A short introduction to pheromones for non-chemists

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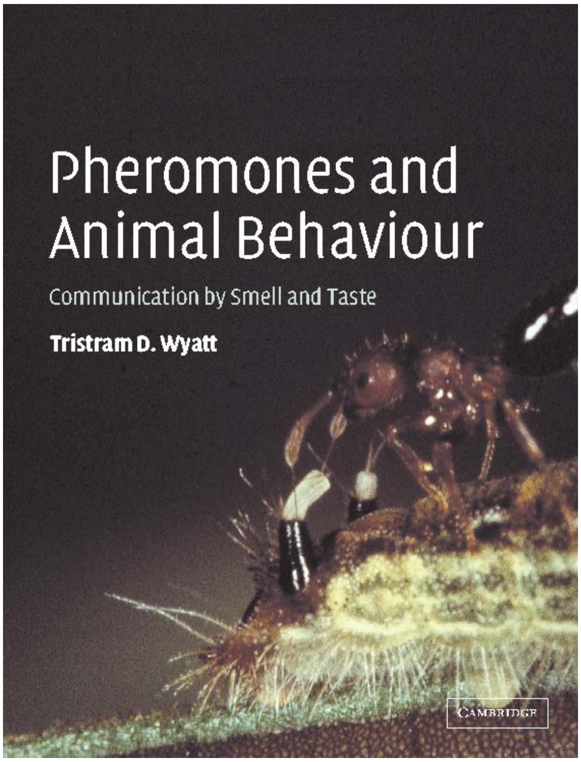
Pheromones and Animal Behaviour **(2003)**
by Tristram Wyatt



Also available for **free** download is the introductory chapter, “Animals in a chemical world” described by Peter Mombaerts in *Nature Neuroscience* as ‘the best overview of pheromones that I have ever come across, and worth reading by itself’ from
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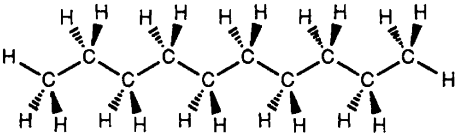
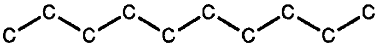
Appendix A1

An Introduction to Pheromones for Non-Chemists

This brief introduction to the chemical structure of pheromones is largely after Stevens in Howse *et al.* (1998). Like other organic molecules, pheromones are based on a chain of carbon and attached hydrogen atoms. The carbon backbone forms a zigzag because of the tetrahedral arrangement of the four carbon bonds (these angles are important for other characteristics of the molecular shape, see Appendix A2 Isomers).

The hydrogen atoms attached to the carbon backbone lie in two planes, above and below the paper, (represented here by bonds as solid wedges (the plane above) and as dashed wedges (the plane below)):





The structure is often simplified to show just the carbon backbone:

When other atoms such as oxygen or nitrogen, or other functional groups, are added to the chain or substituted for hydrogens or carbons, the chemical nature of the molecule changes (see Table A1.1 for common functional groups).

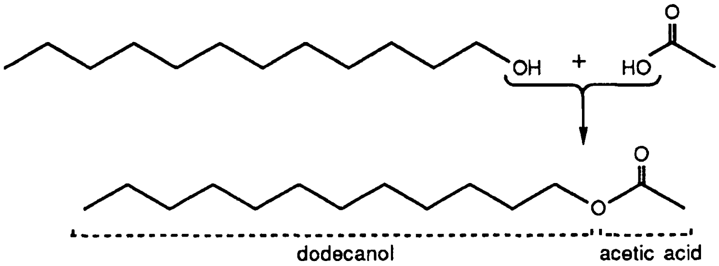
The naming of compounds tells the reader the length of the carbon chain and what and where the important functional groups occur. A common chemical modification of the alcohol group is the combination with an organic acid (with loss of a water) to give an ester. The naming of the

