DOCTOR OF PHILOSOPHY

The Novel Synthesis of Aldehyde Insect Sex Pheromones

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The Novel Synthesis of Aldehyde Insect Sex Pheromones

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ABSTRACT

Three (Z) mono-unsaturated pheromones were synthesised by a method that used catalytic hydrogenation to bring about the reduction of two functional groups in one step. The procedure used inexpensive starting materials to produce the pheromones but, even though the reduction worked well, the introduction of an acid functionality increased the number of steps and the overall yields were reduced.

Continuing the reductive methodology for the synthesis of aldehydes, a range of aldehyde pheromones were prepared including saturated, (Z)-mono-unsaturated and di-unsaturated. They were prepared from inexpensive starting materials and were generally produced, without the use of toxic oxidisers to give the aldehyde functionality. The key intermediates were the bromoaldehydes, which were produced through a range of chain lengths from six to eleven carbons. The aldehydes were protected as an acetal and the bromide coupled with a range of 1-alkynes to chain extend the molecule to the correct length before reducing the alkyne to a *cis* alkene. This gave the protected pheromone, which could be stored indefinitely and deprotected when ready, to give the aldehyde pheromone.

Diene aldehyde pheromones were prepared using the same bromoaldehyde intermediate as a building block. E,Z-2,13-Octadecadienal was synthesised using the same strategies as those used for the mono-unsaturated aldehydes. The Wittig coupling of bromononanal incorporated the conjugated aldehyde into the molecule.

ABBREVIATIONS

b.p.	boiling point
cat.	catalyst
DDT	dichlorodiphenyltrichloroethane
dil.	dilution
DMPU	N,N'-dimethyl-N,N'-propene urea
EAG	electron antennogram responses
equiv.	equivalent
FGI	functional group interconversion
Fig.	figure
g	gram(s)
Gk	Greek
GLC	gas-liquid chromatography
HMPA	hexamethylphosphoramide
Hz	Hertz
IR	infra red
J	coupling constant
M	molar
mg	milligrams
mins.	minutes
mmol.	millimole(s)
mol.	mole
m.p.	melting point
ng	nanogram(s)
NMR	nuclear magnetic resonance
PCC	pyridinium chlorochromate
ppm	parts per million
ppts	pyridinium *p*-tolunensulfonate
rt	room temperature

sat.	saturated
temp.	temperature
THF	tetrahydrofuran
t.l.c.	thin layer chromatography

CHAPTER 1 – Pheromone Biology

1.1.1 Introduction

Life is communication. All organisms no matter how big, or small, impart information in the form of words, sounds, actions or colours. They communicate in order to survive. Any or all of the known senses are employed to make contact. It maybe as simple as the colour of a petal in a flowering plant, the clicking of a grasshopper or more complicated as a developed language; the results are the same – continued survival of the species.

Animals use chemical messages as a means of communication; these chemicals are known as pheromones. These messages carry information that co-ordinates physiological and behavioural activity between individuals of the same species. They are part of a class of chemical substances called semiochemicals (**Diagram 1**).[1]

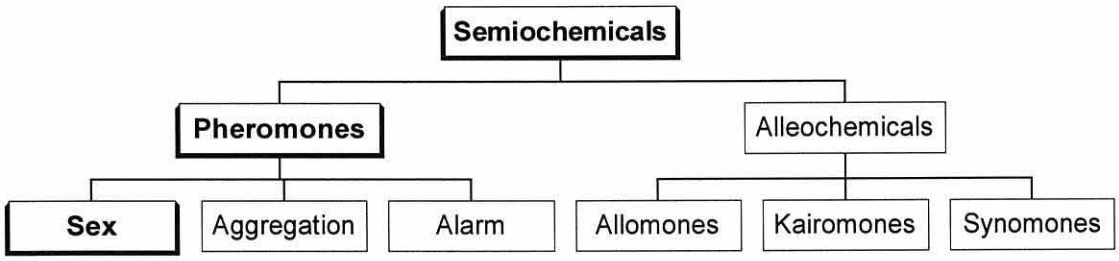


Diagram 1 The sub-classes of semiochemicals

1.1.2 Semiochemicals

Semiochemicals (Gk. Semeon, signal) are chemical signals that are passed between organisms. There are two classes of semiochemicals:

(i) **Alleochemicals**, are chemicals passed between individual organisms of different species - they are interspecific. Alleochemicals are subdivided into several groups. The groups depend on who benefits from the response that the signal produces. An alleochemical that benefits the emitter but not the receiver is an **allomone**. An alleochemical that benefits the receiver but not the emitter is a **kairomone**, and one that benefits both the emitter and the receiver is a **synomone**.

(ii) **Pheromones**. (Gk. pherom, to carry; horman, to excite or stimulate) A pheromone is the name given to a chemical signal that passes between organisms of the same species - they are intraspecific. The type of response that the pheromone produces classifies the compound. Aggregating pheromones attract individuals of the species together, for a common purpose, whether to a source of food, or for defence. Alarm pheromones initiate an escape from an attack. The third and the most important group are the sex pheromones. Sex pheromones are chemical attractants passed between the two sexes of the species, generally attracting the male to the female for the purpose of reproduction. They may be one chemical compound, but are more usually a mixture of chemicals, released together in a specific ratio.[2]

1.1.3 Insect Sex Pheromones

Insect sex pheromones are among the most biologically active compounds known to man. The receptive sites for these compounds are located on the insect's antennae.[3] The antennae contain olfactory receptors that are capable of detecting a single pheromone molecule. An insect may respond and change its behaviour on detection of a hundred or so of these molecules. There is research that can suggest the minimum density of pheromone molecules required, for a particular species; to stimulate a behavioural response in 50 % of the species gives a BR_{50} value. It has been calculated that 200 pheromone molecules per ml of air gives

the BR_{50} value for the silkworm moth. The BR_{50} value for the Chinese silkworm moth was found to be much lower. The female may attract the male of the species over a distance of 11 kilometres.[4]

When the insect detects the pheromones in the air it is attracted, and follows the scent. The male will fly upwind in the airstream of the odour, towards the source, until it has located the female. If the scent is lost then the insect will fly randomly across the wind to try to pick up the trail again.

Sexually receptive females excrete sex pheromones in order to attract the males. The females biosynthesise and excrete the pheromone molecules from a specific gland. The gland is generally situated in the abdomen of the insect but this depends on the species. Only nanograms of pheromone are produced. The compounds slowly volatilise on the surface of the gland, and are dispersed in the wind.

Insects rely on the attraction of the opposite sex, over long distances, for mate location and reproduction. The pheromones must therefore be volatile but not diffuse too quickly; otherwise the concentrations would be too low to allow detection. The molecular masses of pheromones are therefore generally between M_r 200 and 300.

The chain length, degree of unsaturation, functional groups and chirality, dictate the activity of the pheromone. The blend of pheromone components must be in the correct ratio for the pheromone to be effective in attracting the mate. The blend is generally a mixture of two or three of the alcohol, aldehyde and acetate, of the same or different chain length (**Fig. 1**). Each species has its own specific component mixture.

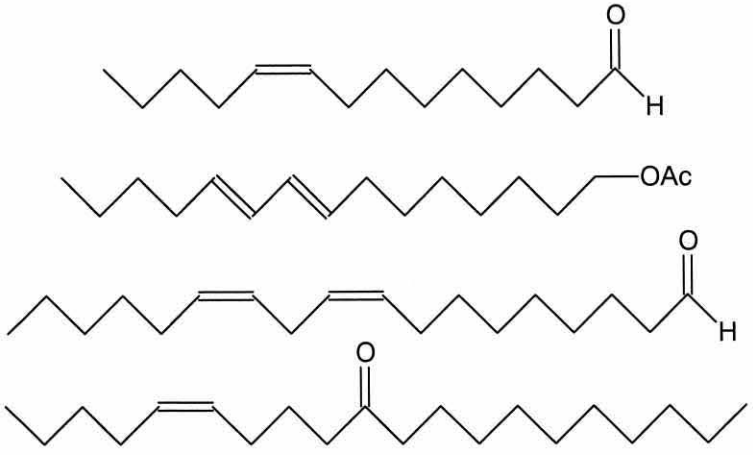


Figure 1 Examples of lepidopteran pheromones.

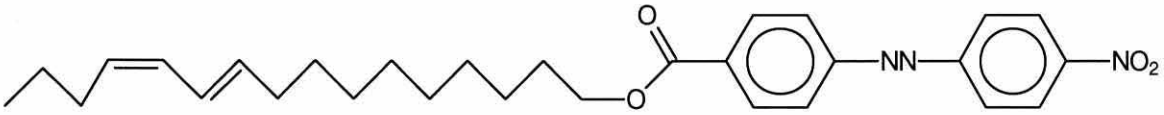
The structures of insect sex pheromones of the lepidopteran species:

- Contain an even number of carbon atoms in an unsaturated chain of between 10 and 24 carbons.
- Contain an oxygen functional group, such as an aldehyde, ketone, acetate or alcohol.
- One, two or three double bonds may be present along the chain; their positioning and stereochemistry is vital for activity.

The first isolation and identification of an insect pheromone was for the female silkworm moth *Bombyx mori*, in 1959 by Butenandt *et al.* The pheromone was termed bombykol and its structure is (E,Z)-10,12-hexadecadien-1-ol (**1**).

(1)

The determination of the first pheromone structure took 22 years and required the crude extraction of 500 000 female abdomens to obtain enough compound to analyse. Each insect gland was washed with ethanol/ether (3:1) and the extractions were subsequently reacted with 4-nitroazobenzene-4-carboxylic acid (NABA) to give the corresponding ester (**2**).



(2)

This gave the pheromone ester (**2**), of which 12 mg was obtained. Ultraviolet absorption and a molecular formula of $C_{29}H_{37}N_3O_4$ for the derivative gave a pheromone formula of $C_{16}H_{30}O$ and suggested a conjugated diene system. Further chemical analysis confirmed the formula. Hydrogenation with platinum oxide gave palmityl alcohol. Oxidative cleavage of the double bonds with potassium permanganate gave carboxylic acid derivatives. These compounds were identified by further analysis of their methyl esters. These studies gave the structure 10,12-hexadecadien-1-ol.[4]

However the exact stereochemistry of the two double bonds in the molecule was still unknown. The four possible geometric isomers had to be synthesised, and each isomer was tested for its BR_{50}, in biological tests, before the correct isomer could be finally revealed as cis-12-trans-10-hexadecadien-1-ol. Some 19 years later in 1978, it was discovered that the silk worm pheromone was actually a mixture of two components. The second pheromone structure was discovered to be (E),(Z)-10,12-hexadecadien-1-al, and was termed bombykal.

From the discovery of the first pheromone structure, thousands of pheromones have been identified and more are still being found. Pheromone compounds are extracted in nanogram amounts; they are separated and characterised by GC/MS, IR and UV analysis. Then the characterised structures are synthesised and compared to the natural compound. The synthetic compound must be tested on the species for its biological activity, before the structure is finally established.

Now new methods of identification have been developed to test for activity in a range of compounds. These modern techniques make the screening for active molecules less laborious. An electroantennogram (EAG) is the measurement of the electrical impulses that are created when a pheromone molecule is passed across the insect's amputated antennae.[4] A current is passed through the antennae tip. When a molecule binds with the olfactory receptors a minute pulse is detected, proving biological activity. The EAG machines have been connected to GC and MS. The extractions from an insect can be separated by gas chromatography and passed over the antennae.[5] The active compounds can therefore be discovered much more quickly and a mass spectrum obtained at the same time.

1.2 Pheromone Biochemistry

1.2.1 Introduction

Pheromones of lepidopteran species are generally a blend of long chain unsaturated aldehydes, alcohols and acetate esters, and they are usually an even number of carbons in length. Their structures are analogous to fatty acids, and their biosynthesis follows the same metabolic pathway. The equivalent fatty acid of the pheromone is produced by the insect and further processes occur which convert the carboxylic acid functionality into aldehydes, alcohols, and acetates, before finally being excreted from the body

1.2.2 Pheromone Biosynthesis

Fatty acid synthesis occurs in the cytosol of the cell. It produces long chains of carbons, in even numbers. The chain length elongates sequentially by the addition of 2-carbon units. These 2-carbon units are derived from acetyl-CoA (**3**), which is the principle building block of the fatty acid pathway. From this point the fatty acid biosynthesis develops.

The first and most important step in fatty acid biosynthesis is the irreversible conversion of acetyl-CoA into malonyl-CoA (**4**), by carboxylation (**Fig 2**). Biotin carboxyl carrier protein (BCCP) (**5**) supplies the CO_2 which adds to acetyl-CoA.[6]

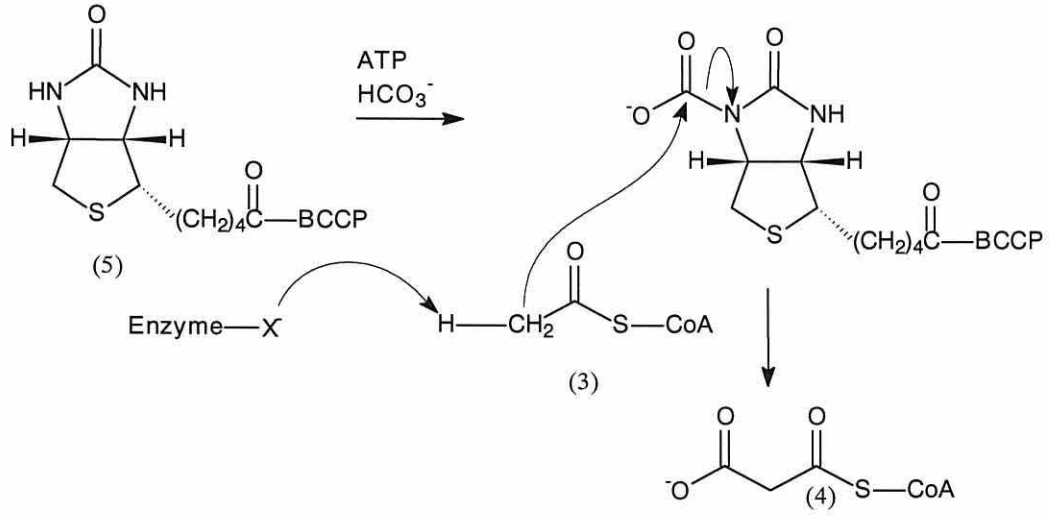


Figure 2

Once malonyl is produced the biosynthesis can begin. The biosynthesis of the fatty acid carbon chain is cyclical. Each cycle is completed in 4 steps. The first step is the union of malonyl and the acetyl (**Fig. 3**). Two different thiol groups attach malonyl-CoA and acetyl-CoA separately to the same acyl carrier protein (ACP). On this protein the rest of the steps in fatty acid synthesis occur. Malonyl-ACP adds in a Claisen condensation type reaction to acetyl-ACP. This reaction is catalysed by acyl-malonyl-ACP condensing enzyme. The addition of a two-carbon unit (acetyl) and a three-carbon unit (malonyl) with the loss of CO_2 forms a four-carbon unit. The condensation reaction is made thermodynamically favourable by the loss of carbon dioxide. The methylene carbon between the carbonyl and the carboxylic acid of the malonyl is activated, making it a good nucleophile; the methylene attacks the carbonyl of the acetyl displacing the protein linkage to give (**6**).

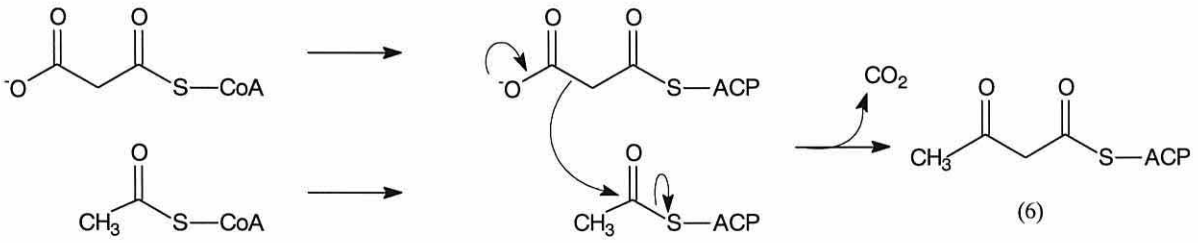


Figure 3

The second step in the metabolic pathway of the fatty acid synthesis is a stereoselective reduction of the keto group to an alcohol (**Fig. 4**). The reducing agent is NADPH. The reaction is catalysed by the enzyme beta keto acyl-ACP reductase, giving the product (3R)-hydroxybutyryl-ACP (**7**).

