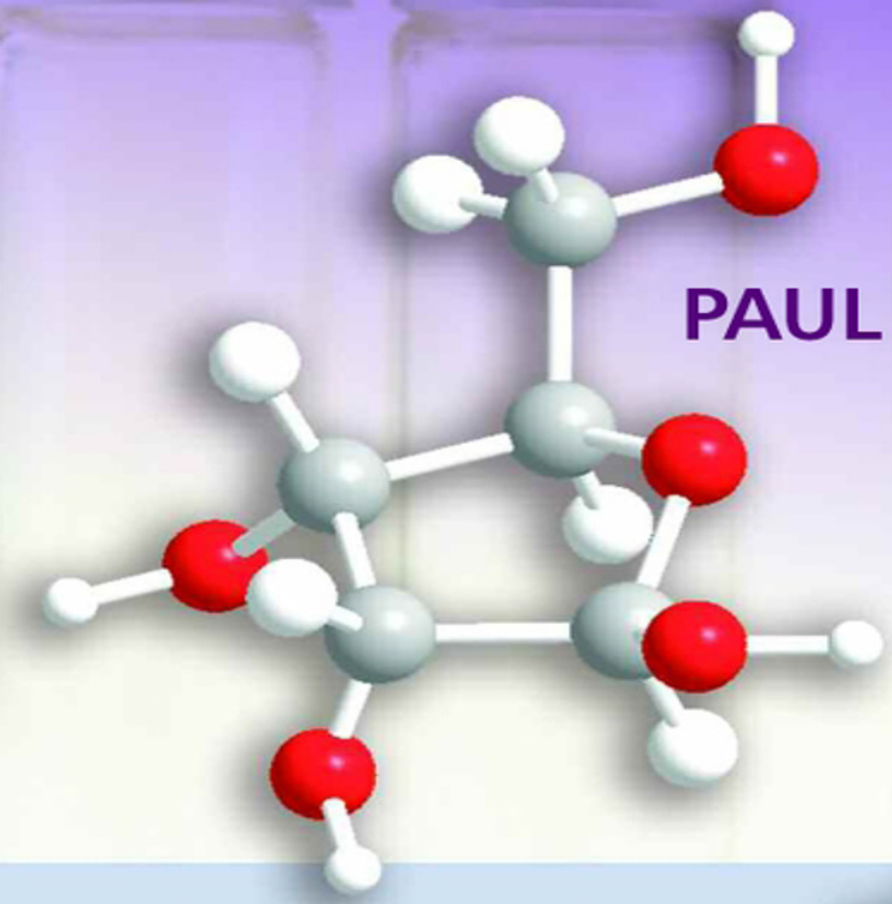
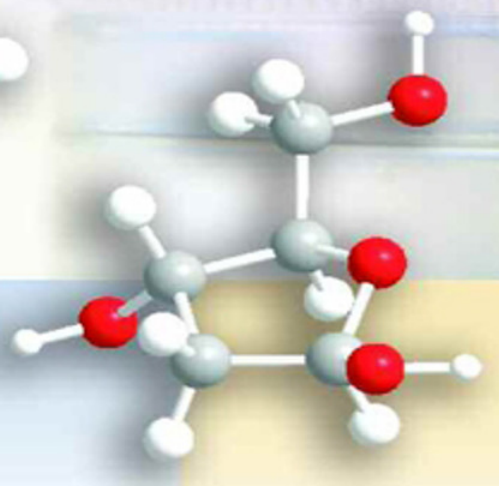
Essentials of Organic Chemistry

For Students of Pharmacy, Medicinal Chemistry and Biological Chemistry



PAUL M DEWICK



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For students of pharmacy, medicinal chemistry
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Contents

Preface

For more years than I care to remember, I have been teaching the new intake of students to the Nottingham pharmacy course, instructing them in those elements of basic organic chemistry necessary for their future studies. During that time, I have also referred them to various organic chemistry textbooks for additional reading. These texts, excellent though they are, contain far too much material that is of no immediate use to pharmacy students, yet they fail to develop sufficiently areas of biological and medicinal interest we would wish to study in more detail. The organic chemistry needs of pharmacy students are not the same as the needs of chemistry students, and the textbooks available have been specially written for the latter group. What I really wanted was an organic chemistry textbook, considerably smaller than the 1000–1500-page tomes that seem the norm, which had been designed for the requirements of pharmacy students. Such a book would also serve the needs of those students on chemistry-based courses, but who are not specializing in chemistry, e.g. students taking medicinal chemistry and biological chemistry. I have wanted to write such a book for a long time now, and this is the result of my endeavours. I hope it proves as useful as I intended it.

Whilst the content is not in any way unique, the selection of topics and their application to biological systems should make the book quite different from others available, and of especial value to the intended readership. It is a combination of carefully chosen material designed to provide a thorough grounding in fundamental chemical principles, but presenting only material most relevant to the target group and omitting that which is outside their requirements. How these principles and concepts are relevant to the study of pharmaceutical and biochemical molecules is then illustrated through a wide range of examples.

I have assumed that readers will have some knowledge of organic chemistry and are familiar with the basic philosophy of bonding and reactivity as covered in pre-university courses. The book then presents material appropriate for the first 2 years of a university pharmacy course, and also provides the fundamental chemical groundwork for courses in medicinal chemistry, biological chemistry, etc. Through selectivity, I have generated a textbook of more modest size, whilst still providing a sufficiently detailed treatment for those topics that are included.

I have adopted a mechanism-based layout for the majority of the book, an approach that best enables the level of detail and selection of topics to be restricted in line with requirements. There is a strong emphasis on understanding and predicting chemical reactivity, rather than developing synthetic methodology. With extensive use of pharmaceutical and biochemical examples, it has been possible to show that the same simple chemistry can be applied to real-life complex molecules. Many of these examples are in self-contained boxes, so that the main theme need not be interrupted. Lots of cross-referencing is included to establish links and similarities; these do not mean you have to look elsewhere to understand the current material, but they are used to stress that we have seen this concept before, or that other uses are coming along in due course.

