will therefore have a *high* pK_a value.
- If B is a *weak* base then BH^+ will be relatively unstable and easily deprotonated. BH^+ will therefore have a *low* pK_a value.

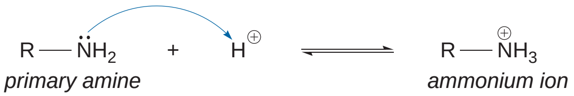
The cation can be stabilised by +I and +M groups, which can delocalise the positive charge. (The more 'spread out' the positive charge, the more stable it is.)

Mesomeric effects are introduced in Section 1.6.3

1.7.2.1 Inductive effects and aliphatic (or alkyl) amines

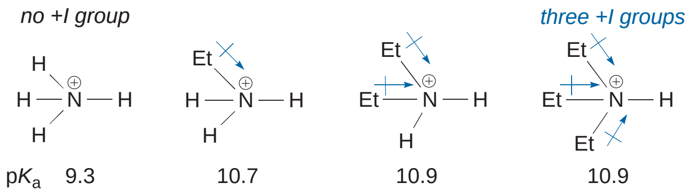
On protonation of amines (e.g. RNH_2), ammonium salts are formed.

Aliphatic amines have nitrogen bonded to one or more alkyl groups; aromatic amines have nitrogen bonded to one or more aryl groups



The greater the +I effect of the R group, the greater the electron density at nitrogen and the more basic the amine. The greater the +I effect, the more stable the ammonium ion and the more basic the amine.

Primary (RNH_2), secondary (R_2NH) and tertiary (R_3N) amines are introduced in Section 2.1

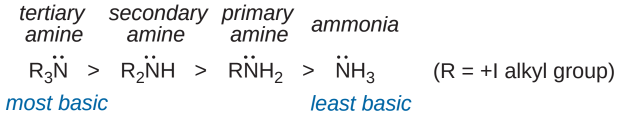


Triethylamine (Et_3N) is commonly used as a base in organic synthesis (Section 5.2.2)

The pK_a values *should* increase steadily as more +I alkyl groups are introduced on nitrogen. However, the pK_a values are determined in *water*, and the more hydrogen atoms on the positively charged nitrogen, the greater the extent of hydrogen bonding between water and the cation. This solvation leads to the stabilisation of the cations containing N–H bonds.

Hydrogen bonds are introduced in Section 1.1

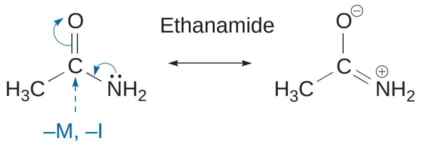
In organic solvents (which cannot solvate the cation) the order of pK_a's is expected to be as follows.



$$R_3\ddot{N} > R_2\ddot{N}H > R\ddot{N}H_2 > \ddot{N}H_3 \quad (R = +I \text{ alkyl group})$$

The presence of −I and/or −M groups on nitrogen reduces the basicity and so, for example, primary amides ($RCONH_2$) are poor bases.

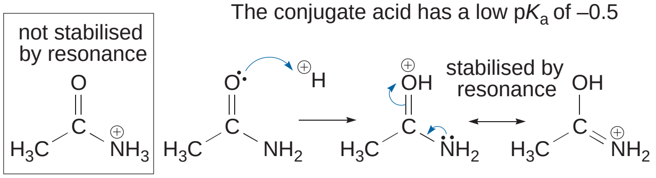
Secondary amides (RCONHR) and tertiary amides ($RCONR_2$) are also very weak bases because the nitrogen lone pairs are stabilised by resonance



The C=O group stabilises the lone pair on nitrogen by resonance – this reduces the electron density on nitrogen

If ethanamide was protonated on nitrogen, the positive charge could not be stabilised by delocalisation. Protonation therefore occurs on oxygen as the charge can be delocalised on to the nitrogen atom.