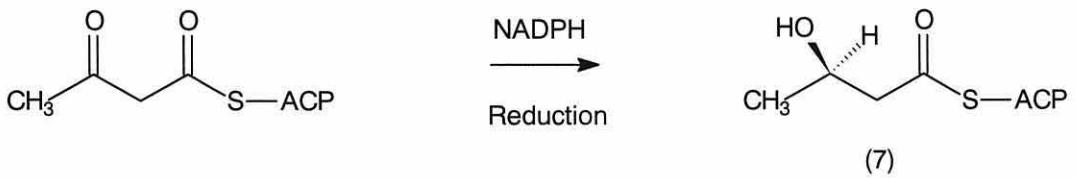


Figure 4

Step three is the dehydration of (3R)-hydroxybutyryl-ACP; the reaction removes H_2O, to form a double bond. The product is (E)- Δ^2-butenoyl-ACP (**8**).

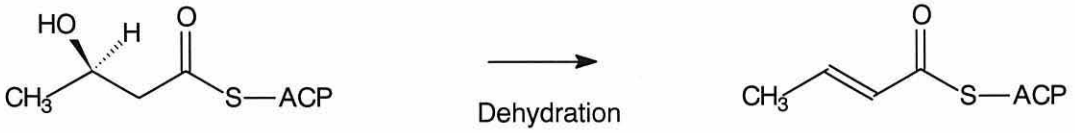


Figure 5

The fourth step, is the reduction of the *trans* double bond to give butyryl-ACP (**9**). NADPH is again used as a reducing agent and the reaction is catalysed by enoyl-ACP reductase.

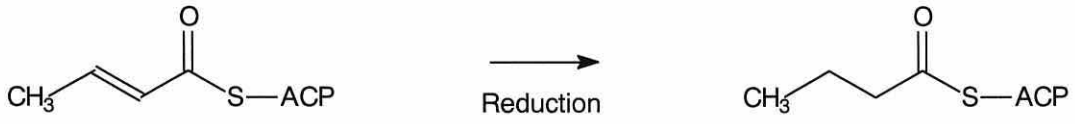


Figure 6

These four steps complete the first cycle of elongation. In the second cycle (**9**) is condensed with malonyl-ACP and the reduction-dehydration-reduction steps are repeated. Thus a series of two carbon units are added until the required chain length is completed.[7]

1.2.3 Desaturation of Pheromone Precursors

The majority of lepidopteran pheromones are monounsaturated acetate esters, alcohols and aldehydes with a long chain carbon backbone 10-18 carbons in length. The mechanism for the insertion of a double bond into the fatty acyl chain is by the action of desaturase enzymes. Each desaturase enzyme introduces a double bond at a specific point along the carbon chain relative to the carbon containing the functional group (**Fig. 7**). The reaction utilises oxygen though the precise mechanism is unknown.

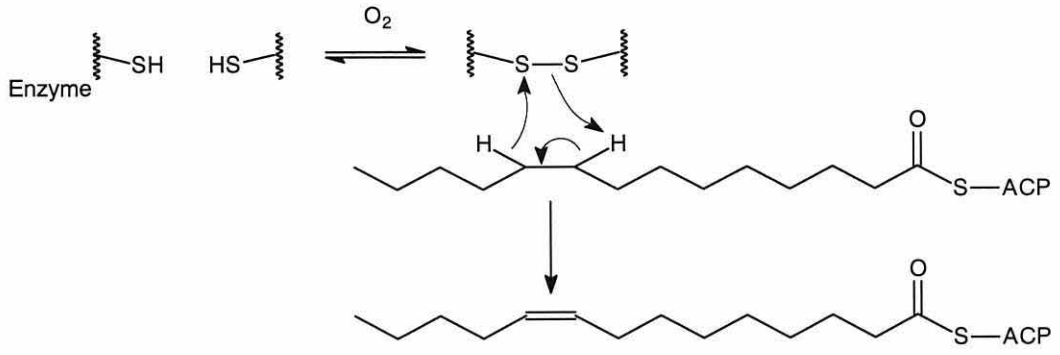


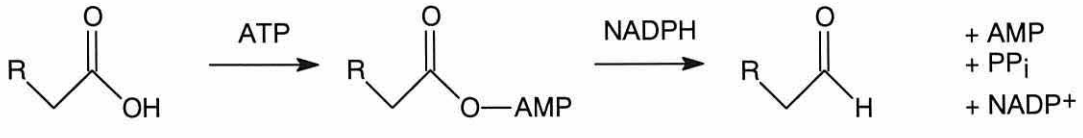
Figure 7

1.2.4 Conversion into Pheromones

Little is known about the biological systems utilised for the conversion of the fatty acid into the corresponding aldehydes, alcohols and acetate pheromone components, however there is some idea about which enzymes are responsible for their biotransformations.

1.2.4.1 Aldehydes

Reductase enzymes have been discovered that reduce fatty acids to aldehydes. The fatty acid is activated with ATP, forming an acyl-AMP intermediate (**10**). This intermediate is then reduced by reductase enzyme to the aldehyde using NADPH (**Fig. 8**).



(10)

Figure 8

The second method for aldehyde biosynthesis, is the oxidation of fatty alcohols (**Fig. 9**). There are two types of enzymes which bring about the reduction of acids to aldehydes. Dehydrogenase enzymes use NADP to accept an electron for oxidation and oxidase enzymes

use oxygen as the electron acceptor. These enzymes have a metal ion centre or a flavin cofactor to mediate the reduction of the oxygen molecule.

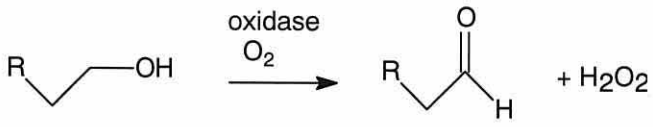


Figure 9

1.2.4.2 Alcohols

Aldehyde reductase enzymes are present in pheromone glands. The fatty aldehyde may be reduced to the fatty alcohol using NADPH as the reducing agent (**Fig. 10**).

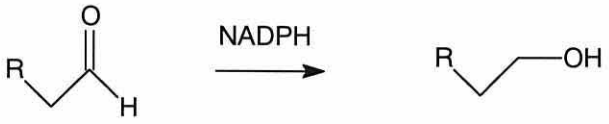


Figure 10 Reduction of an aldehyde.

1.2.4.3 Acetates

The third type of pheromone structure is the acetate esters of the fatty alcohols. These are the most common of the three functionalities of pheromones in lepidopteran species. Fatty alcohols are directly converted into the acetate esters by the action of the enzyme fatty alcohol acetyl transferase with acetyl CoA (**Fig. 11**).

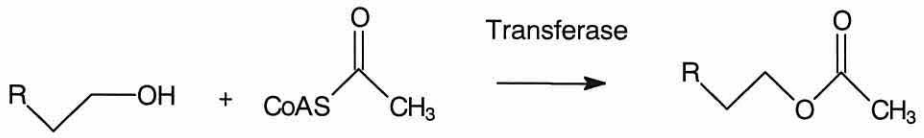


Figure 11 Acetate esterification.

The esters can be hydrolysed *in vivo* to allow the compound to be converted into alcohols and aldehydes for excretion. Their hydrolysis occurs with the action of esterase enzymes (**Fig. 12**).

Figure 12 Acetate hydrolysis.

Acetate esters are found in abundance in the pheromone glands of insects that excrete only alcohol or aldehyde pheromones. It is believed that pheromones are kept in the gland in the less reactive form of the acetate ester until needed. Further conversions into the alcohol and then into the aldehyde are made when necessary. This avoids the storage of fatty aldehydes, which can be toxic to the cells of the gland in high concentration.[8]

1.3 Nomenclature of Insect Pheromones

Originally when pheromone discovery was in its infancy the names of the pheromone compounds were related to the species Latin classification (**Table 1**).

Table 1

Species	Common name	Compound
Lymantria dispar	Disparlure	(Z)-7,8-epoxy-2-methyloctadecane
Bombyx mori	Bombykol	(E,Z)-10,12-hexadecadien-1-ol
Pectinophora gossypiella	Gossyplure	(Z,Z) and (Z,E)-7,11-hexadecadienyl acetate

As the range of species studied increased, similarities and trends were discovered. Also the same pheromone compounds were being discovered in different species (albeit in different ratios and mixtures). So a more logical chemical description of each molecule was introduced. The pheromones of lepidopteran insects often have a greatly similar chemical structure, i.e. that of an unsaturated chain with an oxygen functionality.[9] A general shorthand nomenclature has developed with the continued discovery of hundreds of new compounds (**Table 2**).

Table 2

Chemical Name	Abbreviation
(Z)-7-hexadecenyl acetate	(Z)7-16:Ac
(E),(Z)-10,12-hexadecadien-1-ol	(E)10,(Z)12-16:OH
(Z)-11-tetradecenal	(Z)11-14:Al

The important features, the chain length, the position and stereochemistry of the double bonds and the functionality of the molecule are all recorded in the abbreviated form. The names of seven important insect pests and their pheromone components are listed in **Table 3**.

Table 3

Insect pest common name	**Species**	**Pheromone components**
American Bollworm	*Heliothis armigera*	(Z)11-16:Al, (Z)9-16;Al
Diamond back moth	*plutella xylostella*	(Z)11-16:Al, (Z)11-16:Ac, (Z)11-16:OH
Cotton bollworm	*Heliothis zea*	(Z)11-16:Al, (Z)9-16;Al, (Z)7-16:Al, 16:Al
Tobacco budworm	*Heliothis virescens*	(Z)11-16:Al, (Z)9-16;Al
Gypsy moth	*Lymantria dispar*	-(Z)-7,8-epoxy-2-methyloctadecane
Leaf roller moth	*Argyrotaenia velutinana*	-(Z)11-14:Ac
Silkworm moth	*Bombyx mori*	(E)10,(Z)12-16:OH
Pink bollworm moth	*Pectinophora gossypiella*	(Z)7,(E)11-16:Ac

1.4 Pheromone Use

1.4.1 Introduction

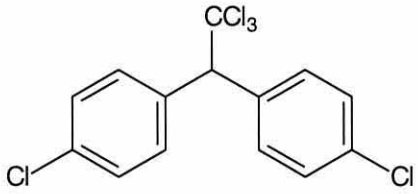
There are many species of insects that are the scourge of the agricultural world. Approximately 15 percent of crops planted are lost through the feeding of insects on agricultural crops and therefore over $20 billion is spent annually on insecticides to protect the produce from destruction. One species, the diamond back moth, alone causes $1 billion of damage in the USA.[10] Lepidopteran insect species are of great significance to the agricultural community; most of the major pests worldwide are from this variety. Therefore it is on these species that most study is concentrated.

Modern legislation and environmental concerns point towards the reduction of the exposure limits in the use of pesticides. Pheromones are part of a program that provides a cleaner and greener alternative. They are authorised for use as pest controls, on organic farming by the European Union. Many countries in the Middle East, Asia and the Americas use pheromones as an alternative for traditional crop protection. In Egypt, the government treats a hundred thousand acres of cotton plantation per year with pheromone traps, for protection against the pink bollworm (*Pectinophora gossypiella*). In Britain the National Resources Institute researches the use of pheromones as an economically viable method of crop protection in India and Southeast Asia.

1.4.2 Pesticides

Pesticides were originally developed to protect man from the pests that attacked food crops. They allowed food production to follow the continued increase in the population throughout the 20th Century. The chemicals were very effective, saving crops from consistent attacks of pests. They prevented the starvation and hunger that was forecast during the industrial revolution. As post war populations grew, pesticides came into worldwide use. Yet, all was not as it seemed.

The first organic pesticides caused problems to the health of those who used the sprays, and eventually those who digested the produce. One of the first, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT) (**11**) was developed in 1939.



(11)

DDT was linked to many environmental problems and biologists feared the possibility of a "Silent Spring" because of the compound's ability to accumulate in the environment and by 1972 it was internationally banned.[11]

Over the years, the full consequences of the release of toxic chemicals into the environment began to show. The pesticides would linger in the food chain, not only killing the pests, but also affecting everything from the soil microbes, to natural predators and harmless species. All wildlife could be effected and eventually the compounds returned to the creators, man. The whole ecosystem could become unbalanced with the future effect incalculable.[12]

The most important effect of the use of pesticides is that on humans. This can be measured directly, by the poisoning of the farmers and workers using or producing the chemicals, and indirectly, through the side effects that have developed from ingesting the contaminated foodstuffs, giving rise to increases in cancers, leukaemia, birth defects, and sterility.

Once sprayed, the pesticide cloud can drift across fields covering non-target crops. The rain washes the spray into the soil, and can kill beneficial microorganisms. The chemicals leach away into adjacent rivers and lakes, killing at first the indigenous insects at the bottom of the food chain then concentrating in and killing the fish populations. The poison also affects birds and mammals as it slowly accumulates in the food chain.[13]

Another serious problem that arises, is the continued development of resistance in the insects. The insects themselves combat the use of the poisons by genetically mutating. Farmers then increase their pesticide usage and demand more potent compounds.

1.4.3 Integrated Pest Management

Insect sex pheromones are used in integrated pest management (IPM) programs. Their uses are for the monitoring of populations of insect species and for mating disruption in agricultural crops. IPM is a system of utilising a range of pest control techniques that protect crops and that will also reduce the amount of pesticides in use. It provides a more environmentally safe alternative to pesticides. Insect pheromones join the armoury of weapons that are currently being used in crop protection. There are three methods used in pheromone insect control:

1. Mating disruption: this involves the dispersion of the pheromones in the air. The insects are disorientated, with the result that the chances of the male finding the real females in the field are greatly reduced. The males' confusion arises as the synthetic pheromones are of a higher concentration than that of the calling females.

2. Mass Trapping: this involves the use of traps that are baited with the pheromone. The aim is to attract the insects to the trap, then capturing and killing them. This method is used to directly control the insect pest.

3. Monitoring: The same traps may be used to gain information on a species population, monitoring the area will determine when and where control measures should be undertaken. Monitor traps are useful in many situations. The pheromone traps can confirm the presence of a species, determining the location and size of the infestation. They can be of use to food manufacturers and retail outlets, warehouse and grain storage facilities, as well as commercial properties like hotels, restaurants and hospitals.

1.4.4 Reasons for Pheromone Use

Insects sex pheromones are of great value in their ability to detect, monitor and control pests in agricultural crops. The current methods of pest control, namely insecticides have many inherent problems - they are toxic and their application leads to insect resistance. Which means that their usage becomes less economical.

Insect Pheromones are non-toxic and are used in relatively small applications, compared with insecticides. The compounds are naturally occurring, and the chance of insects developing resistance is zero. The general structures of the pheromones are related to those of fatty acids and there is research to suggest that exposure to pheromones would result in a biochemical break down in the body, allowing them to be naturally excreted in the same manner as fatty acids. The metabolic pathway would be similar to β-oxidation, the products of which are excreted naturally. The particular blend of pheromone components means that application is species specific, leaving non-target organisms unaffected.

1.4.5 Commercial Prospects

The worldwide use of semiochemicals is relatively small compared with the potential market for their use.

Agrochemicals	$ 28 000 000 000
Insecticides	$ 8 000 000 000
Semiochemicals	$ 70 000 000

Forty percent of the sales for semiochemicals are for pest monitoring. The locations of companies that produce semiochemicals, traps and applicators are quite evenly spread across the world.

USA	$ 20 000 000
Europe/Africa/Middle East	$ 30 000 000
Japan/Australia/N.Z./S.A.	$ 20 000 000

The cost of pheromones is one reason for their limited use. The production of pheromones must be cost effective if they are to make a major penetration into the insecticide market. There is enough backing by governments and environmental agencies to develop the use of pheromones in IPM systems. The regulatory requirements for pheromone use is much less stringent than those for insecticides.[14]

1.5 Aldehyde Pheromones

A recurring group of compounds in most pheromone components is the aldehyde pheromones. Aldehyde compounds are more difficult to synthesis than their complementary alcohols and acetates. It is therefore cost effective synthesis of the aldehydes which is the key to an overall cost reduction in pheromone production. The cost of manufacture could be reduced with a more efficient synthetic route. Almost half of the aldehydic compounds have closely related chemical structures. They have a mono alkenal functionality, with the (Z) isomer predominant (**Table 4**). It is the *cis* (Z) mono unsaturated aldehydes for which it would be most interesting to develop an efficient synthetic route for commercial production.