Table A1.1. *Prefixes and suffixes for common functional groups.*

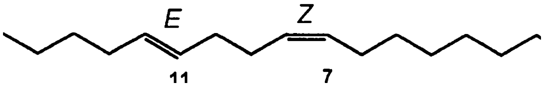
Functional group	**Formula**	**Prefix**	**Suffix**
Alcohol	-OH	Hydroxy-	-ol
Aldehyde	$-CH{=}O$	Formyl-	-al
Amine	$-NH_2$	Amino-	-amine
Carboxylic acid	-COOH	Carboxy-	-oic acid
Ester	-COOR	*R*-oxycarbonyl-	-*R*-oate
Ketone	$>C{=}O$	Oxo-	-one

From Howse et al. (1998).

molecule reflects the addition of the acid, often acetic acid, to the original chain, for example to produce dodecan-1-ol acetate:



The name also indicates the number and position of carbon double bonds (C=C). The formal name for the pheromone of the pink bollworm (*Pectinophora gossypiella*) is (*Z,E*)-7,11-hexadecandien-1-ol acetate (and the *Z,Z* isomer; see Appendix A2) (common name Gossyplure). The 'dien' tells us that there are two double bonds, the '7,11' that these occur at carbons 7 and 11:



Appendix A2

Isomers and Pheromones

Pheromone synthesis is catalysed by enzymes and pheromones are detected by receptors, both of which are proteins, which recognise their substrates and signal molecules (ligands), respectively, by shape in three dimensions. Molecules with atoms in the same formula can also sometimes be put together in a number of different structures. Even more subtly, molecules with the same structure (connections between atoms) can have different shapes in three dimensions. These different variations are called isomers.

This potential variation in molecular shape, in synthesis and reception, has been acted on by natural selection so that now these variations in shape are vitally important to many species for species recognition. Each of the possible isomer types can be important biologically as in each case the shape of the molecule is different and it may stimulate a different range of olfactory receptors (Chapter 9).

There are two main different kinds of isomers: constitutional isomers have the atoms connected in different ways, whereas stereoisomers have the same connectivity but differ in the arrangement of atoms in space.

A2.1 Constitutional isomers

A2.1.1 Functional group isomers

From the same molecular formula the atoms can be connected in ways that produce different functional groups, giving quite different chemical properties to the molecule. For example, *n*-butyl alcohol (below left) and ethyl ether (below right) are both $C_4H_{10}O$

A2.1.2 Positional isomers

Positional isomers differ, for example, in the position of a functional group (e.g. 2-heptanone and 3-heptanone) or the position of a double bond

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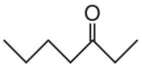
Table A2.1. *Naming of isomers: the meanings of the letters and symbols.*

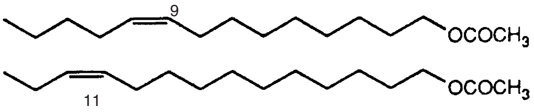
The development of chemical nomenclature has left us with a number of different naming schemes, including some for the same differences, which can be slightly confusing. In addition, some molecular formulae allow for many possible isomers to be made from them so that the range of isomers could include, say, geometrical, positional and optical isomers among the possible molecules sharing the same molecular formula.

Symbols	**Synonym**	**Type of isomer**
E, *Z*		Geometrical spatial arrangement around double bond
l, d	− , +	Optical isomers (*laevo*, *dextro* twist of polarised light)
S, *R*		Different absolute configurations of stereocenters (assymetric centres)

(e.g. *Z*-9-tetradecen-1-ol acetate and *Z*-11-tetradecen-1-ol acetate, the pheromone components of the summer fruit tortrix moth, *Adoxophyes orana*):


2-heptanone


3-heptanone



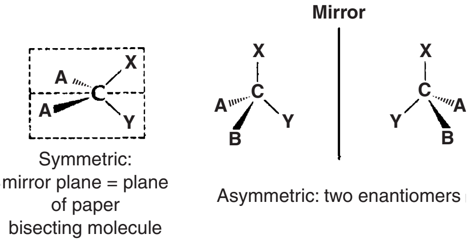
A2.2 Stereoisomers

Stereoisomers are compounds with identical formulae and order of connecting the atoms together, but with different spatial orientations of the atoms. In biological systems, driven by enzymes and receptor proteins sensitive to the shape of molecules, these differences have profound effects. There are a several types of stereoisomer. These are described in Sections A2.2.1 and A2.2.2, and the nomenclature used is shown in Table A2.1.