Reactions of amides are discussed in Section 9.8

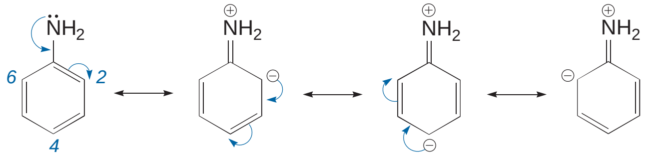


The conjugate acid has a low pK_a of –0.5

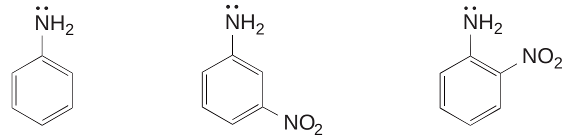
1.7.2.2 *Mesomeric effects and aryl (or aromatic) amines*

For the preparation and reactions of aniline ($PhNH_2$), see Section 7.8

The lone pair of electrons on the nitrogen atom of aminobenzene (or aniline, $PhNH_2$) can be stabilised by delocalisation of the electrons onto the 2-, 4- and 6-positions of the benzene ring. Aromatic amines are therefore less basic than aliphatic amines.



- If −M groups are introduced at the 2-, 4- and/or 6-positions (but not the 3- or 5-positions) the anion can be further stabilised by delocalisation, as the negative charge can be spread on to the −M group. This reduces the basicity of the amine.
- If −I groups are introduced on the benzene ring, the order of −I stabilisation is 2-position > 3-position > 4-position. This reduces the basicity of the amine.



pK_a 4.6 — **Most** basic as no –I or –M groups on the ring

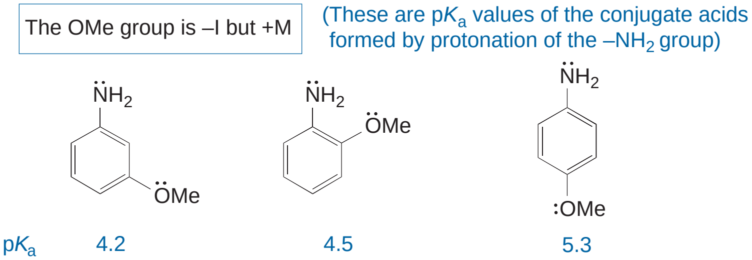
2.45 — The NO_2 can stabilise the lone pair inductively

–0.28 — **Least** basic – the NO_2 can stabilise the lone pair inductively and by resonance

(These are pK_a values of the conjugate acids)

For the Pauling electronegativity scale see Section 1.6.1

- If +M groups (e.g. OMe) are introduced at the 2-, 4- or 6-position of aminobenzene ($PhNH_2$), then the basicity is increased. This is because the +M group donates electron density to the carbon atom bearing the amine group. Note that the nitrogen atom, not the oxygen atom, is protonated – this is because nitrogen is less electronegative than oxygen and is a better electron donor.



The OMe group is –I but +M

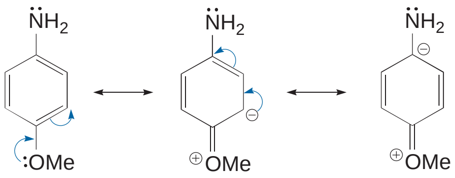
(These are pK_a values of the conjugate acids formed by protonation of the –NH_2 group)

pK_a	4.2	4.5	5.3
	Least basic as the OMe group cannot donate electron density to the carbon atom bearing the nitrogen	The OMe group can donate electron density to the nitrogen but it has a strong –I effect as it is in the 2-position	**Most** basic as the OMe group can donate electron density to the nitrogen and it has a weak –I effect (as well apart from the nitrogen)

The OMe group is called a methoxy group (see Section 2.4 for naming organic compounds)

Curly arrows can be used to show the delocalisation of electrons on to the carbon atom bearing the nitrogen.