Table 4 Monounsaturated aldehydic pheromones

C-10 (Chain length)	**C-12**	**C-14**
(Z)-5-Decenal	(Z)-5-Dodecenal (Z)-7-Dodecenal (Z)-9-Dodecenal	(Z)-5-Tetradecenal (Z)-7-Tetradecenal (Z)-9-Tetradecenal (Z)-11-Tetradecenal (E)-11-Tetradecenal
C-15	**C-16**	**C-18**
(Z)-10-Pentadecenal	(Z)-7-Hexadecenal (Z)-9-Hexadecenal (Z)-10-Hexadecenal (E)-10-Hexadecenal (Z)-11-Hexadecenal (E)-11-Hexadecenal (Z)-12-Hexadecenal	(E)-2-Octadecenal (Z)-9-Octadecenal (Z)-11-Octadecenal (E)-11-Octadecenal (Z)-13-Octadecenal (E)-13-Octadecenal (E)-14-Octadecenal

The basic premise for the research project was to synthesise aldehyde pheromones, avoiding traditional routes that oxidise alcohols using toxic heavy metals, and in the process to develop a more cost effective pathway to their production on a large scale from cheap and convenient starting materials.

1.5.1 Di-unsaturated Pheromones

Once a process had been developed for mono alkenal pheromones, it was then hoped to extend it to include dienic aldehydic pheromones. There are 70 compounds that are attributed to being aldehyde pheromones. Four are saturated, twenty-four are mono-unsaturated, thirty-six are diene and five are triene. The four basic characteristic stereochemical diene systems are shown in **Fig. 13**.

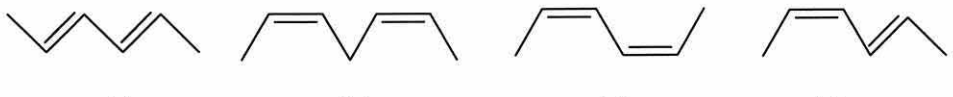


Figure 13

(a) Conjugated *trans-trans*, (b) Skipped conjugated *cis-cis*, (c) Conjugated *cis-cis*, (d) Conjugated *cis-trans*.

There is a range of over twenty different pheromones that feature skip conjugated *cis* double bonds. A range of them contains the double bonds in the same positions on the unsaturated carbon backbone.

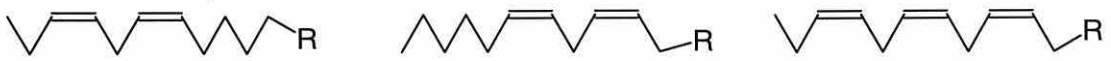


Figure 14

These structures are contained in pheromones of chain lengths 16 to 26 carbons. The **R** group can be an alkyl chain, but some contain an oxygen functionality at the terminal carbon. A full list of aldehyde pheromones are given in the **Appendix**.

1.5.2 Conclusion

Insect pests are, and will remain a great problem to the human race. Unfortunately pesticides which were developed to combat the pests, are turning out to be a destructive power to the environment, causing in some circumstances, more harm than good. Even when nature seems to be tamed, it has a habit of turning on those who affect it. The best inventions always complement and utilise the methods of nature, and do not go against it. This is being realised by farmers and governments throughout the world. In September 1998, the United Nations member states signed an agreement to reduce pesticides levels. The trends are moving away from traditional pesticides to more harmless alternatives.

Throughout many years alternatives to pesticides have been tried and tested to rid pests from the fertile lands on which we grow crops. The Chinese are always interested to developing safer methods of pest control. In a northern city of Tianym the government released 5 million Ichneumon wasps that were bred specifically to eat insect pest that were destroying the harvest. This follows in the footsteps of previous attempts in Chinese pest control. In the 1950's their campaign against sparrows also avoided the use of toxic chemicals; the entire population was mobilised to scare the birds away by banging kitchen utensils in the countryside to keep the birds in flight until they dropped with exhaustion. On the face of it sex pheromones for insect control may not seem so unusual after all.

CHAPTER 2 – Pheromone Chemistry

2.1 Hypothesis

The best method for the production of fatty aldehydes is a reductive one. The reduction of acyl chlorides to aldehydes by catalytic hydrogenation gives a more cost-effective route for the production of a wide range of insect pheromones on a commercial scale. The synthesis of cis alkenal pheromones is possible by a double reductive method, i.e. reducing both the acyl chloride and an acetylene in one step. The synthetic procedure should be easily scaled up and the starting materials would be readily available in bulk quantities.

The subsequent synthesis of di-unsaturated aldehyde pheromones can be produced using the techniques developed from hydrogenation and will give a flexible route that will require few changes to the overall strategy.

2.2 Aldehyde Pheromones

Aldehyde insect pheromones are part of a mixture of compounds, which are excreted by insects for the purpose of attracting a mate. In this mixture, the aldehyde component is generally in the smallest ratio. However, the aldehyde odour is the most prominent and quite distinctive in the blend. It is almost overpowering to humans when concentrated. Like all the best perfumes the most expensive odours are utilised in a subtle manner, yet they are vitally important in terms of the overall success in attraction. The blends of the most economically destructive pests contain aldehydes as part of their attractive scent. This makes these pheromone compounds a desirable commodity. However the main problem is the expense of synthesising the aldehydes. They are expensive due to the methods used in their manufacture. The traditional techniques for the aldehyde synthesis are oxidative. The alcohol is oxidised to the aldehyde by means of metallic oxidising agents; these oxidisers are very toxic to humans and are likely to be carcinogenic. The yields are rarely quantitative and the conditions harsh on the molecule. Though the initial price of the oxidising material is not high, it is not the only cost incurred. Large amounts of the oxidiser must be used - usually two to three equivalents are necessary. The separation and purification of the product from the toxic waste produced is

important, as are the careful disposal and cleaning up procedures that require specialised equipment and training.

2.2.1 Pheromone Synthesis

The first pheromone to be identified was (E),(Z)-10,12-hexadecadien-1-ol (**1**), by Butenandt *et al* in 1962.[15] The compound was extracted from the silkworm moth (*Bombyx mori*). Though it was known to contain two conjugated double bonds, their stereochemistry was not confirmed until all four stereoisomers were synthesised and biologically tested. The isomers were synthesised by two different groups in Germany at the same time. The first synthetic route to bombykol was developed at the Max-Plank Institute of Biochemistry in Munich (**Fig. 15**). The procedure was non-stereoselective. A Wittig reaction produced both *cis* and *trans* isomers which were separated using urea and methanol, before the synthesis was continued.

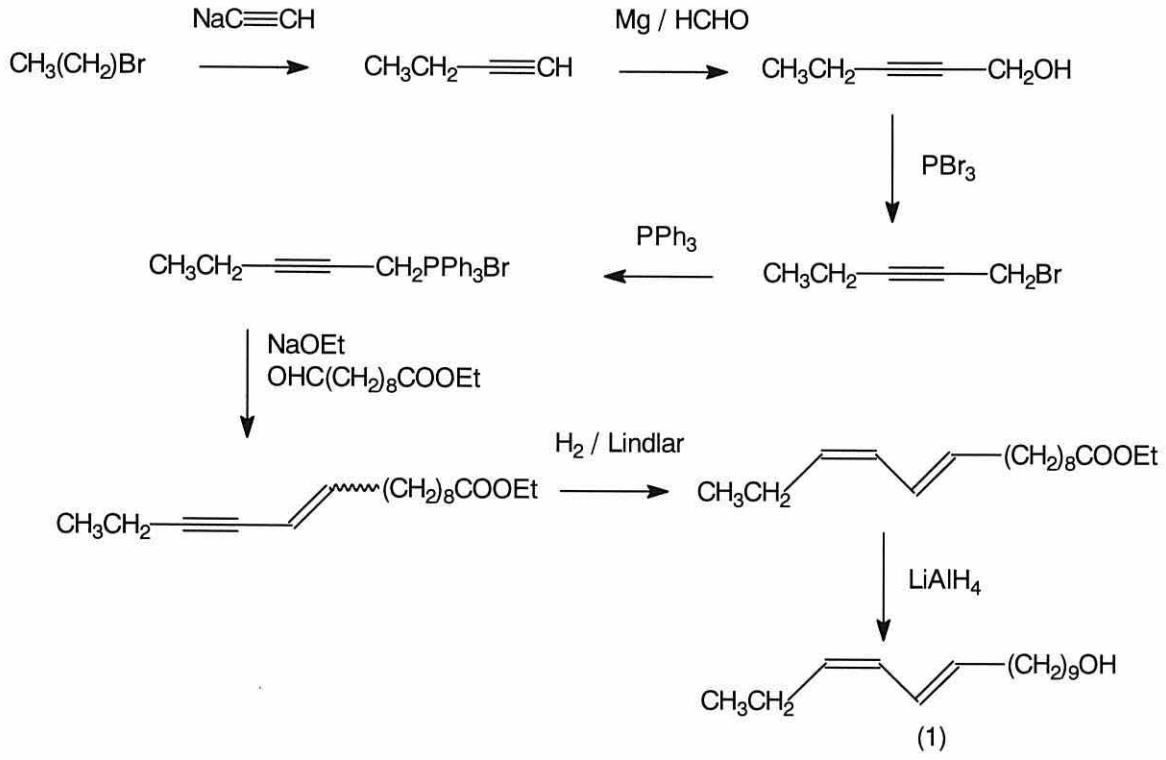


Figure 15

Chemists at Farbenfabriken Bayer AG in Leverkusen achieved the second synthesis of (**1**) in the same year (**Fig. 16**).[16] This route was shorter and also stereoselective. The aldehyde (**12**)

was coupled to propargyl bromide via an organozinc intermediate and the secondary alcohol (**13**) produced was dehydrated to give the *trans* alkene (**14**).

The derived ester was reduced to the alcohol with lithium aluminium hydride and the terminal alkyne was coupled with propyl magnesium bromide to give (**15**). Finally the alkynol was catalytically semi-hydrogenated to the *cis* alkene (**1**).

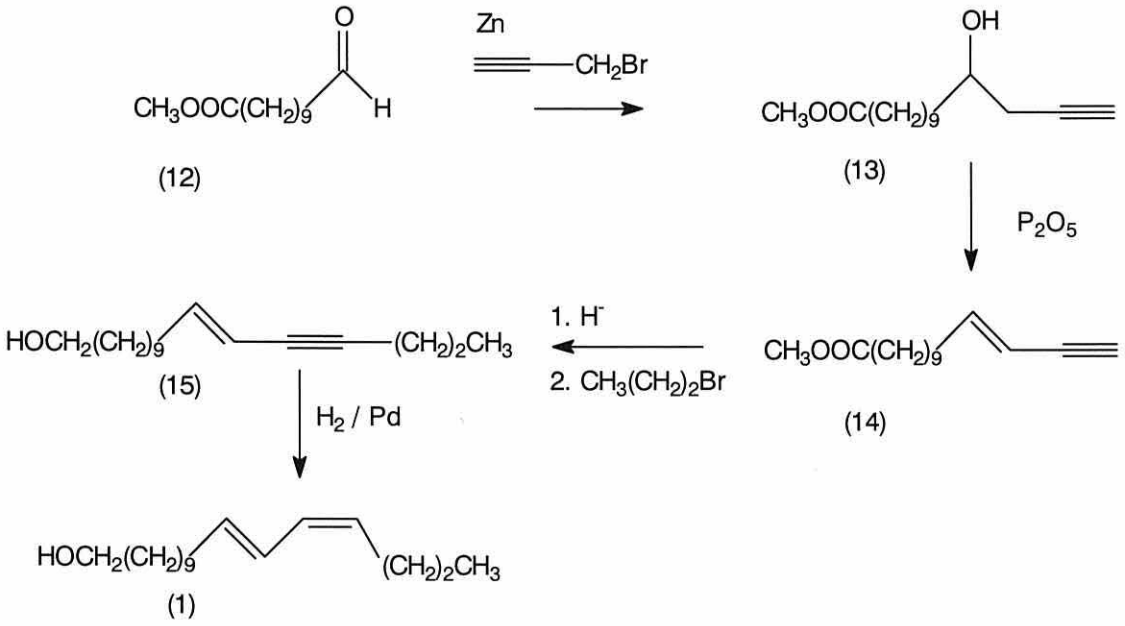


Figure 16

Research continued rapidly, as more new compounds were discovered and identified for a wide range of insect species. Biologists demanded synthetic samples of these compounds, firstly to prove structure and later to study their effect and potential uses. This process still continues, due to the enormous variety of insect species in the world.

The major pheromone compound of the red-banded leaf roller moth (*Argyrotaenia velutinana*) was identified as (Z)-11-tetradecenyl acetate (**16**) and synthesised in 1968 (**Fig. 17**). 10-Bromodecan-1-ol was protected with dihydropyran and the bromide (**17**) coupled to 1-butyne. The compound was then deprotected and partially hydrogenated to the *cis* alkene (**18**). The alcohol was acylated to give the pheromone (**16**) as the product in five steps.[17]

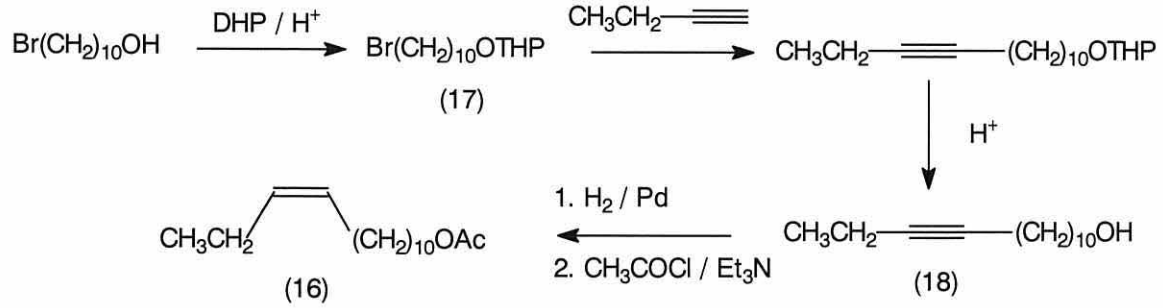


Figure 17

The fall armyworm moth (*Spodoptera frugiperda*) pheromone (Z)-9-tetradecenyl acetate (**19**) is of similar structure and its synthesis in 1968 followed a similar pattern (**Fig. 18**).[18] 8-Chlorooctan-1-ol was protected with DHP and the chloride coupled with lithium acetylide. The terminal acetylene (**20**) was coupled with butyl bromide. Again the alkyne (**21**) was partially hydrogenated to give the *cis* alkene (**22**) and the alcohol was deprotected and converted into the acetate in one pot. This gave (**19**) in six steps, as two coupling reactions were employed instead of using 1-hexyne. Many analogous pheromones were synthesised by this route, giving an overall yield of approximately 35 %, making the method viable for commercial production.[19]

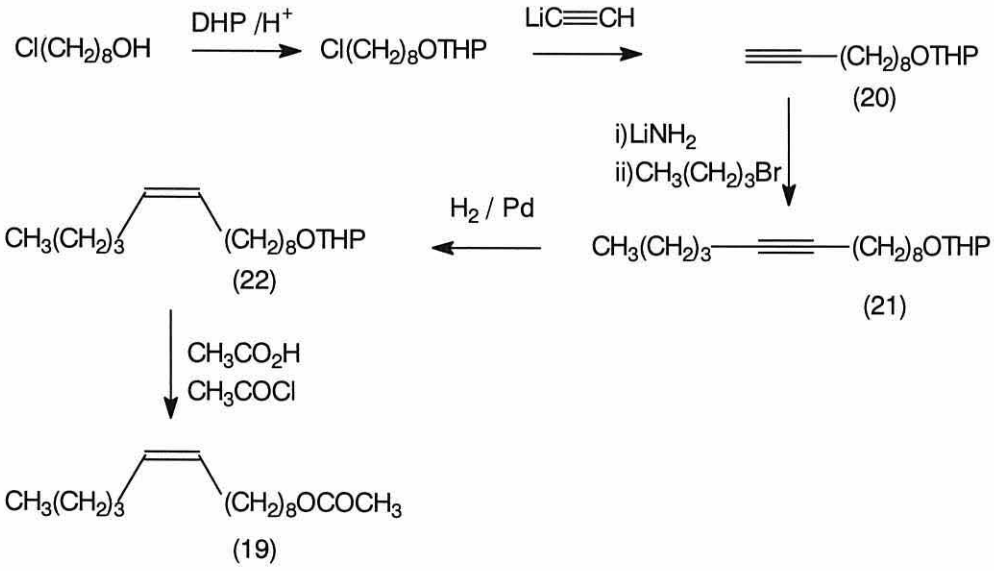


Figure 18

J. Bestmann *et al* developed many syntheses for a wide range of pheromones throughout the 1970's. In 1975 a general method was developed for synthesising (Z)-9-olefins, including