I have endeavoured to provide a friendly informal approach in the text, with a clear layout and easy-to-find sections. Reaction schemes are annotated to keep material together and reduce the need for textual explanations. Where alternative rationalizations exist,

I have chosen to use only the simpler explanation to keep the reasoning as straightforward as possible. Throughout, I have tried to convince the reader that, by applying principles and deductive reasoning, we can reduce to a minimal level the amount of material that needs be committed to memory. Worked problems showing typical examination questions and how to approach them are used to encourage this way of thinking.

Four chapters towards the end of the book diverge from the other mechanism-oriented chapters. They have a strong biochemical theme and will undoubtedly overlap with what may be taught separately by biochemists. These topics are approached here from a chemical viewpoint, using the same structural and mechanistic principles developed earlier, and should provide an alternative perspective. It is probable that some of the material described will not be required during the first 2 years of study, but it could sow the seeds for more detailed work later in the course.

There is a measure of intended repetition; the same material may appear in more than one place. This is an important ploy to stress that we might want to look at a particular aspect from more than one viewpoint. I have also used similar molecules in different chapters as illustrations of chemical structure or reactivity. Again, this is an intentional strategy to illustrate the multiple facets of real-life complex molecules.

I am particularly grateful to some of my colleagues at Nottingham (Barrie Kellam, Cristina De Matteis, Nick Shaw) for their comments and opinions. I would also like to record the unknowing contribution made by Nottingham pharmacy students over the years. It is from their questions, problems and difficulties that I have shaped this book. I hope future generations of students may benefit from it.

Finally, a word of advice to students, advice that has been offered by organic chemistry teachers many times previously. *Organic chemistry is not learnt by reading*: paper and pencil are essential at all times. It is only through drawing structures and mechanisms that true understanding is attained.

Paul M Dewick
Nottingham, 2005

1

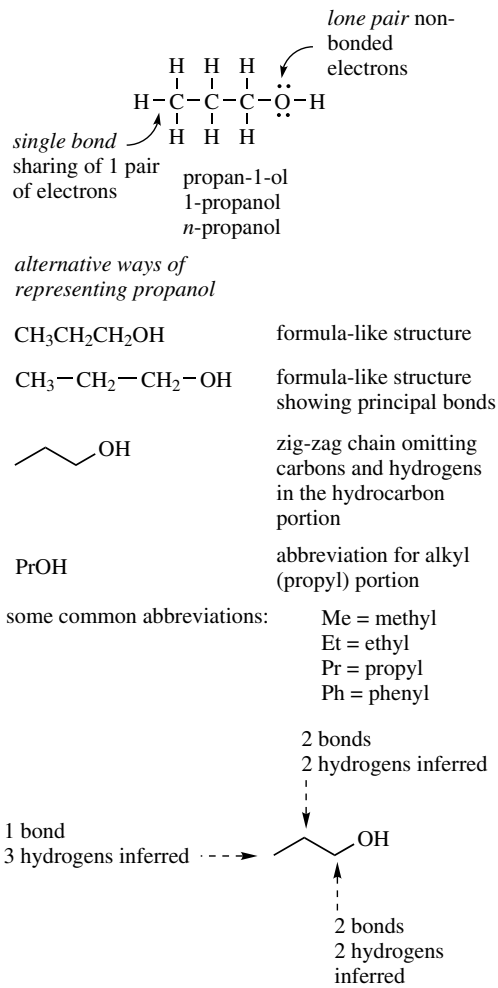
Molecular representations and nomenclature

1.1 Molecular representations

From the beginnings of chemistry, scientists have devised means of representing the materials they are discussing, and have gradually developed a comprehensive range of shorthand notations. These cover the elements themselves, bonding between atoms, the arrangement of atoms in molecules, and, of course, a systematic way of naming compounds that is accepted and understood throughout the scientific world.

The study of carbon compounds provides us with the subdivision 'organic chemistry', and a few simple organic compounds can exemplify this shorthand approach to molecular representations. The primary alcohol propanol (systematically propan-1-ol or 1-propanol, formerly *n*-propanol, *n* signifying normal or unbranched) can be represented by a structure showing all atoms, bonds, and lone pair or non-bonding electrons.

Lines are used to show what we call **single bonds**, indicating the sharing of one pair of electrons. In writing structures, we have to remember the number of bonds that can be made to a particular atom, i.e. the **valency** of the atom. In most structures, carbon is tetravalent, nitrogen trivalent, oxygen divalent, and hydrogen and halogens are univalent. These valencies arise from the number of electrons available for bonding. More often, we trim this type of representation to one that shows the layout of the carbon skeleton with attached hydrogens or other atoms. This can be a formula-like structure without

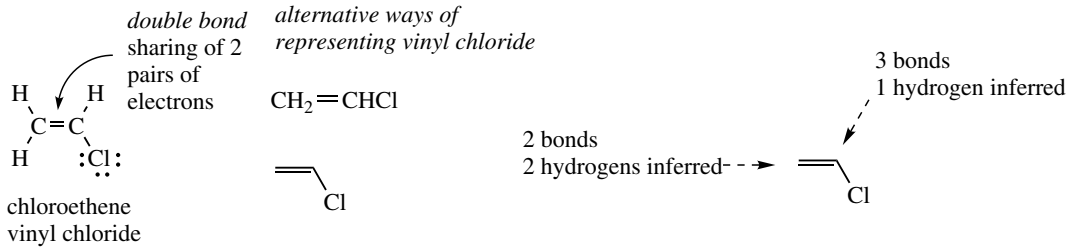


Essentials of Organic Chemistry Paul M Dewick

bonds, or it can be one showing just the principal bonds, those of the carbon chain.