Curly arrows are introduced in Section 4.1

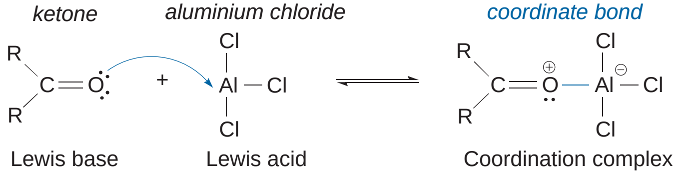


electron density adjacent to the nitrogen increases the basicity

1.7.3 Lewis acids and bases

- A *Lewis acid* is any substance that accepts an electron pair in forming a coordinate bond (Section 1.1). Examples include H^+, BF_3, $AlCl_3$, $TiCl_4$, $ZnCl_2$ and $SnCl_4$. They have unfilled valence shells and so can accept electron pairs.
- A *Lewis base* is any substance that donates an electron pair in forming a coordinate bond. Examples include H_2O, ROH, RCHO, $R_2C{=}O$, R_3N and R_2S. They all have a lone pair(s) of electrons on the heteroatom (O, N or S).

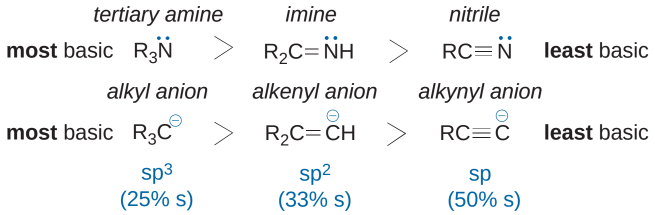
A heteroatom is any atom that is not carbon or hydrogen



Reactions of ketones are discussed in Chapter 8

1.7.4 Basicity and hybridisation

The greater the ‘s’ character of an orbital, the lower in energy the electrons and the more tightly the electrons are held to the nucleus. The electrons in an sp-orbital are therefore less available for protonation than those in an sp^2- or sp^3-orbital, and hence the compounds are less basic.

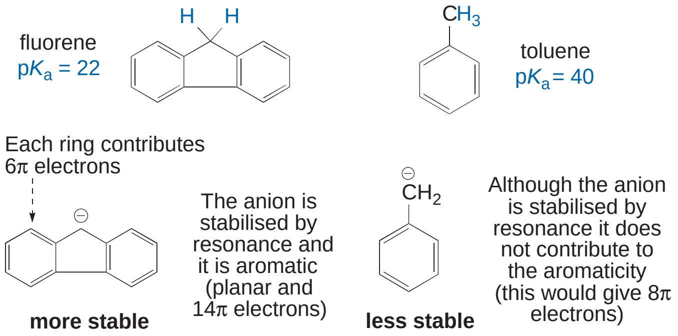


1.7.5 Acidity and aromaticity

Aromatic compounds are planar, conjugated systems which have 4n + 2 electrons (Hückel's rule) (Section 7.1). If, on deprotonation, the anion is part of an aromatic π-system then the negative charge will be stabilised. Aromaticity will therefore *increase* the acidity of the compound.

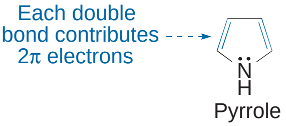
Toluene is a common solvent. Oxidation of the CH_3 group is discussed in Section 7.6

Resonance stabilisation of carbanions is introduced in Section 1.6.3

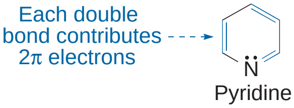


If a lone pair of electrons on a heteroatom is part of an aromatic π-system, then these electrons will not be available for protonation. Aromaticity will therefore *decrease* the basicity of the compound.

Reactions of aromatic heterocycles, including pyrrole and pyridine are discussed in Sections 7.10 and 7.11



The lone pair of electrons contributes to the 6π-electrons in the aromatic ring. Pyrrole is therefore not basic (pK_a –4)



The lone pair of electrons does *not* contribute to the 6π-electrons in the aromatic ring. Pyridine is therefore basic (pK_a 5)

1.7.6 Acid-base reactions

For a table of pK_a values see Appendix 3

The pK_a values can be used to predict if an acid-base reaction can take place. An acid will donate a proton to the conjugate base of any acid with a higher pK_a value.