(Z)-9-dodecenal to (Z)-9-hexadecenal, which were synthesised by using the Swern oxidation in 88 % to 67 % yield.[20]

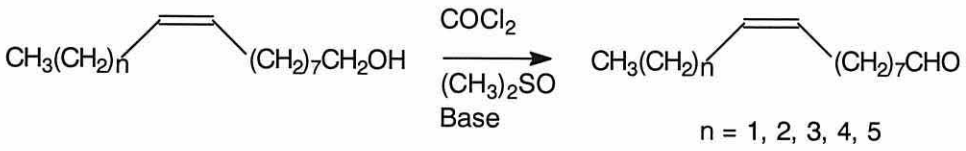


Figure 19

In 1978, Bestmann synthesised (Z)-11-tetradecenal (23) and (Z)-11-hexadecenal (24) using hydroboronation chemistry.[21]

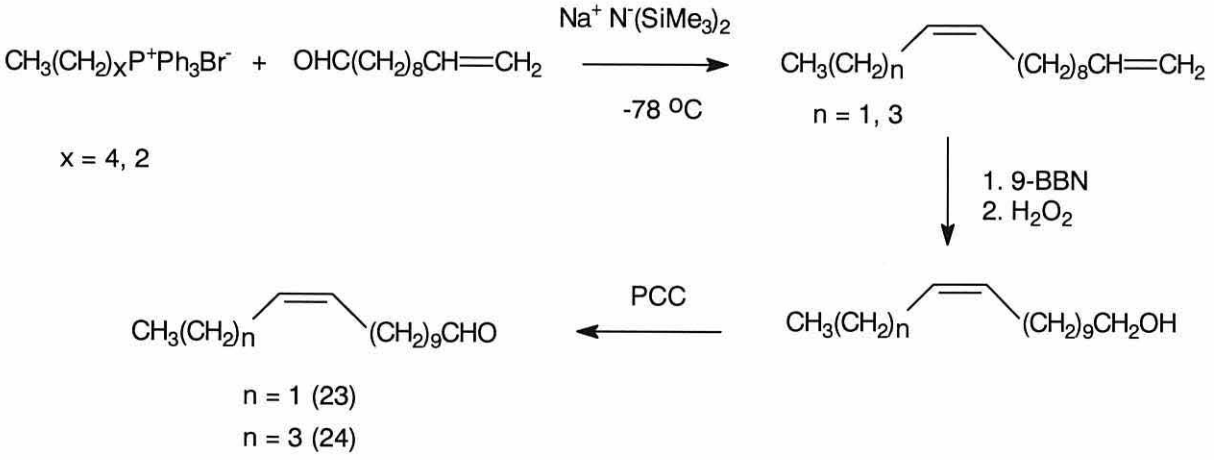


Figure 20

The ylide of the Wittig salt was made using sodium bis(trimethylsilyl)amide at -78 °C and, on the addition of 10-undecenal, the reaction gave the Z-alkene functionality in the correct position. Changing the length of alkyl Wittig salt altered the pheromone chain length. Hydroboration of the terminal alkene was achieved using 9-borabicyclo[3.3.1]nonane (9-BBN), which added regiospecifically *syn* to the less substituted carbon. The organoboron was oxidised to the alcohol on addition of hydrogen peroxide. The R-O-B bond was hydrolysed in the basic solution to give the alcohol. The (Z)-11-alkenols were finally oxidised to the aldehydes (**23**) and (**24**) with PCC in ~80 % yield.

In the 1980's H. C. Brown *et al* also utilised boron chemistry to synthesise lepidopteran insect pheromones. (Z)-7-Tetradecenal (**25**) and (Z)-7-hexadecenal (**26**) were synthesised in 1986 using B-chloroborepane as the starting material.[22] B-methylborepane (**27**) was synthesised from B-chloroborepane, by the addition of methyl lithium at room temperature. 1-Octynyllithium was added to the pot at 0 °C. The complex (**28**) was then cooled to -78 °C in order to add iodine and effect an oxidation with hydrogen peroxide. The product, an alkyneol (**29**), was distilled from the crude product in 73 % yield. 7-Tetradecynol was treated with dicyclohexylborane at 0 °C.

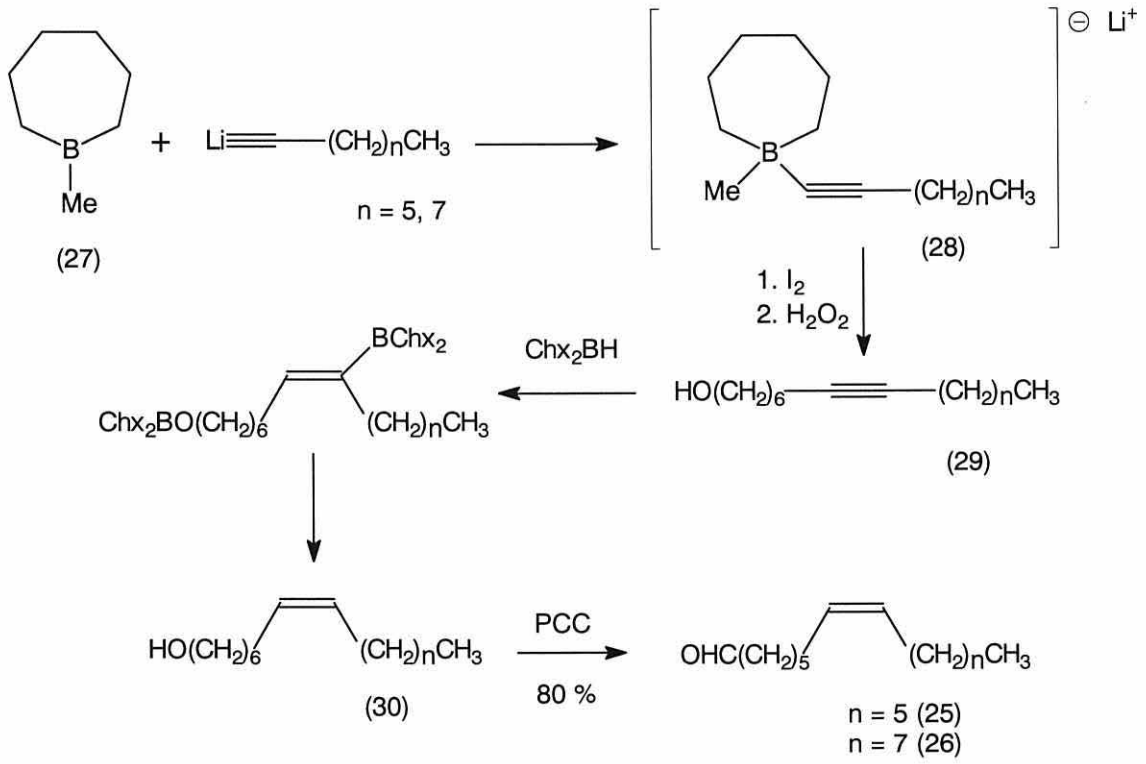


Figure 21

The organoborane was oxidised to give (Z)-7-tetradecenol (**30**) (n = 5) in 80 % yield. Finally the alcohol was oxidised with PCC to give the aldehyde (**25**). The procedure was repeated using 1-decyne to give (Z)-7-hexadecenal (**26**) (n = 7) in similar yields. The synthesis is novel but is limited to the shorter chained pheromones due to the limitations on the boropane ring size. Again, this synthesis relies on PCC oxidation.

(Z)-12-Hexadecenal (**31**) was synthesised in 1992 (**Fig. 22**). 1-Pentyne was coupled to the THP ether of 11-bromoundecan-1-ol in 93 % using butyllithium at -78 °C. HMPA was added to the reaction vessel as co-solvent to THF. The alkyne (**32**) was hydrogenated to the *cis*

olefin in 78 % yield, and the THP ether (**33**) deprotected with *p*-toluenesuphonic acid to give the alcohol (**34**) (73 %). The alcohol was finally oxidised using PCC to give the product (**31**) in a yield of 88 %.[23]

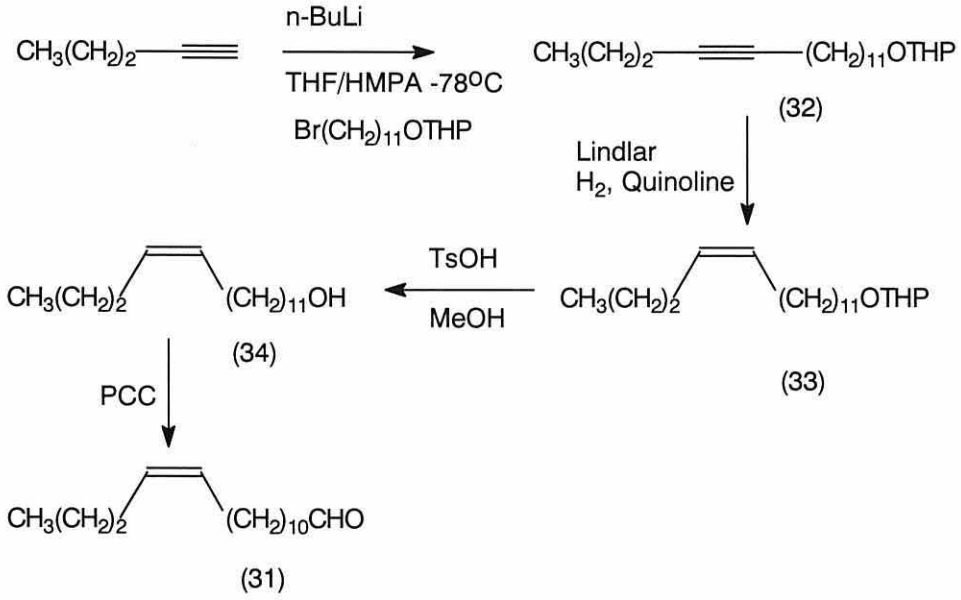


Figure 22

In the 1990's, Mestres[24] synthesised a range of monoalkenal pheromones; the most efficient synthesis is shown below, giving the pheromone (Z)-9-hexadecenal in 9 steps from cyclooctene (**36**) (**Fig 23**).

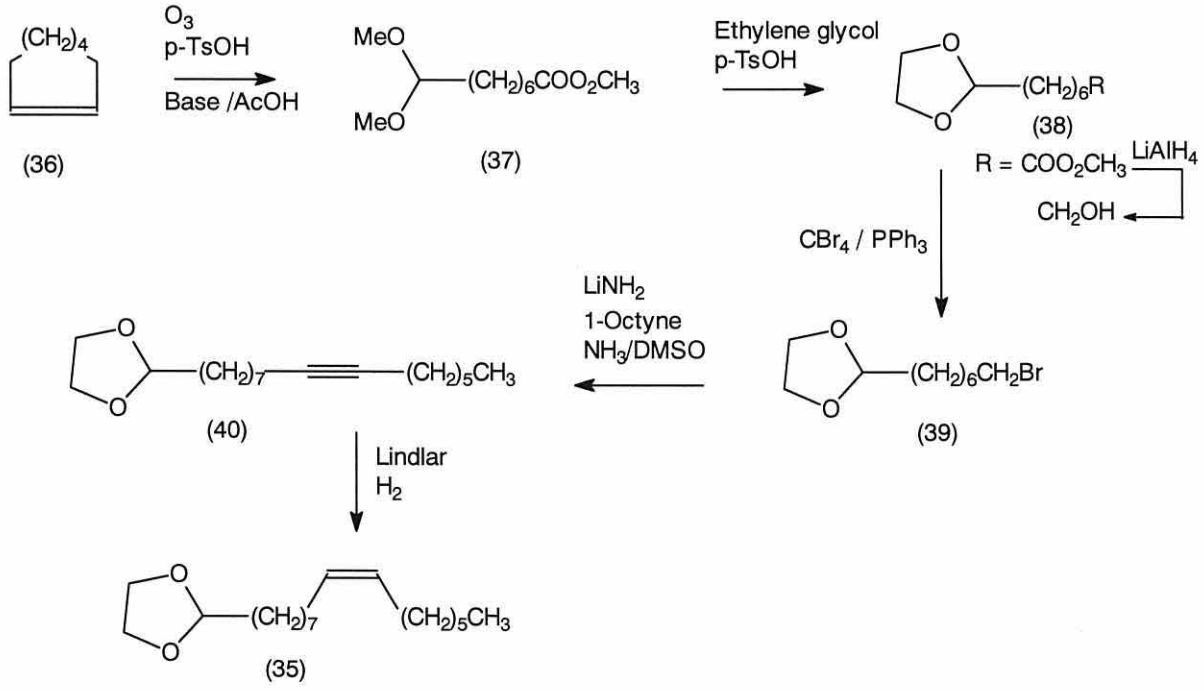


Figure 23

The first step, an ozonolysis of cyclooctene (**36**) curiously gave an acid aldehyde as product, instead of the dialdehyde or di-acid, which is normally the product; however the experimental details are not included in the paper. The aldehyde was protected by an acyclic methyl acetal as it was formed. The acyclic acetal (**37**) was further converted into the more stable cyclic 1,3-dioxolane acetal (**38**). The ester functionality was reduced to an alcohol with lithium aluminium hydride, and the alcohol was brominated using carbon tetrabromide and triphenylphosphine (65 %); some deprotection of the acetal occurred during the bromination due to the mild acidity of the reaction. The bromoalkyl dioxolane (**39**) was coupled to a terminal alkyne in 87 % yield, using lithium amide as base, in liquid ammonia and DMSO as co-solvent. The alkyne (**40**) was partially hydrogenated to the *cis* olefin, 2-((Z)-8-pentadecenyl)-1,3-dioxolane (**35**), in 93 % yield.

The first pheromones that were discovered and eventually synthesised were alcohols and acetates. To give the flexibility of producing the complementary range of alcohol, acetate and aldehydes, the method adopted was to oxidise the alcohol as the final step (**Fig. 24**). This oxidative approach to the aldehyde synthesis has continued to be used over the past 20 years. In almost all the syntheses the pheromone compounds were produced on a laboratory scale of < 5 g and more usually < 1 g, which is enough for biological testing, but is insufficient for long term testing in field experiments or application.

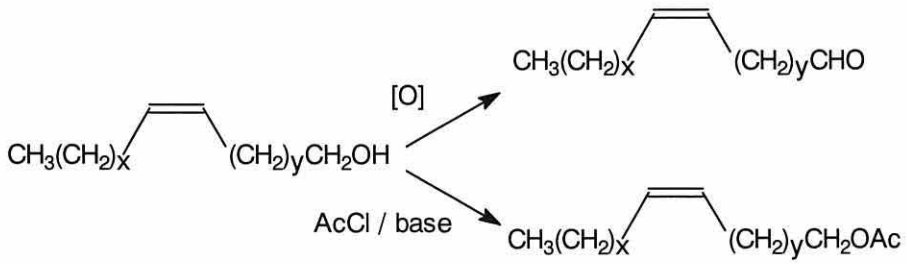


Figure 24

Unsurprisingly, a great many of these synthetic routes use common reactions in most of the steps. The reactions that are common to pheromone synthesis involve organobromine reactions, acetylenic coupling, protections and partial hydrogenations of alkynes to alkenes. There are reactions that rely on the same laboratory apparatus, and which if exploited to their full potential would be more effective in cost, space and time.

Two examples are:

1. Hydrogenation equipment for the semi-hydrogenation of acetylene to produce *cis*-olefins is also capable of producing aldehydes by catalytic hydrogenation.
2. A liquid ammonia reactor is used for the coupling of 1-alkynes to alkyl halides using lithium amide in liquid ammonia, and alkynes may be reduced to *trans* olefins by sodium in liquid ammonia.

2.3 Oxidative Methods

The principle method of producing aldehydes has been to use transition metal oxidants. Chromium (IV), the main transition metal used, is a very strong oxidising agent. Varying the ligands attached to the metal and the use of different can control its precise reactivity. Throughout this century, oxidants have been developed in the search for better yields and ease of use for a wide range of reactants. Some examples are:

For primary alcohols -

- Jones' reagent, (chromic acid and sulphuric acid in water).[25]
- Collins's reagent, (dipyridine Cr (IV) oxide).[26]
- Corey's reagent, (pyridinium chlorochromate (PCC)).[27]
- Pyridinium dichromate, (PDC).[28]
- Magtrieve™ (Chromium dioxide).[29]

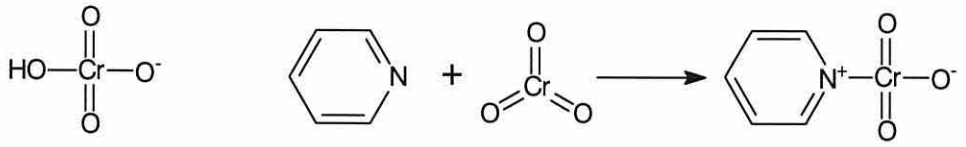
Other examples are -

- Swern reaction, (dimethyl sulphoxide and oxalyl chloride).[30]
- Catalytic dehydrogenation, (using Copper chromite).
- Activated manganese dioxide.[31]

These reagents are described below.