However, for many complex structures, even these approaches become too tedious, and we usually resort to a shorthand version that omits most, if not all, of the carbon and hydrogen atoms. Propanol is now shown as a **zig-zag chain** with an OH group at one end. The other end of the chain, where it stops, is understood to represent a methyl group; three attached hydrogens have to be inferred. At a point on the chain, two hydrogens are assumed, because two bonds to carbons are already shown. In a structure where three bonds joined, a single additional hydrogen would be assumed (see vinyl chloride, below).

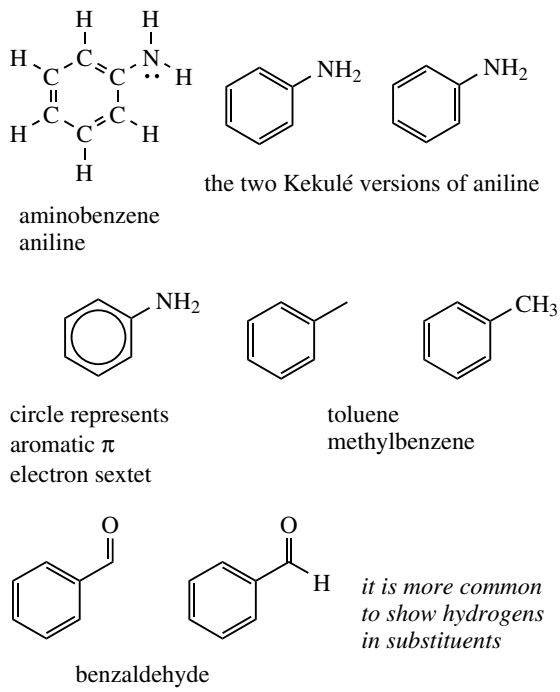
The zig-zag arrangement is convenient so that we see where carbons are located (a long straight line would not tell us how many carbons there are), but it also mimics the low-energy arrangement (conformation) for such a compound (see Section 3.3.1). Note that it is usual to write out the hydroxyl, or some alternative group, in full. This group, the so-called **functional group**, tends to be the reactive part of the molecule that we shall be considering in reactions. When we want an even more concise method of writing the molecule, abbreviations for an alkyl (or aryl) group may be used, in which case propanol becomes PrOH. Some more common abbreviations are given later in Table 1.3.



Double bonds, representing the sharing of two pairs of electrons, are inferred by writing a double line. Vinyl chloride (systematically chloroethene) is shown as two different representations according to the conventions we have just seen for propanol. Note that it is customary always to show the reactive double bond, so that CH_2CHCl would not be encountered as an abbreviation for vinyl chloride.

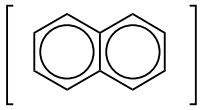
The six-membered cyclic system in **aromatic rings** is usually drawn with alternating double and single bonds, i.e. the **Kekulé form**, and it is usually immaterial which of the two possible versions is used. Aniline (systematically aminobenzene or benzenamine) is shown with and without carbons and hydrogens. It is quite rare to put in any of the ring hydrogens on an aromatic ring, though it is sometimes convenient to put some in on the substituent, e.g. on a methyl, as in toluene (methylbenzene), or an aldehyde group, as in benzaldehyde.

Benzene strictly does not have alternating double and single bonds, but the aromatic sextet of electrons is localized in a π orbital system and bond lengths are somewhere in between double and single bonds



(see Section 2.9.4). To represent this, a circle may be drawn within the hexagon. Unfortunately, this version of benzene becomes quite useless when we start to draw reaction mechanisms, and most people continue to draw benzene rings in the Kekulé form. In some cases, such as fused rings, it is actually incorrect to show the circles.

two Kekulé versions of naphthalene

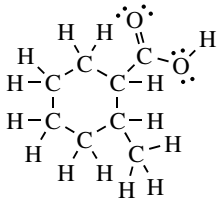


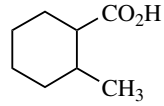
each circle must represent six aromatic π electrons

this is strictly incorrect!

Thus, naphthalene has only 10 π electrons, one from each carbon, whereas the incorrect two-circle version suggests it has 12 π electrons.

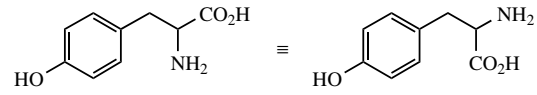
We find that, in the early stages, students are usually happier to put in all the atoms when drawing structures, following earlier practices. However, you are urged to adopt the shorthand representations as soon as possible. This saves time and cleans up the structures of larger molecules. Even a relatively simple molecule such as 2-methylcyclohexanecarboxylic acid, a cyclohexane ring carrying two substituents, looks a mess when all the atoms are put in. By contrast, the line drawing looks neat and tidy, and takes much less time to draw.





2-methylcyclohexanecarboxylic acid

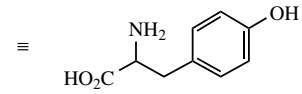
Do appreciate that there is no strict convention for how you orientate the structure on paper. In fact, we will turn structures around, as appropriate, to suit our needs. For example, the amino acid tyrosine has three functional groups, i.e. a carboxylic acid, a primary amine, and a phenol. How we draw tyrosine will depend upon what modifications we might be considering, and which functional group is being altered.



tyrosine

we might use this version if we were considering reactions of the carboxylic acid group

we might use this version if we were considering reactions of the amine group



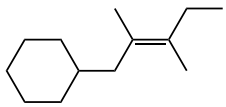
we might use this version if we were considering reactions of the phenol group

You will need to be able to reorientate structures without making mistakes, and also to be able to recognize different versions of the same thing. A simple example is with esters, where students have learnt that ethyl acetate (ethyl ethanoate) can be abbreviated to $CH_3CO_2C_2H_5$. When written backwards, i.e. $C_2H_5OCOCH_3$, the ester functionality often seems less recognizable.