A2.2.1 Chirality and enantiomers (optical isomers)

Chiral molecules are mirror images of each other and, just like your hands, cannot be superimposed on each other (chiral comes from the Greek word *cheir*, meaning ‘hand’). The two mirror images are called **enantiomers**. The ability to distinguish between a pair of enantiomers requires a chiral agent; a glove is a chiral agent that distinguishes right and left hands. Enzymes and receptors are just such systems in biology. Nature is inherently chiral.

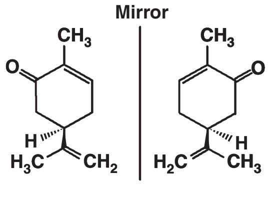
The chirality is a consequence of the tetrahedral geometry of carbon atoms: if different groups are attached to each of the four bonds of one of the carbon atoms, the molecule can be made in two different ways (or as two enantiomers, see diagram below). Such a carbon atom is termed a stereocentre or asymmetric centre (in some books this is called a chiral centre). In this and other diagrams, dotted lines |||||| represent bonds going away from you behind the plane of the paper, solid, thick lines ▶ represent bonds coming out of the page towards you. Lines — are bonds in the plane of the paper.



Symmetry and asymmetry in tetrahedral carbon.

A special property of chiral compounds, which led to the discovery of the phenomenon, is optical activity. Solutions of pure enantiomers rotate the plane of polarisation of plane–polarised light passing through them: opposite enantiomers rotate it in opposite directions. l-Molecules rotate the plane of polarisation to the left, and d-molecules rotate it to the right. The abbreviations come from Latin: l (*laevo*, for 'left') and d (*dextro*, 'right'). l and d are often called − and +, respectively.

An example of our sensitivity to enantiomers is (−)-carvone: this gives us the smell of spearmint whereas its mirror image, (+)-carvone, is perceived by us as the very different spicy smell of caraway:



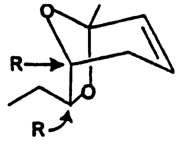
(−)-carvone
smell: spearmint

(+)-carvone
caraway

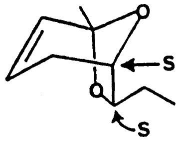
A **racemic mixture** or **racemate** is an equal mix of the two enantiomers. As they cancel each other out optically, such solutions do not rotate the plane of polarisation of light, so they are optically inactive. Most chemically synthesised compounds, unless enzymes or other special steps are used in synthesis or purification, are racemic mixtures.

The l, d naming system is based on the observation of the direction in which polarised light is shifted but does not tell us the actual position of all atoms in space around a molecule. This is done by the **absolute configuration**, which uses a rather complicated set of rules which allow the chemist to describe the absolute configuration at each of the asymmetric centres as either *R* (from *rectus* = 'right') and *S* (from *sinister* = left). As the *R* and *S* are defined according to a set of nomenclatural rules, these do not necessarily predict which way the whole molecule will shift polarised light (l/d). (You will see L and D in some chemical names: these symbols are used to define the absolute configuration of a sugar or of an amino acid, based on the absolute configuration of glyceraldehyde (Fischer nomenclature). D, L (absolute configuration) should not be confused with d, l (rotation of the plane of polarization of plane–polarized light). The rules for naming are not important here, but biologically, the differences *are* important (see Howse *et al.* 1998, p. 152).