2.3.1 Metallic Oxidisers

The Jones reagent was one of the first reagents to use chromium as an oxidiser. The reagent uses an acidic aqueous solution of chromate (**41**) which can be used for simple primary alcohols to give the aldehyde but in poor yields of ~50 %.[32]



(41) (42)

Figure 25

A chromium trioxide-pyridine complex (**42**) was synthesised by Collins *et al* in 1968. Adding pyridine to chromium tri-oxide in dichloromethane produced the reagent. The use of chromium trioxide gives very high yields for oxidations to ketones (~95 %)[33] and aldehydes (~70 %).[34]

In 1975 Corey, produced pyridinium chlorochromate (PCC) by adding chromium trioxide to pyridine in hydrochloric acid. This gave CrO_3ClH-py. as a bright orange product. In the right conditions, PCC produces aldehydes from alcohols in ~80 % yield. The reactivity of the chromium metal centre is reduced due to its surrounding ligands, and the solvent. Addition of water to PCC will produce pyridinium dichromate (PDC) which will oxidise primary alcohols to carboxylic acids or secondary alcohols to ketones in good yields.

Allylic alcohols can be oxidised with PCC or activated manganese dioxide. The latter is a milder oxidiser, and not will react unless the alcohol is allylic. It must be carefully produced and stored to retain its activity.

The latest oxidiser available is Magtrieve™, which is a mild and selective oxidant for alcohols to aldehydes or ketones and is more reliable than MnO_2. Magtrieve™ from DuPont uses tetravalent chromium dioxide (CrO_2) as oxidant. CrO_2 is a solid crystalline material, which

has a magnetic moment. Excess is used in the oxidation of an alcohol as it is a heterogeneous reactant, but the reduced form is easily recoverable by the use of a magnet.

Catalytic dehydrogenation oxidises an alcohol by passing its vapours over copper chromite. The conditions of the reaction are very vigorous, requiring high temperatures and aqueous acidic solvents, thus are unsuitable for fatty alcohols.

2.3.2 Swern Oxidation

An alternative oxidative method of alcohols that uses mild conditions without transition metals is the Swern oxidation. Dimethyl sulphoxide (DMSO) is a selective oxidant when used in conjunction with N,N-dicyclohexylcarbodiimide (Pfitzner-Moffatt)[35] or oxalyl chloride (Swern)[36] as an activator which electrophiles. The DMSO nucleophilic attacks the electrophile at -78 °C generating the sulphonium halide. The alcohol is added and the hydroxyl group attacks the sulphur of the intermediate generating an alkoxysulphonium salt (**43**). On addition of triethylamine the ylide (**44**) rearranges to give the corresponding carbonyl.

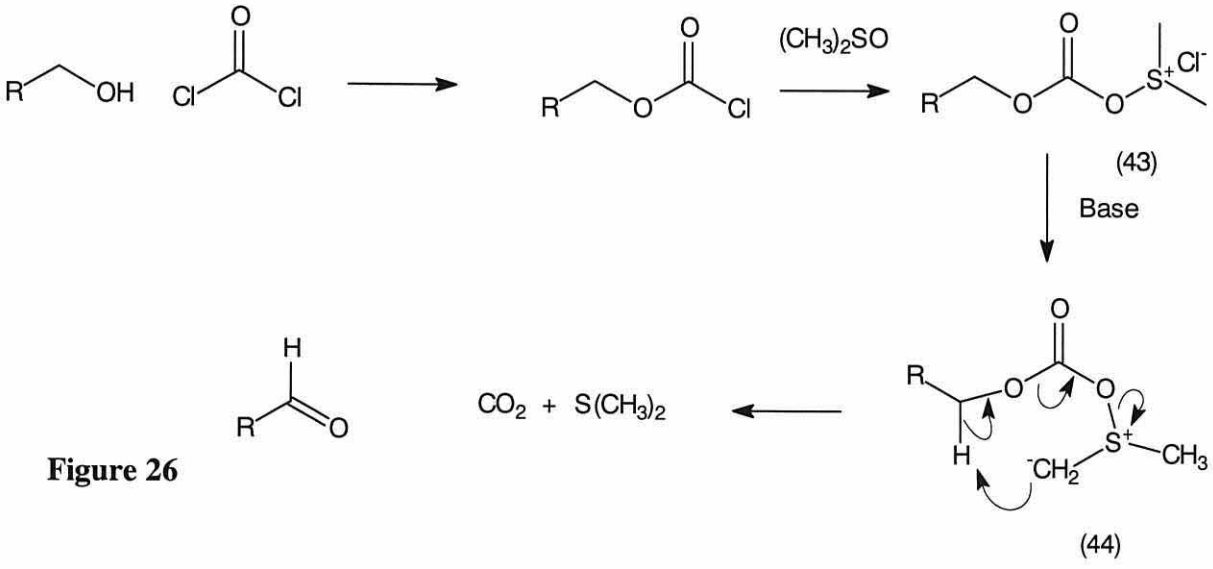


Figure 26

The commercial use of these oxidative methods is not very convenient for a number of reasons. The procedures oxidise the alcohol effectively to the aldehyde, but there are drawbacks for their use on a large scale. The oxidation normally requires two to three molar equivalents of the oxidant. Oxidation reactions must be carefully monitored so that the aldehyde is not further oxidised to the carboxylic acid. The chromate reagents leave a sticky waste product of the reduced metal, which takes the form of an insoluble black gum. The gum makes the separation of the aldehyde more difficult, requiring several extractions and filtrations. The cleaning of the reaction vessel is also a problem. The product must be purified to remove unwanted by-products, and the resulting heavy metal waste must be safely disposed of. Finally, and most importantly, all the chromium oxidising compounds are corrosive and very hazardous to health, with prolonged exposure causing cancer.

2.4 Reductive Methods

The alternative approach to the synthesis aldehydes is to reverse the procedure from oxidation to use reductive methods, i.e. the reduction of the carboxylic acid, its derivatives or nitriles to the aldehyde.

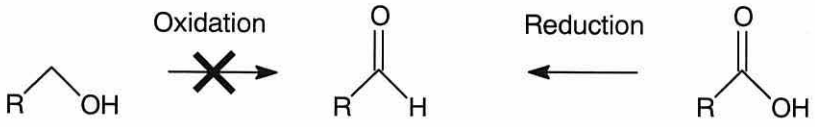


Figure 27

2.4.1 Reduction of Carboxylic Acids and Esters

Carboxylic acids are more difficult to reduce to aldehydes than esters, because acids are less reactive than aldehydes. So when the aldehyde is produced the hydride preferentially reduces it further to the alcohol. A carboxylic acid may be converted to an imino alcohol salt when reacted with lithium in methyl amine and the aldehyde is formed on quenching the salt with water.

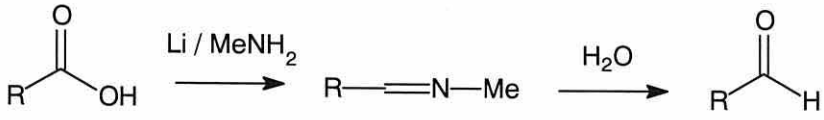


Figure 28

Carboxylic esters can be reduced at temperatures below -78 °C, using metal hydrides, such as diisobutylaluminium hydride.[37] The reason for doing the reaction at low temperatures is because the partial reduction of the ester relies on the relative stability of the intermediate. The intermediate of the metal hydride and the ester is stable at low temperatures, and no aldehyde is actually produced until the reaction is worked up. At higher temperatures the intermediate will undergo elimination and reduce the esters directly to alcohols.

There are however problems associated with the use of hydrides on an industrial scale. The difficulties are in the equipment required to achieve the reaction conditions necessary to avoid over-reduction. The cooling process is costly and the equipment expensive. Stoichiometric equivalents of the metal hydride are used which means large quantities of the reducing agent must be handled and the reagents are toxic and expensive. The hydrides require careful handling due to their reactivity to air and water.

2.4.2 Reduction of Nitriles

The reduction of a nitrile can be achieved by the Stevenson method (**Fig. 29**).[38] Anhydrous tin (II) chloride and dry hydrogen chloride react with the nitrile to give the aldimine hydrochloride salt. On addition of water the salt is hydrolysed to the aldehyde. Though the Stevenson reaction is normally used for aromatic aldehydes, it is possible to use the procedure for the preparation of aliphatic aldehydes.

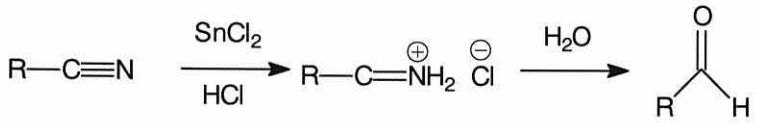


Figure 29

Nitriles may also be reduced to an imino group using metal hydrides, e.g. diisobutylaluminium hydride,[39] or lithium triethoxyaluminohydride (**Fig. 30**).[40] One molar equivalent of the hydride is added to the cyano group at low temperature, and the resulting imine is hydrolysed to the aldehyde on work up with addition of acid.

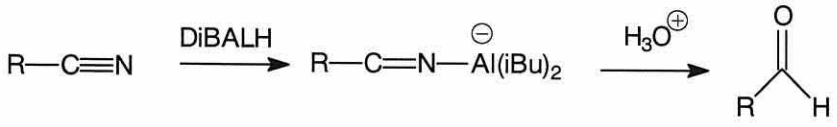


Figure 30

The incorporation of the cyano group requires the addition of cyanide salts, which are poisonous, and demand careful handling procedures. The addition of the cyanide functionality also extends the chain length by one carbon. This means that odd numbered carbon chained starting materials would have to be used, which are generally more expensive than even numbered carbon chained compounds.

2.4.3 Reduction of Acyl Chlorides

Acyl chlorides are the most reactive of the carboxylic acid derivatives, and are the easiest functionality to reduce to aldehydes. It is possible to reduce the acyl chloride with metal hydride reducing agents. Lithium tri-tert-butoxyaluminium hydride may be used for this reduction.[41] The reason that this hydride is used is because the metal centre is surrounded by bulky substituents which lower its reactivity. The tert-butoxy groups cause steric hindrance around the metal centre, which prevents further reduction at low temperatures (< -78 °C).

2.4.4 Rosenmund Reduction

Before the development of metal hydrides, or the refining of modern oxidative methods, the synthesis of aldehydes was principally achieved by the catalytic hydrogenation of acyl chlorides. This reaction is called the Rosenmund reduction.[42]

The Rosenmund reduction uses a palladium catalyst and hydrogen gas, to reduce an acyl chloride to an aldehyde. Hydrogen is bubbled through refluxing toluene or xylene and is adsorbed onto the catalyst. The acyl chloride is adsorbed on the Pd surface and is reduced to the aldehyde producing hydrogen chloride as a secondary product of the reaction. The exhaust gases are bubbled through a water trap, where the HCl is collected. The acidic aqueous trap is titrated in order to follow the reaction and discover the end point.

The main by-product is the alcohol of the acid chloride. The alcohol is formed from the subsequent reduction of the aldehyde. Over reduction is prevented by the addition of a catalytic poison or regulator, which reduces its activity. Originally quinoline-S (thioquinanthrene) was used as the regulator, though alternative regulators were tried, which were generally aromatic amines, e.g. dimethylaniline and pyridine.

The Rosenmund reaction required very careful control of the reaction conditions. The use of an open system bubbling hydrogen through the refluxing solvent is complicated and potentially dangerous. The progression of the reaction is difficult to follow as it relies on the collection and titration of the free hydrogen chloride produced. The conditions are also favourable to produce a range of by-products due to the effects free HCl, and the high temperatures.

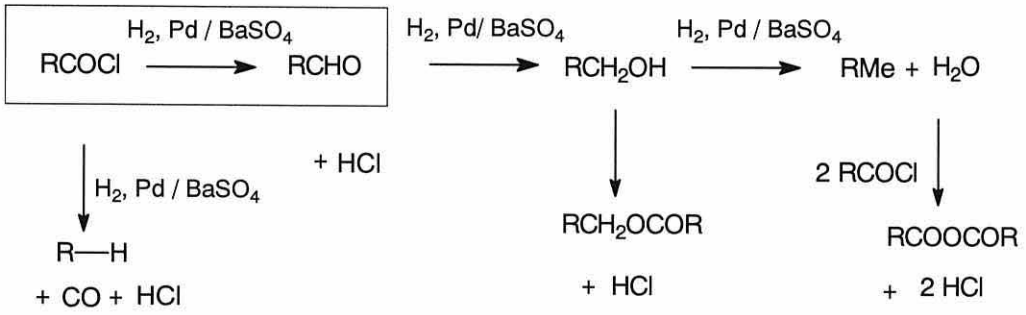


Figure 31

The over-reduction of the aldehyde to the alcohol leads to further loss of yield as it reacts with the acyl chloride to form esters. The alcohol can also be reduced further by hydrogenolysis to produce water. The water will react with the acid chloride to form carboxylic acids, and they may combine to give anhydrides. Once started, a cascade of by-products soon develops. The numerous by-products and the delicate nature of the original method, which was full of specific reaction conditions, makes the procedure a difficult one to carry out. Nevertheless, the Rosenmund reaction was the best method to reduce acid chlorides to aldehydes until the 1960's, when metal hydrides were introduced. Due to the exacting conditions required by the Rosenmund reaction, it was replaced by metal hydrides for reactions carried out on a laboratory scale.

A number of papers have been published that have tried to refine Rosenmund's original method. The changes allowed the reaction to proceed in a closed system, at room temperature.

The closed system meant that by following the volume of hydrogen consumed the reaction could be monitored, and the low temperature reduced the chance of side reactions. The main modification that allowed this development to occur was, to add an aromatic amine to the reaction vessel. The amine would absorb the HCl and help drive the reaction to aldehyde formation. This alteration was named, the "amine modified" Rosenmund reaction.

The first amine modification was by Sakuri and Tanabe in 1944.[43] They used *N,N*-dimethylaniline as HCl acceptor and acetone as solvent. Unfortunately *N,N*-dimethylaniline was also reduced under the reaction conditions. It was not until the 1970's that further papers were published which gave better results and used more convenient procedures. Peters and Van Bekkum changed the acceptor to ethyldiisopropylamine and used acetone as solvent.[44] In 1976 Burgstahler used 2,6-dimethylpyridine, in dry THF at room temperature in a closed system.[45] The reduction proceeded smoothly in good yields and the products were of high purity.