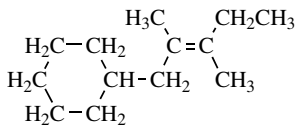
1.2 Partial structures

We have just seen that we can save a lot of time and effort by drawing structures without showing all of the atoms. When we come to draw reaction sequences, we shall find that we are having to repeat large chunks of the structure each time, even though no chemical changes are occurring in that part of the molecule. This is unproductive, so we often end up writing down just that part of the structure that is of interest, i.e. a **partial structure**. This will not cause problems when you do it, but it might when you see one and wish to interpret it.

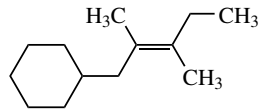
In the representations overleaf, you can see the line drawing and the version with methyls that stresses the bond ends. Both are satisfactory. When we wish to consider the reactivity of the double bond, and perhaps want to show that reaction occurs irrespective of the alkyl groups attached to the double bond, we put in the abbreviation R (see below), or usually just omit them. When we omit the attached groups, it helps to show what we mean by using wavy lines across the bonds, but in our urge to proceed we tend to omit even these indicators. This may



a typical line drawing

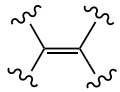


this is what the line drawing conveys



this version emphasizes the chain ends

using the R abbreviation for an unspecified alkyl group; different R groups may be indicated by R^1, R^2, R^3, etc., or R, R′, R″, etc.



a partial structure; this shows the double bond that has four groups attached; wavy lines indicate bonds to something else

in context, this might mean the same, but could be mistaken for a double bond with four methyls attached

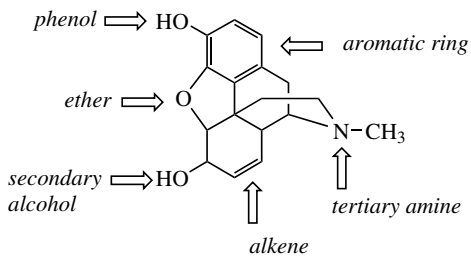
this would be better; putting in the carbons emphasizes that the other lines represent bonds, not methyls

cause confusion in that we now have what looks like a double bond with four methyls attached, not at all what we intended. A convenient ploy is to differentiate this from a line drawing by putting in the alkene carbons.

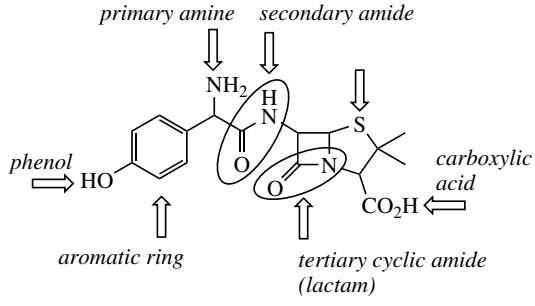
1.3 Functional groups

The reactivity of a molecule derives from its **functional group** or groups. In most instances the hydrocarbon part of the molecule is likely to be unreactive, and the reactivity of the functional group is largely independent of the nature of the hydrocarbon part. In general terms, then, we can regard a molecule as R–Y or Ar–Y, a combination of a functional group Y with an alkyl group R or aryl group Ar that is not participating in the reaction under consideration. This allows us to discuss reactivity in terms of functional groups, rather than the reactivity of individual compounds. Of course, most of the molecules of interest to us will have more than one functional group; it is this combination of functionalities that provides the reactions of chemical and biochemical importance. Most of the functional groups we shall encounter are included in Table 1.1, which also contains details for their nomenclature (see Section 1.4).

It is particularly important that when we look at the structure of a complex molecule we should visualize it in terms of the functional groups it contains. The properties and reactivity of the molecule can generally be interpreted in terms of these functional groups. It may sometimes be impossible to consider the reactions of each functional group in complete isolation, but it is valuable to disregard the complexity and perceive the simplicity of the structure. With a little practice, it should be possible to dissect the functional groups in complex structures such as morphine and amoxicillin.

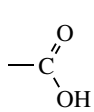
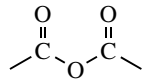
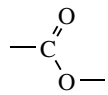
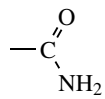
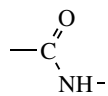
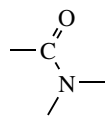


morphine



amoxicillin

Table 1.1 Functional groups and IUPAC nomenclature (arranged in order of decreasing priority)

Functional group	Structure		Suffix	Prefix
Cation				
ammonium			-ammonium	ammonio-
phosphonium			-phosphonium	phosphonio-
sulfonium			-sulfonium	sulfonio-
Carboxylic acid		—CO_2H	-oic acid	carboxy-
Carboxylic acid anhydride (anhydride)			-oic anhydride	
Carboxylic acid ester (ester)		—CO_2R	alkyl -oate	alkoxylcarbonyl- (or carbalkoxy-)
Acyl halide		—COX	-oyl halide	haloalkanoyl-
Amide				
primary amide		—$CONH_2$	-amide	carbamoyl-
secondary amide		—CONHR		
tertiary amide		—$CONR_2$		
Nitrile		—CN	-nitrile (or -onitrile)	cyano-
Aldehyde		—CHO	-al	formyl-
Ketone		—COR	-one	-oxo-

(*continued overleaf*)

Table 1.1 (*continued*)

Functional group	Structure		Suffix	Prefix
Alcohol				
primary alcohol	$-CH_2OH$		-ol	hydroxy-
secondary alcohol	$>CHOH$			
tertiary alcohol	$-C(-)(-)-OH$			
phenol	$Ar-OH$			
Thiol (mercaptan)	$-SH$		-thiol	mercapto-
Amine				
primary amine	$-NH_2$		-amine	amino- (or aza-)
secondary amine	$>NH$	$-NHR$		
tertiary amine	$>N-$	$-NR_2$		
Ether	$-O-$	$-OR$	(ether)	-oxa- (or alkoxy-)
Sulfide (thioether)	$-S-$	$-SR$	(sulfide)	alkylthio- (or thia-)
Alkene	$>C=C<$		-ene	alkenyl-
Alkyne	$-C\equiv C-$		-yne	alkynyl-
Halides	$-X$		(halide)	halo-
Nitro	$-N^{\oplus}(=O)-O^{\ominus}$	$-NO_2$		nitro-
Alkanes	$-C(-)(-)-C(-)(-)-$		-ane	alkyl-