An example of stereoselectivity in a mammalian pheromone is dehydro-*exo*-brevicomin, which comes in *R*, *R* and *S*, *S* forms; only the *R*, *R* form is active biologically and only this form is produced by male mice (Novotny *et al.* 1995):



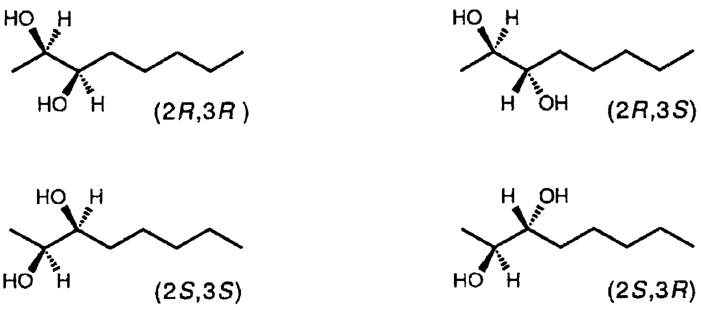
(*R*,*R*)-3,4-dehydro-*exo*-brevicomin



(*S*,*S*)-3,4-dehydro-*exo*-brevicomin

A2.2.2 Diastereoisomers

When a molecule has more than one asymmetric centre, a second form of stereoisomerism is possible, diastereoisomerism. Each of the asymmetric centres can be in one of the two forms, *R* and *S*. If there are two asymmetric centres there will be 2^2 stereoisomers, that is four. For example, 2,3-octandiol (a pheromone produced by the grape borer beetle *Xylotrichus pyrrhoderus*) occurs in four forms: (2*R*,3*R*), (2*R*,3*S*), (2*S*,3*S*) and (2*S*,3*R*):



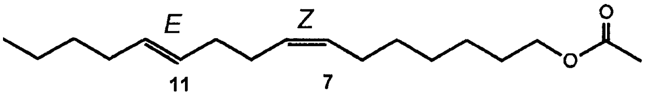
The four optical isomers of 2, 3-octandiol.

Some of these molecules represent mirror images of each other, for example, (2*S*,3*S*) and (2*R*,3*R*) and are called enantiomers. Other pairs of isomers, such as (2*R*,3*R*) and (2*S*,3*R*) are not mirror images and these are called **diastereoisomers**, that is, they are stereoisomers that are not enantiomers. These are common in branched compounds. In the case of the grape borer beetle, only one of the four isomers is attractive (2*S*,3*S*).