The modified Rosenmund reactions have a number of features that may be beneficial for the synthesis of aldehyde pheromones. Firstly, all major pheromone producers have hydrogenator apparatus for the partial hydrogenation of acetylenes to *cis* alkenes. Secondly, the raw materials are inexpensive to use. Hydrogen is cheap and abundant, and palladium catalysts are already used on a large scale with the metal easily to recover. Thirdly, the reaction conditions are mild, occurring at room temperature and atmospheric pressure, with little purification necessary to give the pure product.[46]

2.4.5 Hydrogenation of Acetylenes

The hydrogenation of acetylenes has always been a most important reaction in pheromone synthesis. The majority of pheromones contain a *cis* alkene in the aliphatic chain. The most convenient method of introducing a *cis* alkene into a molecule is the partial hydrogenation of an alkyne by catalytic means. The catalysts used are generally heterogeneous. They are made from the transition metals, e.g. palladium or nickel. The palladium catalyst is supported on a substrate; barium sulphate, carbon or calcium carbonate (Lindlar) may all used.[47]

Reductions by catalytic hydrogenation methods are generally extremely clean reactions with little or no by-products. The reaction proceeds quickly at room temperature and does not require elevated pressures. The catalysts are metals in the form of a powdered solid, generally supported on an inert support which when separated may be recycled

The mechanisms of these types of hydrogenations are not fully understood, but there is a general understanding of the system. Hydrogen is adsorbed onto reactive sites on the metal, forming metal- hydrogen bonds. The alkyne is also adsorbed onto the surface of the catalyst which bonds with both carbon atoms through their π-orbitals. A hydrogen is added to the adsorbed alkyne, then the second hydrogen is added to the same face of the molecule.[48]

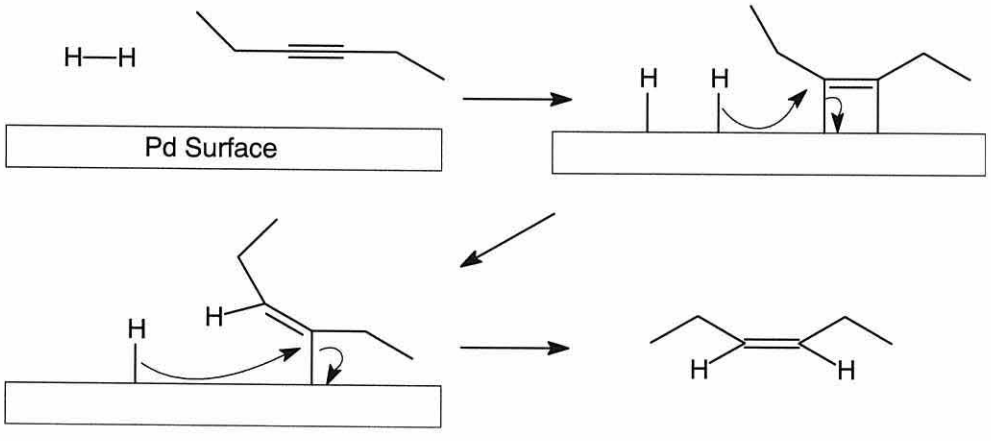


Figure 32

Hydrogen is contained in a closed system and is allowed to adsorb onto the metal surface. It is the surface of the metal where the reaction occurs. The hydrogen adds to one face of the alkyne, to give the *cis* isomer. The volume of hydrogen is monitored and when one molar equivalent has added the reaction is stopped. The work up is simple, the catalyst is filtered off and the solvent is evaporated to leave the product.

Acetylenes are strongly adsorbed on to the catalyst surface and are preferentially absorbed even when in competition with alkenes. However if the reaction is left unchecked, once all the alkyne is reduced, then the alkene begins to be reduced to the alkane.

Nickel (P2) is also used as an alternative catalyst in the hydrogenation of acetylenes to *cis* alkenes in a hydrogen atmosphere. Nickel tetraacetate is reduced to nickel (P2) on the addition of sodium borohydride in ethanol. The nickel (P2) is a good catalyst and will easily hydrogenate the acetylene to the alkane unless ethylendiamine is added, which stops the reaction selectively at the *cis* alkene.[49]

Hydrogenation reactions generally slow down or stop when all the alkyne has reacted, but this may not be relied on. The experiment must be monitored and the reaction stopped when the calculated amount of hydrogen has been absorbed. When using palladium catalysts, modifiers such as quinoline are added. These modifiers stop the reaction when all the alkene is formed. Modifiers effect the catalysts by decreasing the rate of hydrogen adsorption onto the metal surface. The modifier can be incorporated into the catalyst on its preparation, such as the Lindlar catalyst, which is palladium-lead on calcium carbonate. Others are added in the reaction vessel, e.g. quinoline. There are a wide range of modifiers including the metal salts of zinc, lead, tin, cadmium, zirconium, gold and silver and additives, which are usually amines.

The hydrogenation process is already an integrated part of the synthesis of the Z-alkenes of insect pheromones. Many of the most important aldehydes are a necessary and an important part of the attractants. Both the reduction of the alkyne and that of the acyl chloride require very similar conditions and use an amine base, though for different reasons. A double reduction method would give the advantage of doing these two reactions in one step.

2.5 Protecting Group Chemistry

2.5.1 Introduction

A serious problem arises for the organic chemist, when during a synthesis, a molecule contains two or more functionalities which are prone to attack. One is the desired target and the other not. The answer is to select the unwanted functionality and temporarily remove its reactivity from the molecule. The offending group cannot be physically removed, but it can be converted into an inert functionality. This allows the correct reaction to proceed. The procedure is "protecting" the functional group during the necessary reaction. The protection of a reactive species is carried out in three steps:

1. The synthesis of the inert functionality.
2. The execution of the desired reaction(s).
3. The removal of the protecting group.

The type of protecting group used depends on many factors. The main considerations are: The functional group to be protected, the type of reaction that will follow and the effect on the rest of the molecule on protection and deprotection, i.e. the ease of introduction and removal. Other considerations may be the costs of the reaction process, the materials, and the availability of the substrates. [50]

2.5.2 Aldehydes

The efficient protection and deprotection of carbonyl groups are of great importance. In organic chemistry the carbonyl group is often incorporated into a molecule as a useful intermediate, due to its high reactivity to many reagents. This allows for a wide range of functional group interconversions. However its reactivity also makes it a prime candidate for unwanted side reactions. The protection of carbonyls has long been an important issue; the methods have changed little. Aldehydes and ketones are converted into acetals protecting them from nucleophilic attack. Acetals are stable in basic environments and will survive a

wide range of conditions and reagents, including metal hydrides, catalytic hydrogenations and alkali metals in liquid ammonia.

There are three types of acetals (**Fig. 33**); *O,O* acetals (including cyclic and acyclic), *S,S* acetals and *O,S* acetals.

Figure 33

1,2-Glycols and 1,3-glycols are used to convert aldehydes into their cyclic acetals, 1,3-dioxolanes and 1,3-dioxanes respectively (**Fig. 34**). Acyclic dimethyl and diethyl acetals are produced using 2,2-dimethoxypropane, or 2,2-diethoxypropane. The reactions of protection and deprotection are reversible and are acid catalysed.[51]

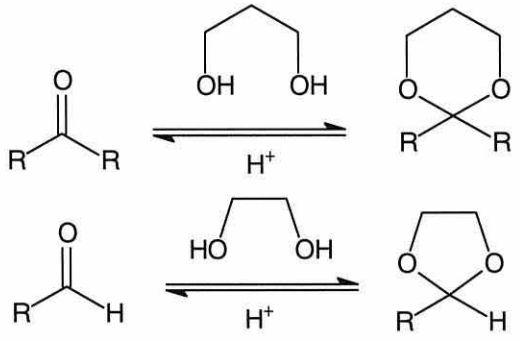


Figure 34

Acetals of aldehydes are more readily prepared than ketones. The ring size of the acetal has an effect on the rate of protection / deprotection. 1,3-Dioxolanes formed from aldehydes hydrolyse faster than 1,3-dioxanes, and *vise versa* for ketones. For both aldehydes and ketones, cyclic acetal rates of formation are generally preferential to the equivalent acyclic acetal.

During the formation of the acetal, a molar equivalent of water is produced, which must be removed to prevent the reaction reversing. The removal of water from the reaction is achieved azeotropically using either toluene or benzene as solvent. Alternatively drying agents have been used to shift the equilibrium of the reaction to the acetal. The reaction is acid catalysed, usually by pyridinium *p*-toluene sulphonate.[52] The acetal can be easily hydrolysed to the aldehyde in aqueous acid conditions.

The developments of carbonyl protection have sought to find alternative methods of acetal cleavage using milder reagents and conditions and to give a more efficient hydrolysis. Some recent papers have suggested copper chloride $CuCl_2.2H_2O$ in MeCN at room temperature,[53] lithium chloride in water/DMSO with heat[54] or ferric chloride hexahydrate.[55] There have also been developments in the use of more environmentally friendly heterogeneous catalysts, which can be easily recycled: montmorilonite K10[56] - an acid clay, and zeolite HSZ-360.[57] Both produce high yields, give an easy recovery of the catalyst by filtration and are easy to recycle. Conveniently both of these catalysts have been proved to also catalyse the acylation of alcohols which is also an important reaction for pheromone synthesis.

New types of carbonyl protecting groups have been developed using modified diols to give a smoother protection and alternative methods of deprotection. Such examples are bromomethyl ethylene acetals,[58] 4-pentenyl acetals,[59] and acetals of 3-phenylsulfonyl 1,2-propane diol (**Fig. 35**).

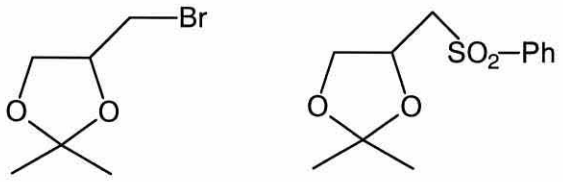


Figure 35

2.5.3 Alcohols

Alcohols are converted into acetals for protection. The cheapest and easiest hydroxyl-protecting group is the tetrahydropyranyl ether (THP). Adding dihydropyran (DHP) to the alcohol in dry conditions with an organic catalyst such *p*-toluenesulphonic acid produces the THP ether.[60]

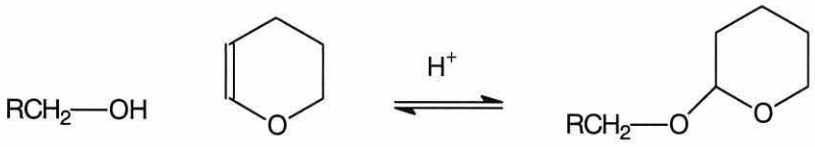


Figure 36

The THP ether is unreactive to nucleophilic attack, hydride reducing agents, organometallic reactions and oxidations. The THP ether is removed in acid conditions.

Another example of an alcohol-protecting group is the methoxymethyl ether (MOM). MOM ethers are formed easily using methoxymethyl chloride. Unfortunately this reactant is a potent carcinogen, and therefore must be handled with great care. An alternative is to use $MeOCH_2OMe$, which gives a slightly lower yield but avoids the methoxymethyl chloride. The MOM ethers are easily deprotected under acidic conditions.

2.6 The Coupling of Acetylenes

The acetylene functionality must be integrated into a pheromone molecule at the correct position. The use of a range of terminal acetylenes is necessary for coupling with organo bromides to give the correct structure.

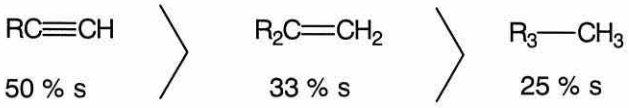


Figure 37

The terminal alkyne is acidic due to its carbon *sp*-hybridization (**Fig. 37**). The more *s* character a carbon has, the more acidic the protons attached to it are. The carbanion of the terminal alkyne is therefore most stable with the highest *s* character as the electrons are held tightest around the nucleus at a lower energy level as the *s* orbital has lower a energy than the *p* orbitals. The 1-alkyne proton has an acidity of pK_a 25 compared with: alkanes pK_a 50, alkenes pK_a 45, amines pK_a 35, alcohols pK_a 15, and carboxylic acids pK_a 5.[61]

Although more acidic than alkenes or alkanes, alkynes are not good acids. The low acidity of the 1-alkyne means that a strong base is required to form the ionic species. The solvent system that is required for coupling reactions of this type must have a lower acidity than the 1-alkyne anion, thus allowing the ion to remain solvated. The following solvents may be used: liquid ammonia, tetrahydrofuran, ether and hydrocarbons. When an anion is formed it will readily undergo alkylation. Metallation of a 1-alkyne can be achieved using liquid ammonia and either lithium or sodium to produce lithium or sodium amide.

In pheromone chemistry the most popular method is to use lithium amide in liquid ammonia. Ammonia gas (boiling point -33 ^{o}C) must be condensed in the reaction vessel before the lithium is added. The solvated lithium in the ammonia forms a solvated electron. This electron produces the deep blue colour seen in the flask. Ferric nitrate is added in a catalytic amount to remove a proton from the ammonia forming lithium amide. Lithium amide strips away the terminal proton from the *sp* carbon. The anion is now ready to attack.

The problem with liquid ammonia is the handling. It must be kept condensed throughout the reaction (which is exothermic). There are few commercial liquid ammonia reactors used in industry.

Butyllithium is an alternative base which may be used in conjunction an aprotic solvent. Hexamethylphosphorous triamide (HMPA) is used as a co-solvent which helps co-ordinate the anion making it more reactive. However HMPA is a potent carcinogen, toxic at very low levels.

CHAPTER 3

3.1 Synthesis of Mono-unsaturated aldehyde pheromones.

3.1.1 Introduction

There have been fourteen mono-unsaturated aldehyde pheromones discovered over the past 30 years. Of these there are some specific pheromones that are of great interest for commercial use. These include for example - (Z)-7-tetradecenal, (Z)-9-tetradecenal and (Z)-11-hexadecenal. A general procedure that will allow the synthesis of these and possibly all the other mono-unsaturated pheromones was the primary objective of this project.

When developing a commercially viable method there are many factors that must be taken into consideration. Is there a market that can be exploited and is the product in demand? Hopefully the answer to this question is yes, and has been explored in the introduction.

A list of considerations has been drawn up below that will have to be taken into account at some stage in the development of a successful process.

- The cost and availability of raw materials,
- The need for specialised equipment,
- The duration of reactions,
- The cost of heating/cooling during reaction,
- The feasibility of the reaction on a large scale,
- The purification procedures,
- The disposal of waste materials,
- Labour and premises.

The work leading to the synthesis of the full range of aldehyde pheromones centres around the use of catalytic hydrogenation for the synthesis of the aldehyde functionality. Hydrogenation reactors are in general use by all major chemical companies. The palladium catalyst used is easily recoverable by filtration and therefore can be recycled for repeated use.

3.1.2 Saturated Aldehydes

The first pheromones to be synthesised by catalytic reduction were the four saturated aldehydes – dodecanal (**45**), tetradecanal (**46**), hexadecanal (**47**) and octadecanal (**48**). Starting from the precursor carboxylic acids, they were first converted into the acid chloride. The cheapest and easiest method by which to do this FGI was to use thionyl chloride – which is an inexpensive liquid, that may be distilled off easily at low temperature and the excess recycled. The reaction itself was carried out at room temperature and was followed by GLC with yields high at approximately 90 %.

The acid chloride products were distilled pure under vacuum, in each case giving a colourless liquid. It was found that this was an important purification step as the following reduction would not occur if the reactant acid chloride was impure. When pure however, the reduction reaction proceeded quickly at room temperature and gave the desired aldehyde products in good yields. It is important to have a good vacuum (0.01 mm Hg) as there was some difficulty in distilling the longer chained pheromones (> 14 carbons), because they would begin to decompose when exposed to temperatures above 180 °C.

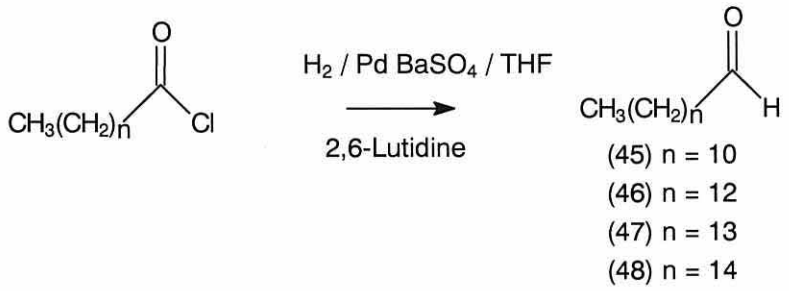


Figure 38

5% Palladium on barium sulphate in THF was put under a hydrogen atmosphere and stirred until the catalyst turned black. The longer the catalyst was left to adsorb the hydrogen, the sooner the hydrogen uptake began on the introduction of the reactant. An equivalent of 2,6-lutidine was added to the reaction vessel, followed after 10 minutes, by the acid chloride. The hydrogen uptake could be seen to begin almost immediately. The 2,4-lutidine absorbed the HCl by-product and, when hydrogen uptake had ceased, the contents of the vessel were filtered through silica to remove the catalyst. The 2,6-lutidine salt could be removed either by distillation of the product or by washing with water. The ^{1}H NMR spectrum of the aldehydes each showed a doublet of triplets at δ 2.4 with coupling constant of 7.2 and 1.8 Hz, and a triplet at δ 9.7 with a coupling constant of 1.8 Hz. The ^{13}C NMR spectrum gave the carbonyl carbon at δ 202. The infrared spectrum showed the shift of the carbonyl peak from 1800 cm^{-1} to 1720 cm^{-1} as expected for the conversion of the acid chloride into the aldehyde.

The success in producing the four fatty aldehydes in high yields proved that the reactions could run cleanly and efficiently. These test reactions also showed that the acid chloride reactant must be carefully distilled before any attempt was made to reduce it to the aldehyde.