1.4 Systematic nomenclature

Organic compounds are named according to the internationally accepted conventions of the International Union of Pure and Applied Chemistry (IUPAC). Since these conventions must cover all eventualities, the documentation required spans a book of similar size to this volume. A very much-abbreviated version suitable for our requirements is given here:

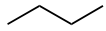
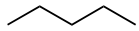
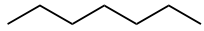
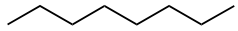
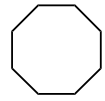
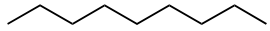
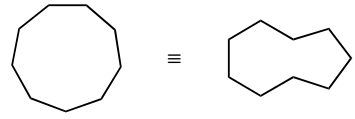
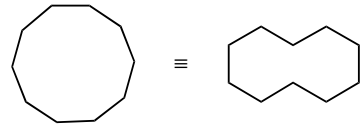
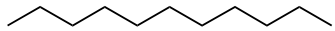
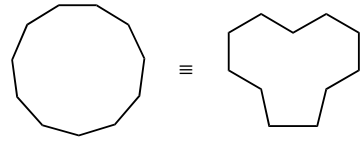
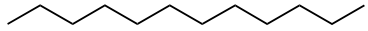
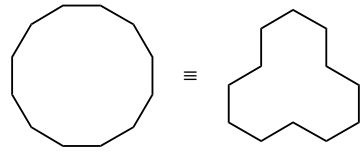
- the functional group provides the suffix name;
- with two or more functional groups, the one with the highest priority provides the suffix name;

- the longest carbon chain containing the functional group provides the stem name;
- the carbon chain is numbered, keeping minimum values for the suffix group;
- side-chain substituents are added as prefixes with appropriate numbering, listing them alphabetically.

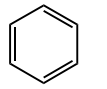
The stem names are derived from the names of hydrocarbons. Acyclic and cyclic saturated hydrocarbons (alkanes) in the range C_1–C_{12} are listed in Table 1.2.

Aromatic systems are named in a similar way, but additional stem names need to be used. Parent aromatic compounds of importance are benzene,

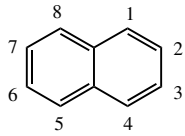
Table 1.2 Names of parent hydrocarbons

Acyclic hydrocarbon		Cyclic hydrocarbon	
Methane	CH_4		
Ethane	$H_3C–CH_3$		
Propane		Cyclopropane	
Butane		Cyclobutane	
Pentane		Cyclopentane	
Hexane		Cyclohexane	
Heptane		Cycloheptane	
Octane		Cyclooctane	
Nonane		Cyclononane	
Decane		Cyclodecane	
Undecane		Cycloundecane	
Dodecane		Cyclododecane	

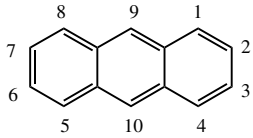
naphthalene, anthracene, and phenanthrene. The last three contain fused rings, and they have a fixed numbering system that includes only those positions at which substitution can take place.



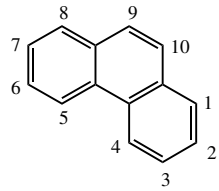
benzene



naphthalene



anthracene



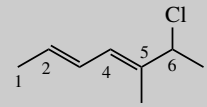
phenanthrene

It is anticipated that readers will already be familiar with many of the general principles of nomenclature and will be able to name a range of simple compounds. It is not the object of this section to provide an exhaustive series of instructions for naming every class of compound. Instead, the examples chosen here (Box 1.1) have been selected to illustrate some of the perhaps less familiar aspects that will be commonly encountered, and to foster a general understanding of the approach to nomenclature.

Alternative names are shown in some cases; this should emphasize that there is often no unique 'correct' name. Sometimes, it can be advantageous to bend the rules a little so as to provide a neat name rather than a fully systematic one. Typically, this might mean adopting a lower priority functional group as the suffix name. It is important to view nomenclature as a means of conveying an acceptable unambiguous structure rather than a rather meaningless scholastic exercise. Other examples will occur in subsequent chapters, and specialized aspects, e.g. **heterocyclic nomenclature**, will be treated in more detail at the appropriate time (see Chapter 11). **Stereochemical descriptors** are omitted here, but will be discussed under stereochemistry (see Sections 3.4.2 and 3.4.3).

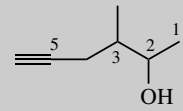
Box 1.1

Systematic nomenclature: some examples



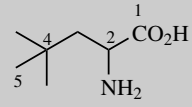
6-chloro-5-methylhepta-2,4-diene
6-chloro-5-methyl-2,4-heptadiene

- alkenes have higher priority than halides; suffix is -ene
- longest carbon chain is seven carbons: heptane
- numbering is chosen to give lowest numbers for the double bonds; 2-ene denotes 2,3-double bond, 4-ene denotes 4,5-double bond
- the European system hepta-2,4-diene is less prone to errors than the US system 2,4-heptadiene
- an additional syllable -a- is used but is not obligatory; heptadiene is easier to say than heptdiene



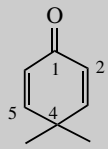
3-methylhex-5-yn-2-ol
3-methyl-5-hexyn-2-ol

- alcohols have higher priority than alkynes; suffix is -ol
- longest carbon chain is six carbons: hexane
- numbering is chosen to give lowest number for alcohol
- the European system hex-5-yn-2-ol keeps numbers and functionalities together



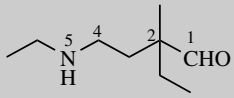
2-amino-4,4-dimethylpentanoic acid

- acids have higher priority than amines; remember 'amino acids'
- suffix is -oic acid
- one of the methyls is part of the five carbon chain, the others are substituents
- note the use of 4,4-, which shows both methyls are attached to the same carbon; 4-dimethyl would not be as precise