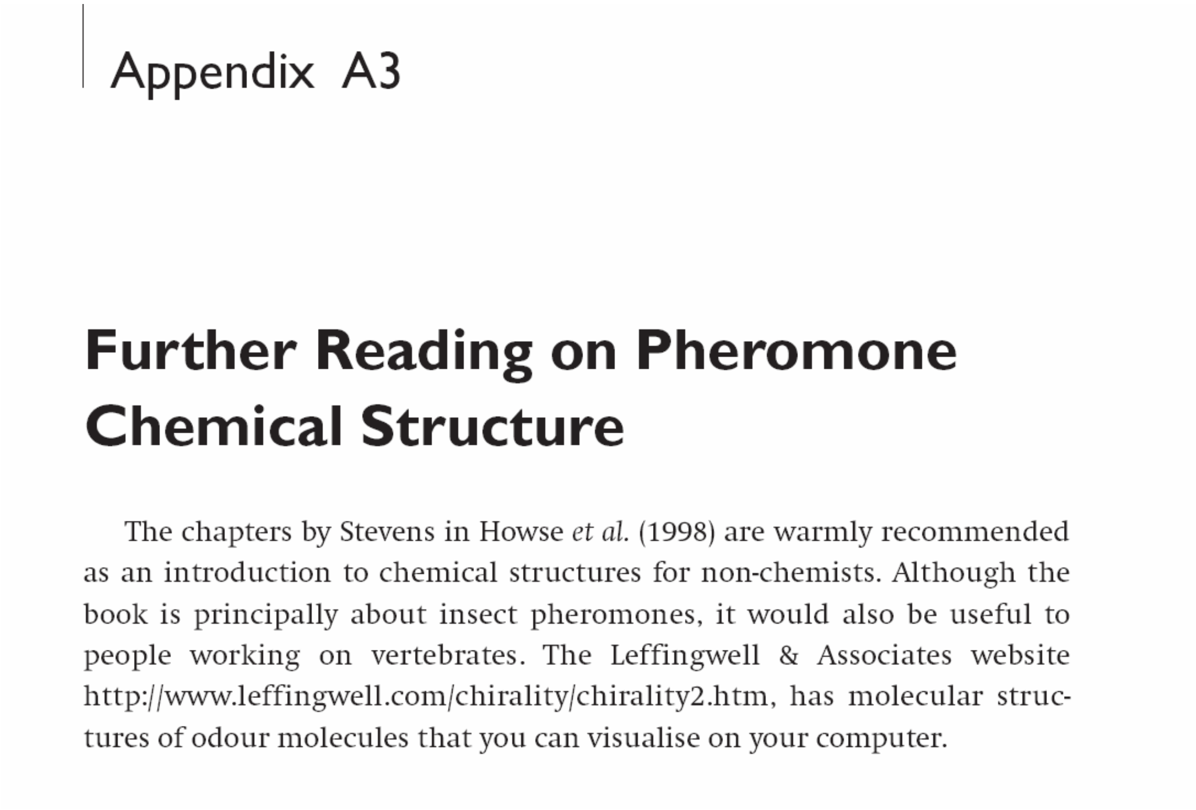
If there are three asymmetric centres in the molecule there will be eight isomers (2^3), as the number of optical isomers is 2^N where N is the number of asymmetric centres.

A2.2.2.1 Geometrical isomers

Geometrical isomers are a particular form of diastereoisomer. Many moth pheromones have particular hydrogens removed, catalysed by specific desaturase enzymes, to leave double bonds. The double bond makes the carbon chain rigid at that point. Because of the angles of the chain, there are two versions of the molecule depending on whether the remaining chains are connected to (i.e. spatially arranged around) the double bond on opposite sides (*E*) or the same side (*Z*) (from the German *Entgegen*, opposite, and *Zusammen*, together). These two forms are different chemical compounds with characteristic chemical and physical properties. You will also come across the older terms *trans* and *cis*, often roughly equivalent, though not strictly so by modern objective naming rules, to *E* and *Z* respectively.



(*Z*,*E*)-7,11-hexadecandien-1-ol acetate



Appendix A3

Further Reading on Pheromone Chemical Structure

The chapters by Stevens in Howse *et al.* (1998) are warmly recommended as an introduction to chemical structures for non-chemists. Although the book is principally about insect pheromones, it would also be useful to people working on vertebrates. The Leffingwell & Associates website http://www.leffingwell.com/chirality/chirality2.htm, has molecular structures of odour molecules that you can visualise on your computer.

References:

Howse, P. E., Stevens, I. D. R. & Jones, O. T . (1998). *Insect pheromones and their use in pest management*. London: Chapman and Hall.

Novotny, M. V., Xie, T. M., Harvey, S., Wiesler, D., Jemiolo, B. & Carmack, M. (1995). Stereoselectivity in mammalian chemical communication – male-mouse pheromones. *Experientia*, **51**, 738–743.