3.2 Mono-unsaturated Aldehydes

3.2.1 Introduction

The synthesis of monounsaturated aldehydes began with the hypothesis that *cis*-alkenal aldehydes could be synthesised using only one reductive step, i.e. the reduction of the acetylene and the acid chloride on the same molecule in one catalytic reaction (**Fig. 39**).

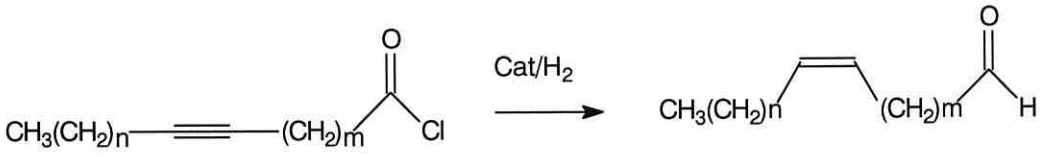


Figure 39

In order to attempt this reaction, first the acetylenic acid must be synthesised. The most obvious way to produce an acetylenic acid would be to couple a terminal alkyne with a bromo acid. This was attempted by Ames in the 1960's to synthesise fatty acids; however, using a ratio of 3 equivalents of the bromoacid to 1 equivalent of the alkyne, and refluxing for 8 hrs gave poor yields of between 25 and 42 % (**Fig. 40**).[62] Increasing the ratio to ten equivalents of the bromoacid gave better yields; however this is a very wasteful procedure, so further research was need to give a more viable method of producing alkynoic acids.

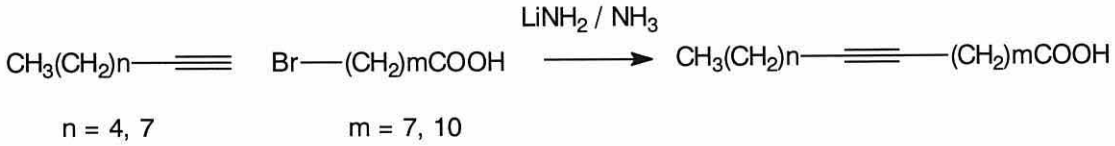


Figure 40

Oxidation of alcohols to the carboxylic acids using potassium permanganate ($KMnO_4$) is a simple procedure that can be carried out cleanly. However the $KMnO_4$ would also oxidise the acetylene, first to a di-ketone then to form two carboxylic acids (**Fig 41**).[124]

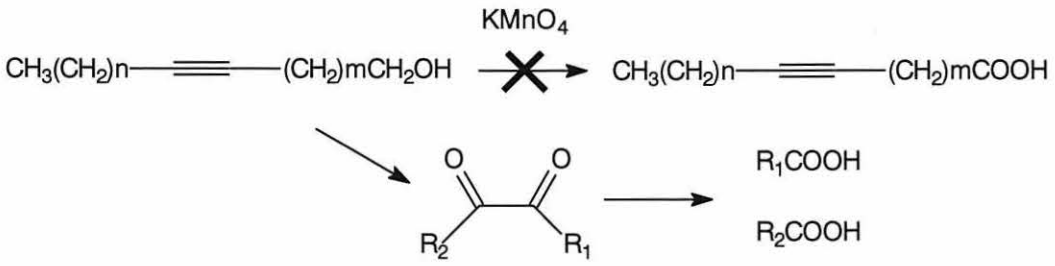


Figure 41

An alternative method that introduces a carboxylic acid is to couple an alkynyl bromide with diethyl malonate, then to deesterify and decarboxylate to give the monoacid. It was this procedure that was initially adopted. This method also chain extended the alkynyl bromide by two carbons, so it follows that the alkynyl bromide must be made 2 carbons shorter on the bromide side of the molecule to ensure that the final product gave the correct chain length.

3.2.2 (Z)-11-Tetradecenal

The synthesis of the first target molecule (Z)-11-tetradecenal is outlined in **figure 42** and **43**.

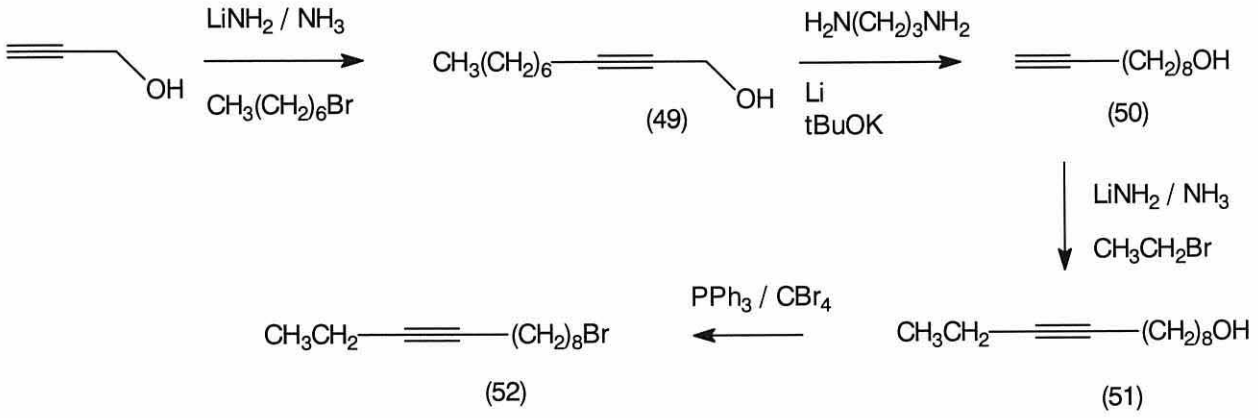


Figure 42

The first step coupled propargyl alcohol to bromoheptane. Lithium amide was used as base and the reaction was carried out at -33 °C, the boiling point of amm
onia, using a mixture of liquid nitrogen and methylated spirits as coolant. 2.2 Molecular equivalents of lithium amide were used to remove the proton from the alcohol and the terminal acetylenic proton of propargyl alcohol. The di-anion was reacted with the alkyl bromide. The acetylene anion reacted in preference to the hydroxyl anion due to the difference in the reactivity and the frontier orbital energy. This gave the product, dec-2-yn-1-ol, (**49**) in a yield of 57 %. The ^{13}C NMR spectrum showed the expected signals with the acetylenic group at δ 78.2 and δ 86.5. The ^{1}H NMR spectrum showed the terminal methyl group at δ 0.89 as a triplet with coupling constant (J 6.8 Hz) and the methylene protons adjacent to the alcohol at δ 4.26 with long range coupling to the methylene group on the other side of the acetylene (J 2.0 Hz). The infrared spectrum gave the expected acetylene peak at a frequency of 2225 cm^{-1}, and a broad OH band at 3332 cm^{-1}.

The acetylene group of dec-2-yn-1-ol was intermolecularly repositioned to the terminal carbon of the alkyl chain, giving dec-9-yn-1-ol (**50**). Known as the "zipper isomerisation", it utilises a mixture of three different bases to shift the triple bond along the hydrocarbon chain.

Lithium is added to 1,3-diaminopropane, it deprotonates the amine groups and forms di-lithio anionic species. Potassium *t*-butoxide is added when all the lithium has reacted with 1,3-diaminopropane. The ^{1}H NMR spectrum of the product showed that the terminal methyl group had been removed. A triplet resonance for the terminal acetylene proton with long range coupling across the acetylene (J 2.7 Hz) appeared at δ 1.93. This established that the acetylene had shifted to the terminal position. The methylene group beside the alcohol appeared as a triplet (J 6.6 Hz) at δ 3.6. The ^{13}C NMR spectrum showed 10 carbons with the two acetylenic carbons at δ 68.1 and δ 84.7.

The isomerisation of the triple bond to the terminal position allowed a second coupling to be achieved, which put the acetylene in the correct position for hydrogenation. The liquid ammonia reaction was repeated and the dianion of dec-9-yn-1-ol was alkylated with bromoethane to give 10-dodecyn-1-ol (**51**) in 72 % yield. The ^{1}H NMR spectrum showed the terminal methyl protons as a triplet at δ 1.13. The terminal *sp* proton at δ 1.93 had been removed. The ^{13}C NMR spectrum showed 12 carbons with the acetylene carbons at δ 79.42 and δ 81.50.

Bromination of the primary alcohol was achieved using carbon tetrabromide and triphenylphosphine. This gave 1-bromododec-9-yne (**52**), in 80 % yield. The ^{1}H NMR spectrum showed a shift of the methylene group adjacent to the alcohol slightly up-field of the hydroxyl-methylene absorbance of (**51**), from δ 3.65 to δ 3.48. The IR spectrum showed no broad alcohol peak at 3361 cm^{-1}.

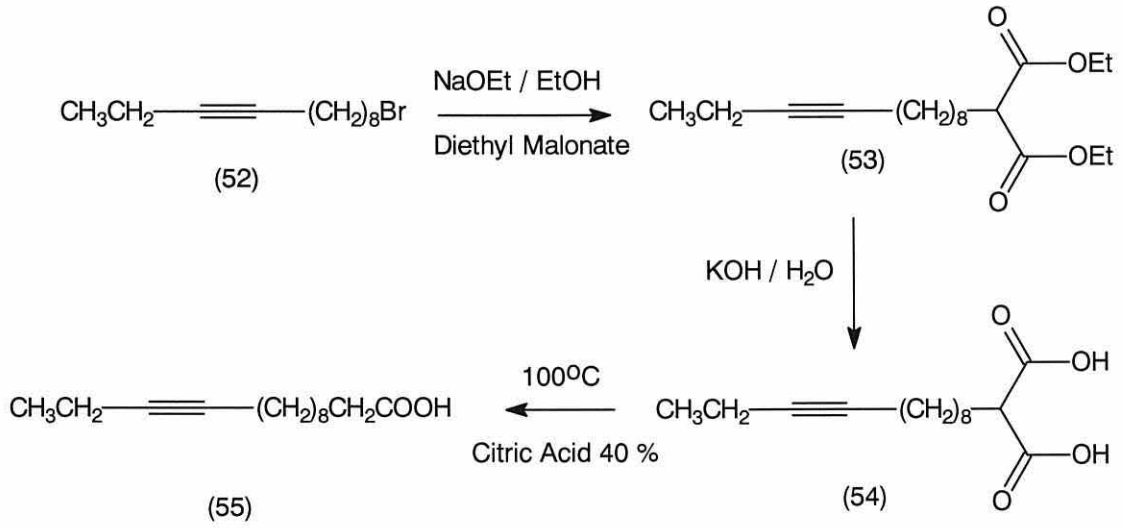


Figure 43

Diethyl malonate was coupled to 1-bromododec-9-yne (**52**). Sodium ethoxide was generated by refluxing sodium in ethanol. The base removed the proton from diethyl malonate from the central carbon between the two carbonyls, where the anion was stabilised by resonance. The anion nucleophilically attacked the methylene next to the bromine of (**52**), to give the diethyl 11-tridecyn-1,1-dioate(**53**). The ^{1}H NMR spectrum of this showed the proton adjacent to the carbonyl as a triplet (J 7.2 Hz) at δ 3.31. The ethyl ester produced a four proton integration (J 7.5 Hz) at δ 4.19 and a six proton integration (J 7.5 Hz) at δ 1.27. The IR spectrum showed the two carbonyl peaks at 1731 cm^{-1} and 1736 cm^{-1}.

The di-ester was hydrolysed by refluxing gently for three hours with aqueous potassium hydroxide. This produced the di-acid, 11-tridecyn-1,1-dioic acid (**54**). The ^{1}H NMR spectrum gave a broad OH peak at δ 9 and the ethyl ester peaks had disappeared from the spectrum. The mono-acid (**55**) was produced by the decarboxylation of the di-acid. This was achieved by the use of aqueous citric acid (25 %) at 100 °C for 12 hrs. The ^{1}H NMR spectrum of the product showed that the single proton at δ 3.43 in (**54**) had been removed.

The mono acid (**55**) was converted into the acid chloride (**58**) by refluxing with thionyl chloride for 30 mins. This gave the product (**58**) in 71 % yield. The ^{1}H NMR of this showed a shift in the position of the signal for the methylene adjacent to the carbonyl from δ 2.35 to δ 2.8 triplet (J 7.2 Hz). The IR spectrum gave the carbonyl of the acid chloride at 1799 cm^{-1} and the broad hydroxyl peak had disappeared. The ^{13}C NMR had the expected number of carbons, with the carbonyl peak at δ 173.8.

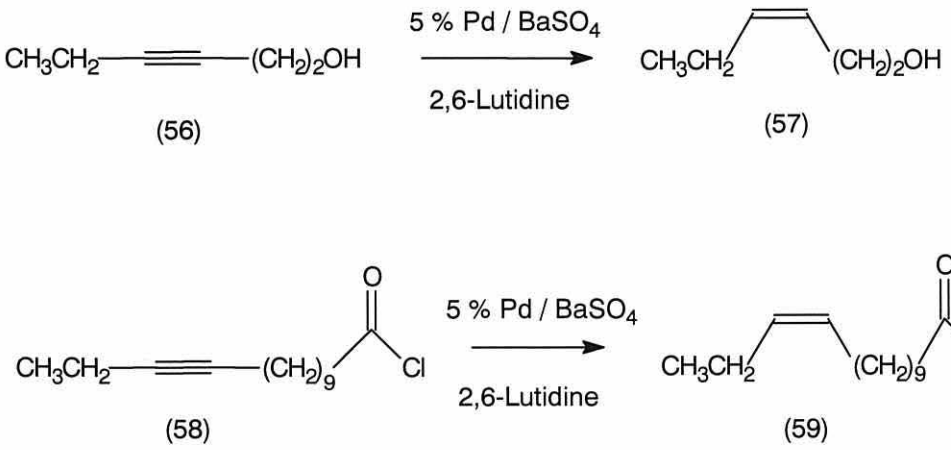


Figure 44

The final step in the synthesis was the dual reduction of tetradec-11-yn-1-oyl chloride (**58**). Before proceeding with the actual molecule, a test reaction was performed to see if the reaction conditions were suitable to reduce the acetylene functional groups. Hex-3-yn-1-ol (**56**) was used as a test material to prove the effectiveness of the reaction. The acetylene was reduced of a *cis*-alkene. Hex-3-yn-1-ol was reduced under the same conditions as the acid chloride. The reaction used palladium on barium sulphate substrate as catalyst, in dry THF and 2,6-lutidine. Hydrogen absorbed quickly until one molar equivalent was absorbed. When hydrogen uptake ceased the product, (Z)-3-hexen-1-ol (**57**), was to obtained in a good yield (98 %).

Tetradec-11-yn-1-oyl chloride (**58**) was then reacted under the same conditions. The reaction proved successful and the target molecule (Z)-11-tetradecenal was synthesised, although in low yield (30 %). However starting material was recovered and therefore could be recycled. The ^{1}H NMR spectrum data of (**59**) showed the aldehyde proton as a triplet (J 1.87 Hz) at δ 9.76. The methylene adjacent to the carbonyl showed a double triplet (J 1.8 and 7.2 Hz) at δ 2.41. The alkene protons appeared as a complex doublet of triplets (J 5.7, 3.1 Hz) at δ 5.33. The ^{13}C NMR spectrum showed the aldehyde at δ 202.9 and the alkene carbons at δ 129.2 and δ 131.5.

The above sequence established that the pheromone- (Z)-11-tetradecenal (**59**) could be produced in nine steps using a double reduction of the acid chloride in the final step. The overall yield was approximately 12-15 %.

The final step gave an unexpectedly very low yield. There could be a possibility that the reaction is affecting the active surface of the palladium leading to this low yield. During a reaction the active palladium becomes slowly deactivated through time As there are two different reactions occurring using the same palladium then the deactivation may be faster than the time taken to complete the dual reduction.

The organic base, 2,6-lutidine, is present to absorb the free HCl that is produced from the acid chloride reduction. Given time, this would regulate the palladium's catalytic activity. During the reaction the catalyst is being asked to do twice the workload, firstly, catalysing the alkyne hydrogenation and secondly catalysing the acid chloride reduction. Normally when the acid chloride is reduced it reacts quickly from the beginning and would not allow the lutidine to completely bind to the catalyst surface. The alkyne and the acid chloride are in competition for the same catalytic surface; this would necessarily effect the reaction time, slowing it down. There is now an extended period of time which would allow the 2,6-lutidine to act as a regulator and effect the activity of the palladium, eventually stopping the reaction before completion and therefore reducing the yield as there is no more active surface available.

The alkynyl acid chloride had to be carefully distilled pure, but the product easily decomposed at high temperatures during distillation. This meant that the acid chloride was being distilled out of the steadily decomposing residue. This could cause small amounts of impurities to be carried over with the distillate and directly effect the reaction.