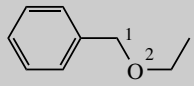
4,4-dimethylcyclohexa-2,5-dienone

- highest priority group is ketone; suffix -one
- longest carbon system is the ring cyclohexane
- numbering is around the ring starting from ketone as position 1
- 2,5-diene conveys 2,3- and 5,6-double bonds
- note 2,5-dienone means two double bonds and one ketone; contrast endione which would be one double bond and two ketones



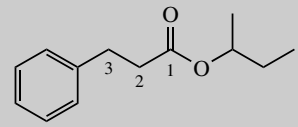
2-ethyl-4-ethylamino-2-methylbutanal
2-ethyl-2-methyl-5-azaheptanal

- highest priority group is aldehyde; suffix -al
- amino group at 4 is also substituted; together they become ethylamino
- the alternative name invokes a seven-carbon chain with one carbon (C-5) replaced by nitrogen; this is indicated by using the extra syllable -aza-, so the chain becomes 5-azaheptane

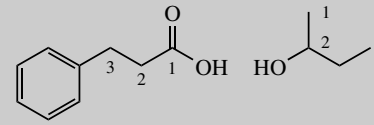


benzyl ethyl ether
benzyloxyethane
1-phenyl-2-oxa-butane

- simple ethers are best named as an alkyl alkyl ether
- the phenylmethyl group is commonly called benzyl
- an acceptable alternative is as an alkoxy alkane: the alternative ethoxytoluene would require an indication of the point of attachment
- the second alternative invokes a three-carbon chain with one carbon replaced by oxygen; this is indicated by using the extra syllable -oxa-, so the chain becomes 2-oxabutane

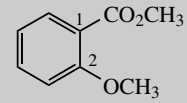


but-2-yl 3-phenylpropanoate



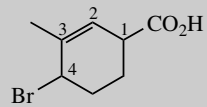
3-phenylpropanoic acid 2-butanol

- esters are named alkyl alkanoate – two separate words with no hyphen or comma
- alkyl signifies the alcohol part from which the ester is constructed, whilst alkanoate refers to the carboxylic acid part
- but-2-yl means the ester is constructed from the alcohol butan-2-ol; 3-phenylpropanoate means the acid part is 3-phenylpropanoic acid
- note the numbers 2 and 3 are in separate words and do not refer to the same part of the molecule



methyl 2-methoxybenzoate

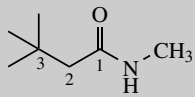
- this is a methyl ester of a substituted benzoic acid; the ring is numbered from the point of attachment of the carboxyl
- the acid portion for the ester is 2-substituted
- the ether group is most easily treated as a methoxy substituent on the benzene ring



4-bromo-3-methylcyclohex-2-enecarboxylic acid

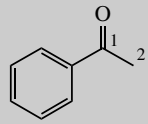
- the carboxylic acid takes priority; suffix usually -oic acid
- the carboxylic acid is here treated as a substituent on the cyclohexane ring; the combination is called cyclohexanecarboxylic acid

Box 1.1 (continued)



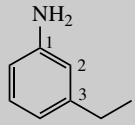
N,3,3,-trimethylbutanamide

- this is a secondary amide of butanoic acid; thus the root name is butanamide
- two methyl substituents are on position 3, and one on the nitrogen, hence *N*,3,3-trimethyl; the *N* is given in italics

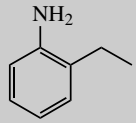


1-phenylethanone
methyl phenyl ketone
acetophenone

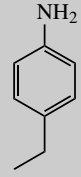
- a ketone in which the longest chain is two carbons; thus the root name is ethanone
- the phenyl substituent is on the carbonyl, therefore at position 1
- without the 1-substituent, ethanone is actually an aldehyde, and would be ethanal!
- the alternative methyl phenyl ketone is a neat and easy way of conveying the structure
- this structure has a common name, acetophenone, which derives from an acetyl (CH_3CO) group bonded to a phenyl ring



3-ethylaniline
m-ethylaniline
3-ethylphenylamine
3-ethylbenzenamine

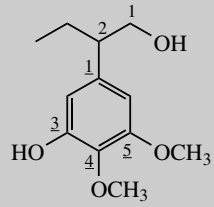


o-ethylaniline

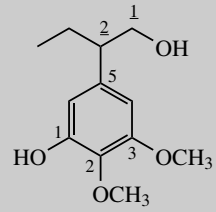


p-ethylaniline

- an amine; suffix usually -amine
- the root name can be phenylamine, as an analogue of methylamine, or the systematic benzenamine; in practice, the IUPAC accepted name is aniline
- the ring is numbered from the point of attachment of the amino group
- the prefixes *ortho*-, *meta*-, and *para*- are widely used to denote 1,2-, 1,3-, or 1,4-arrangements respectively on an aromatic ring; these are abbreviated to *o*-, *m*-, and *p*-, all in italics

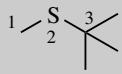


2-(3-hydroxy-4,5-dimethoxyphenyl)butanol



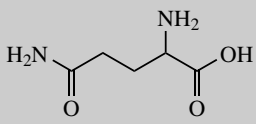
5-(1-hydroxybut-2-yl)-2,3-dimethoxyphenol

- this could be named as an alcohol, or as a phenol
- as an alcohol (butanol), there is a substituted phenyl ring attached at position 2
- note the phenyl and its substituents are bracketed to keep them together, and to separate their numbering (shown underlined) from that of the alcohol chain
- as a phenol, the substituted butane side-chain is attached through its 2-position so has a root name but-2-yl to show the position of attachment; again, this is in brackets to separate its numbering from that of the phenol
- di-, tri-, tetra-, etc. are not part of the alphabetical sequence for substituents; dimethoxy comes under m, whereas trihydroxy would come under h, etc.