Pheromones and Animal Behaviour

Communication by Smell and Taste

Tristram D. Wyatt
University of Oxford

We are entering one of the most exciting periods in the study of chemical communication since the first pheromones were identified some 40 years ago. This rapid progress is reflected in this book, the first to cover the whole animal kingdom at this level for 25 years. The importance of chemical communication is illustrated with examples from a diverse range of animals including humans, marine copepods, Drosophila, Caenorhabditis elegans, moths, snakes, goldfish, elephants and mice. It is designed to be advanced and up-to-date, but at the same time accessible to readers whatever their scientific background. For students of ecology, evolution and behaviour, this book gives an introduction to the rapid progress in our understanding of olfaction at the molecular and neurological level. In addition, it offers chemists, molecular and neurobiologists an insight into the ecological, evolutionary and behavioural context of olfactory communication.

> ‘Pheromones are by far the most important signals used by organisms of all kinds. Wyatt’s book is an excellent text and review: up-to-date, comprehensive, balanced, detailed, clearly written, and nicely illustrated.’
>
> Edward O. Wilson

Contents: 1. Animals in a chemical world; 2. Discovering pheromones; 3. Sex pheromones: finding and choosing mates; 4. Coming together and keeping apart: aggregation and host-marking pheromones; 5. Scent marking and territorial behaviour; 6. Pheromones and social organization; 7. Pheromones and recruitment communication; 8. Fight-or-flight: alarm pheromones; 9. Perception and action of pheromones: from receptor molecules to brains and behaviour; 10. Finding the source: pheromones and orientation behaviour; 11. Breaking the code: illicit signallers and receivers of semiochemical signals; 12. Using pheromones: applications; 13. On the scent of human attraction: human pheromones?; Appendix A: An introduction to pheromones for non-chemists; References.

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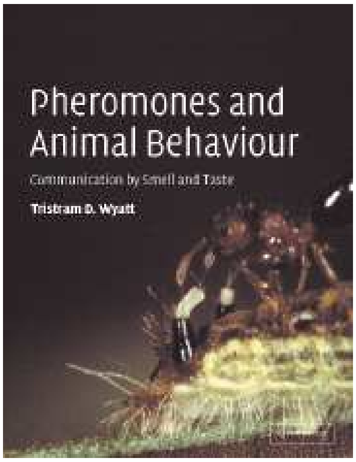

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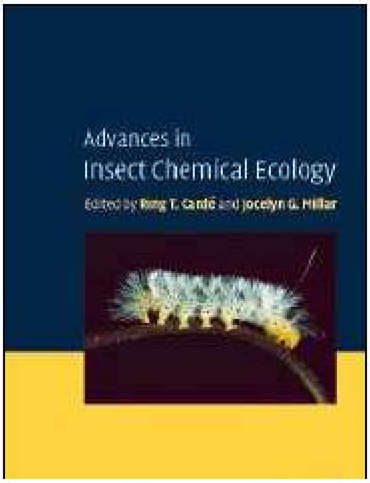

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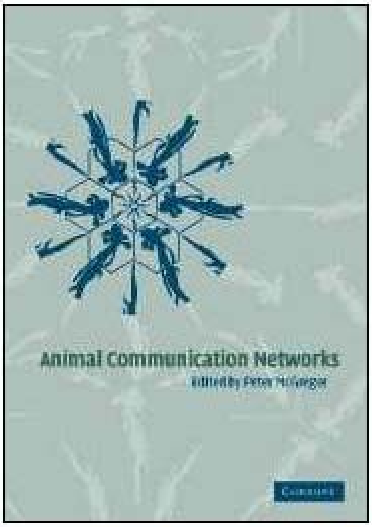

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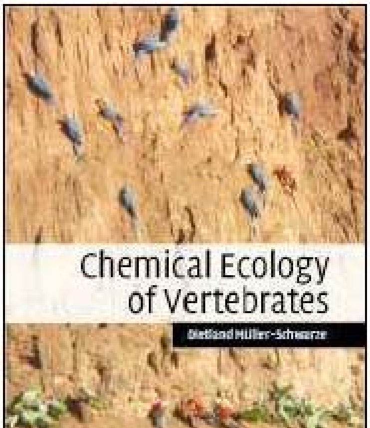

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