tert-butyl methyl thioether
tert-butyl methyl sulfide
3,3-dimethyl-2-thiabutane

- this is a thioether, which can be named as a thioether or as a sulfide
- an alternative invokes a four-carbon chain with one carbon replaced by sulfur using the extra syllable -thia-; this chain thus becomes 2-thiabutane
- note how the (trimethyl)methyl group is most frequently referred to by its long-established name of tertiary-butyl, abbreviated to *tert*-butyl, or *t*-butyl



2-amino-4-carbamoylbutanoic acid
2,5-diamino-5-oxo-pentanoic acid
glutamic acid

- this contains an amine, an amide, and a carboxylic acid; the acid takes priority
- the amide group as a substituent is termed carbamoyl; this includes one carbon, so the chain length remaining to name is only four carbons – butane
- it is rather easier to consider the amide as amino and ketone substituents on the five-carbon chain
- the ketone is indicated by oxo-; do not confuse this with -oxa-, which signifies replacement of one carbon by oxygen
- the common name is glutamic acid; it is an amino acid found in proteins

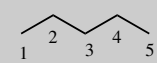
There now follow a number of examples demonstrating how to convert a systematic name into a structure, with appropriate guidance hints (Box 1.2). For added relevance, these are all selected from routinely used drugs. Again, any stereochemical aspects are not included.

Box 1.2

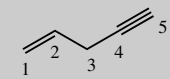
Converting systematic names into structures: selected drug molecules

1-chloro-3-ethylpent-1-en-4-yn-3-ol (ethchlorvynol)

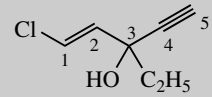
- main chain is pentane (C_5) number it

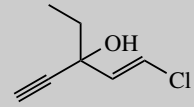


- put in unsaturation
  1-ene (=1,2-ene)
  4-yne (=4,5-yne)



- put in substituents
  1-chloro
  3-ethyl
  3-hydroxy (3-ol)

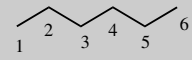




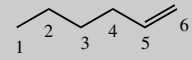
ethchlorvynol

4-aminohex-5-enoic acid (vigabatrin)

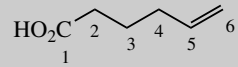
- main chain is hexane (C_6) number it



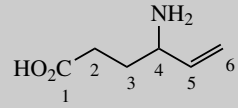
- put in unsaturation
  5-ene (=5,6-ene)

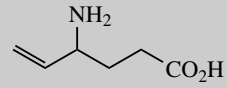


- main functional group is an acid (-oic acid)
  this will be carbon-1



- put in substituent
  4-amino

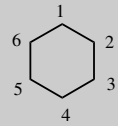




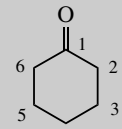
vigabatrin

2-(2-chlorophenyl)-2-methylaminocyclohexanone (ketamine)

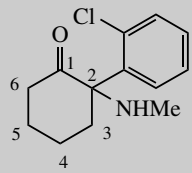
- main chain is cyclohexane (C_6) number it



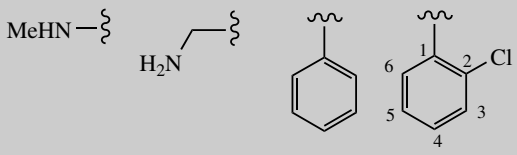
- main functional group is a ketone (-one) this will be carbon-1

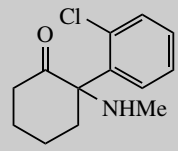


- put in substituents
  2-methylamino = 2-amino carrying a methyl (contrast aminomethyl = methyl carrying an amino)
  2-(2-chlorophenyl) = 2-chlorophenyl at position 2; the phenyl carries a chloro substituent at its own position 2;
  note the use of brackets to separate the two types of numbering



methylamino aminomethyl phenyl 2-chlorophenyl

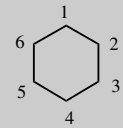




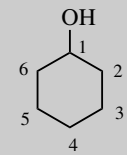
ketamine

5-methyl-2-(2-propyl)-cyclohexanol (menthol)

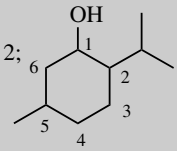
- main chain is cyclohexane (C_6) number it



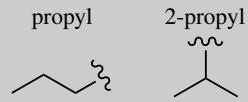
- main functional group is an alcohol (-ol) this will be carbon-1

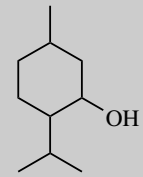


- put in substituents
  5-methyl
  2-(2-propyl) = 2-propyl at position 2;
  2-propyl is a propyl group joined via its 2-position



propyl 2-propyl





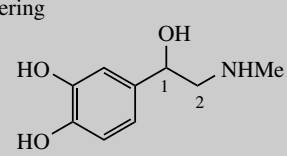
menthol

1-(3,4-dihydroxyphenyl)-2-methylaminoethanol (adrenaline; epinephrine)

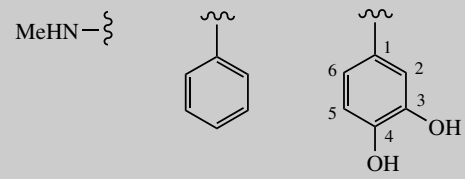
- main chain is ethane (C_2) number it

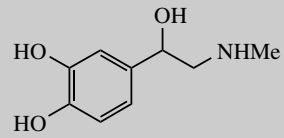
- main functional group is an alcohol (-ol) this will be carbon-1

- put in substituents
  2-methylamino = 2-amino carrying a methyl
  1-(3,4-dihydroxyphenyl) = 3,4-dihydroxyphenyl at position 1;
  the phenyl carries hydroxy substituents at its own positions 3 and 4;
  note the use of brackets to separate the two types of numbering



methylamino phenyl 3,4-dihydroxyphenyl

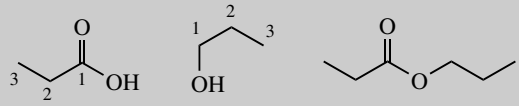




adrenaline

1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl propionate (dextropropoxyphene)

- this is an ester (two words, -yl -oate)
  the -oate part refers to the acid component, the -yl part to the esterifying alcohol
- main chain of acid is propane (C_3)
  main chain of alcohol is propane (C_3)
  these are numbered separately (the ester has two separate words)



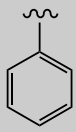
propionic acid
propanoic acid

propanol

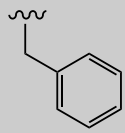
propyl propionate
propyl propanoate

- no substituents on acid component
- put in substituents on alcohol component
  1-phenyl; 1-benzyl; 2-methyl; 3-dimethylamino

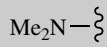
phenyl

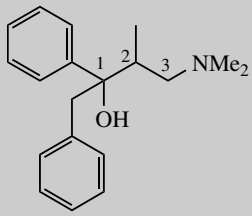


benzyl

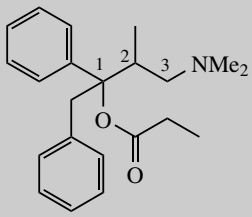


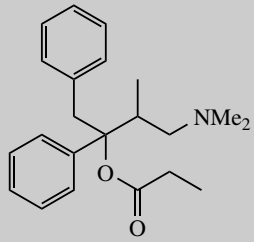
dimethylamino





- join with acid component via ester linkage



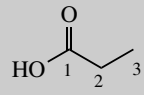


dextropropoxyphene

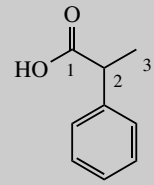
2-[4-(2-methylpropyl)phenyl]propanoic acid (ibuprofen)

- main chain is propane (C_3)
  number it

- main functional group
  is an acid (-oic acid)
  this will be carbon-1

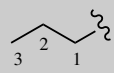


- put in substituents
  consider brackets;
  we have square brackets
  with curved brackets inside
  initially ignore the contents
  of the curved brackets and
  its numbering (4);
  this reduces to 2-[phenyl]
  propanoic acid, which indicates
  phenyl at position 2 on propanoic acid
  4-(2-methylpropyl)phenyl = 2-methylpropyl
  at position 4 of the phenyl;
  2-methylpropyl = propyl with methyl at position 2
  note the brackets separate different substituents
  and their individual numbering systems

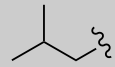


2-phenylpropanoic acid

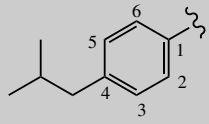
propyl

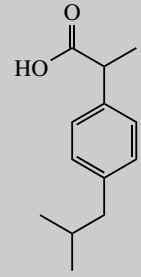


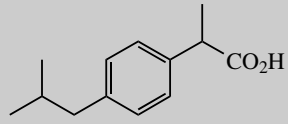
2-methylpropyl



4-(2-methylpropyl)phenyl



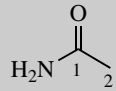




ibuprofen

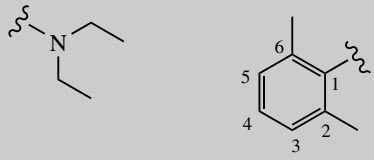
2-(diethylamino)-*N*-(2,6-dimethylphenyl)acetamide (lidocaine; lignocaine)

- this is an amide; acetamide is the amide of acetic acid (C_2)
- number it; the carbonyl carbon is C-1

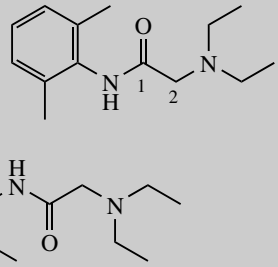


- there are two main substituents, on C-2 and the nitrogen, with brackets to keep the appropriate groups together
  the substituent at C-2 is diethylamino, an amino which is itself substituted with two ethyl groups
  the substituent on the nitrogen is 2,6-dimethylphenyl, a phenyl group substituted at positions 2 and 6 on the phenyl

diethylamino 2,6-dimethylphenyl



- put in substituents

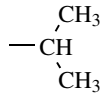
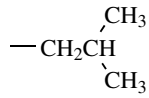
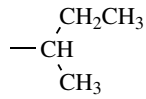
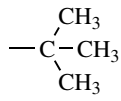
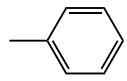
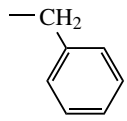
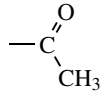
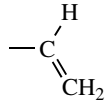
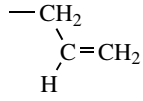


lidocaine

1.5 Common groups and abbreviations

In drawing structures, we are already using a sophisticated series of **abbreviations** for atoms and bonding. Functional groups are also abbreviated further, in that $–CO_2H$ or –CHO convey considerably more information to us than the simple formula does. Other common abbreviations are used to specify particular alkyl or aryl groups in compounds, to speed up our writing of chemistry. It is highly likely that some of these are already familiar, such as Me for methyl, and Et for ethyl. Others are included in Table 1.3.

Table 1.3 Some common structural abbreviations

Group	Abbreviation	Structure
Alkyl	R	
Aryl	Ar	
Methyl	Me	—CH_3
Ethyl	Et	—CH_2CH_3
Propyl	Pr or *n*-Pr	—$CH_2CH_2CH_3$
Butyl	Bu or *n*-Bu	—$CH_2CH_2CH_2CH_3$
Isopropyl	*i*-Pr or ^{i}Pr	
Isobutyl	*i*-Bu or ^{i}Bu	
sec-Butyl	*s*-Bu or ^{s}Bu	
tert-Butyl	*t*-Bu or ^{t}Bu	
Phenyl	Ph	
Benzyl	Bn	
Acetyl	Ac	
Vinyl		
Allyl		
Halide	X	—F —Cl —Br —I