3.2.3 (Z)-9-Tetradecenal

The next pheromone to be synthesised was (Z)-9-tetradecenal. The synthetic route was altered to avoid the use of the zipper isomerisation and the second acetylene coupling reaction. These reactions were replaced by more straightforward synthesis that would be easier to develop on a larger scale.

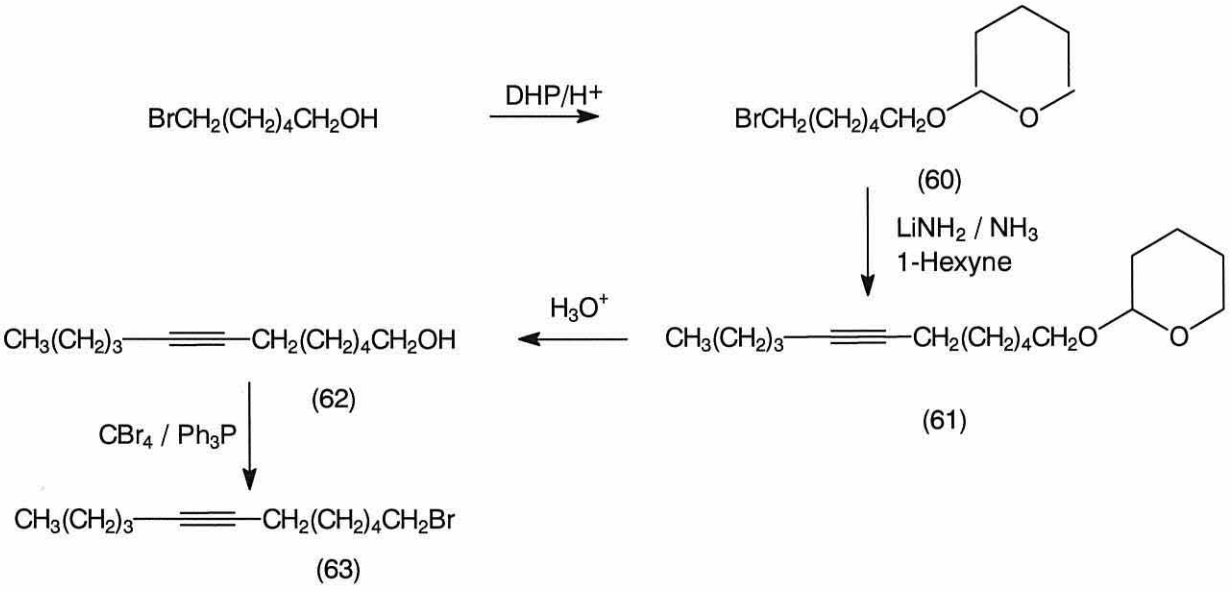


Figure 45

The starting material for this synthesis was hexanediol. Hexanediol was monobrominated with aqueous hydrogen bromide (48 %) by continuous extraction using toluene. The product bromohexanol was protected as its tetrahydropyran ether (**60**) in 98 % yield. The ^{1}H NMR spectrum showed that the methylene alcohol at δ 3.63 was replaced by a complex multiplet at δ 3.51. The multiplet was caused by the chiral proton between the two oxygens. The chiral proton effects the two protons of the methylene adjacent to the oxygen, making them magnetically inequivalent. The IR spectrum shows that the broad absorbance of the alcohol had disappeared.

The ether was coupled to 1-hexyne using lithium amide in liquid ammonia to deprotonate the acetylenic carbon. This gave the product 2-(dodec-7-ynyloxy)tetrahydropyran (**61**) in 79 % yield. The tetrahydropranyl ether was deprotected under acid conditions using pyridinium *p*-toluene sulphonic acid at ambient temperature for 18 hours. The ^{1}H NMR spectrum revealed the triplet at δ 3.65, which is methylene of the alcohol. The IR spectrum contained a broad absorbance at 3361 cm^{-1}.

The alcohol was converted to the bromide (**63**) by reacting carbon tetrabromide and triphenylphosphine in 70 % yield. The ^{1}H NMR of (**63**) showed that the methylene of the alcohol at δ 3.65 had shifted to δ 3.43.

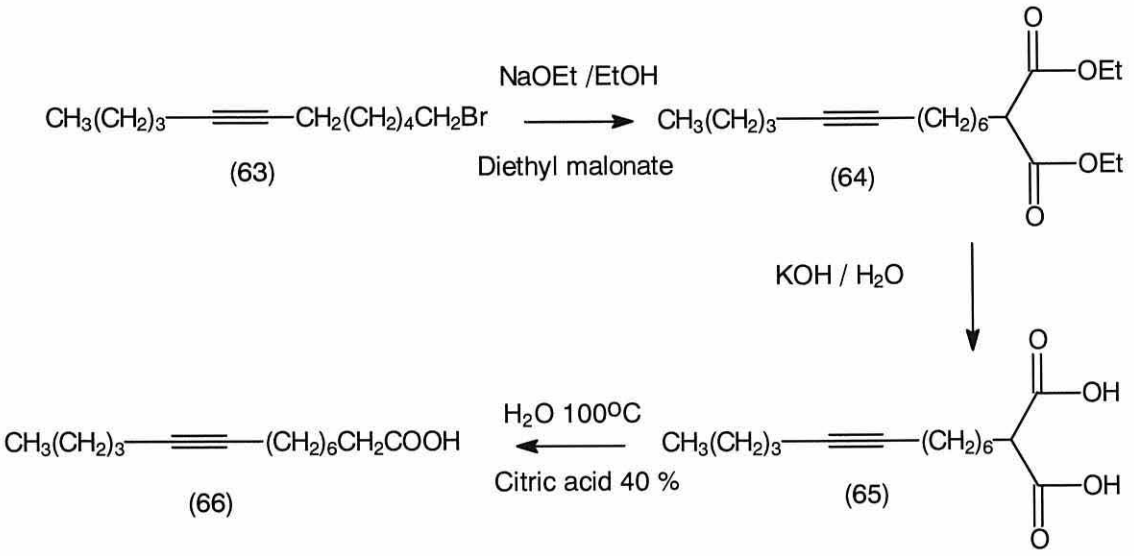


Figure 46

Diethyl malonate was coupled to 1-bromododec-7-yne (**63**) to give The diester product (**64**) in 62 % yield. The ^{1}H NMR showed that the tertiary proton between the two carbonyls at δ 3.31 (J 7.5 Hz). The diester was first hydrolysed with potassium hydroxide, then refluxed in acidic conditions. This caused the decarboxylation of the diacid to give tetradec-9-ynoic acid (**66**) in 73 % yield.

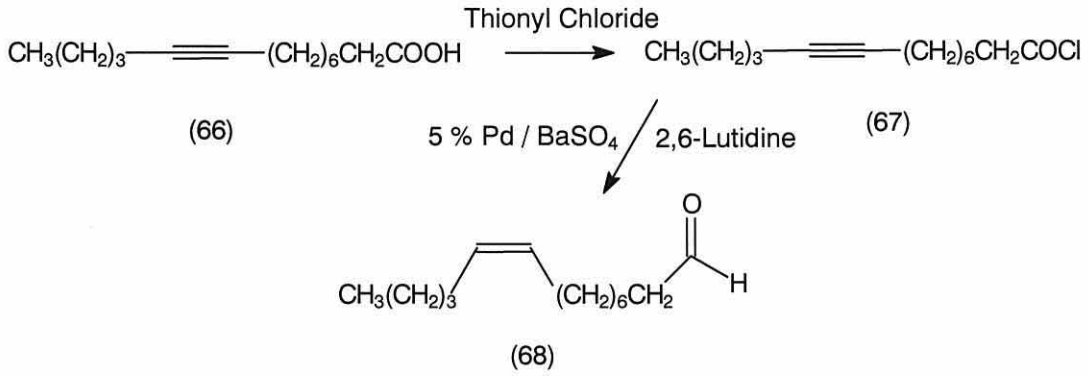


Figure 47

Tetradec-9-ynoic acid (**66**) was dissolved in thionyl chloride and refluxed for 30 minutes. This gave a brown product which had to be distilled pure. This produced the acid chloride (**67**) in a yield of 55 %. The pure acid chloride was hydrogenated using palladium on barium sulphate as catalyst. The reaction converted the acid chloride to the aldehyde and the alkyne was reduced to the alkene in one reaction step of 68 % yield.

3.2.4 (Z)-9-Octadecenal

The reduction was repeated again from the commercially available stearolic acid. The acid was dissolved in thionyl chloride and stirred at room temperature for 1 hr. The crude product was very carefully distilled pure to give octadec-9-ynoyl chloride (**69**) in 98 % yield. The acid chloride was then reduced under a hydrogen atmosphere using palladium on barium sulphate to give the double reduced product (**70**) in 4 hours. The reaction mixture was filtered through silica and the product was isolated in 89 % yield.

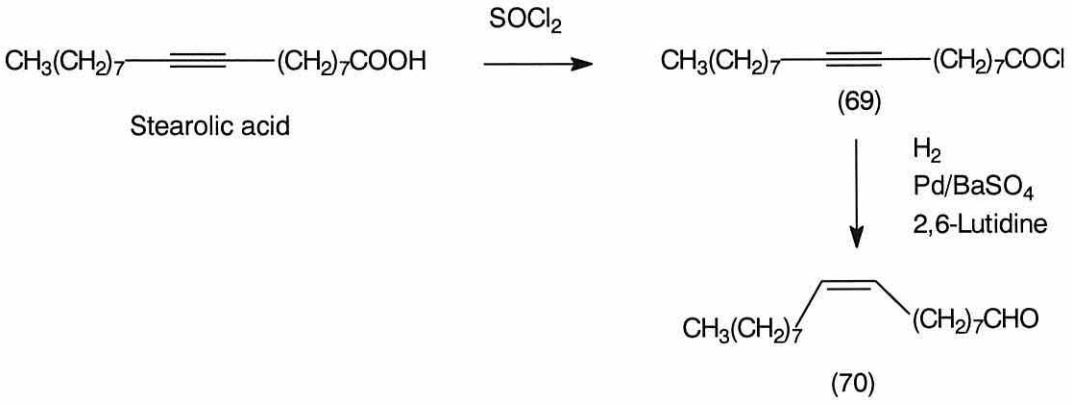


Figure 48

3.2.5 (Z)-5-Alkenals

Having achieved the synthesis of an example of a (Z)-9 and a (Z)-11 aldehyde, the same procedure was used to produce the shorter chained pheromones. with the alkene at the (Z)-5 and (Z)-7 position. Using 3-butyn-1-ol, the terminal alkyne was coupled to 1-bromobutane to give oct-3-yn-1-ol (**71**). The alcohol was brominated with carbon tetrabromide and triphenylphosphine to give (**72**). The coupling of diethyl malonate with the bromide to gave (**73**) in a very poor yield of 3 %. The triple bond situated close to the bromide, seemed to effect the nucleophilic attack of the malonate, therefore reducing the reaction yield.

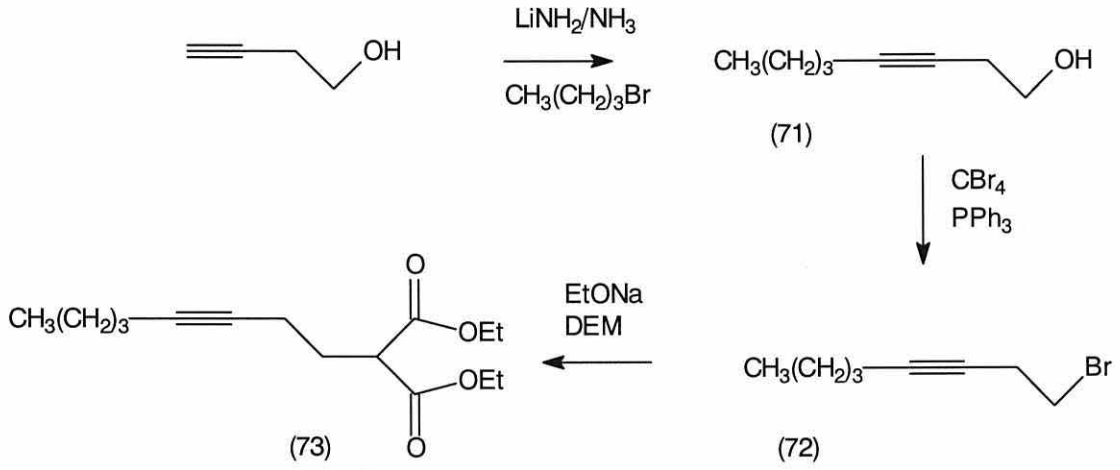


Figure 49

The development for the synthesis of (Z)-5 alkenal pheromones by a double hydrogenation method was halted due to the low yield of the diethyl malonate coupling reaction. A new pathway was devised for these short chained pheromones which adopted the method for catalytic hydrogenation of acid chlorides in a new synthesis. This new development is discussed in **Section 3.3**.

3.2.6 Order of Reactivity in the "Double Reduction"

The order of the reactivity of the dual reduction was explored to find out how the two individual reactions proceeded.

An alkynoyl chloride was reduction using the catalytic hydrogenation procedure. When one molar equivalent of hydrogen had been absorbed, a sample was taken from the reaction vessel. The sample was analysed by GC. It showed one peak with the same retention time as the starting material. Hydrogen uptake stopped when 1.8 molar equivalents was absorbed. A second sample was taken and analysed. It showed one peak and the retention time had shifted. This would be the aldehyde product (**76**).

I believe that during the first half of the reaction the alkyne is reduced to the alkene, hence no discernible shift in retention time. After the alkyne has reacted, the acid chloride begins to react absorbing the second equivalent of hydrogen. The shift in the GC is due to difference in retention time between the acid chloride and the aldehyde.

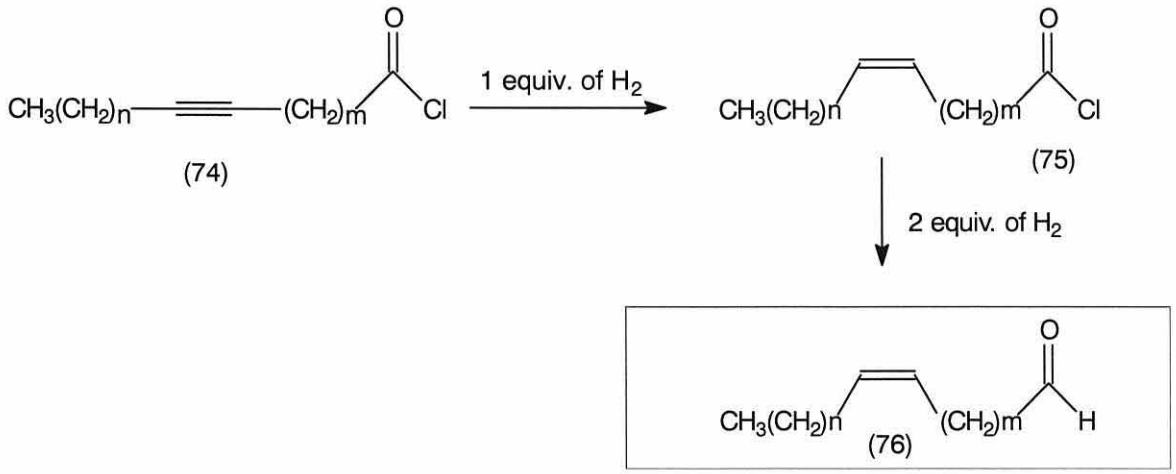


Figure 50

Therefore the reaction is a two-step process. Firstly, the alkyne is reduced to the alkene, then the acid chloride is reduced to the aldehyde. The absorption of hydrogen slows after the formation of the aldehyde, but, the over-reduction of the alkene will occur if the reaction is left too long (**Fig. 51**). It was essential to monitor the reaction and stop it after two equivalents of hydrogen had been absorbed.

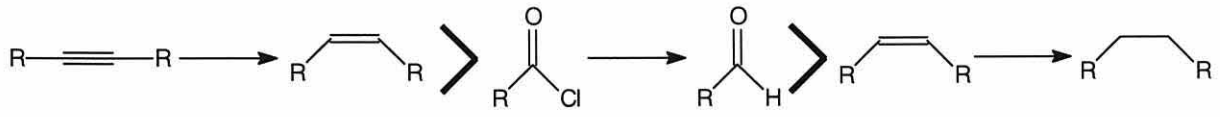


Figure 51

3.2.7 Conclusion

The synthesis of mono-unsaturated aldehyde pheromones was successfully made by a double reduction method. Though there are some difficulties in the development of the procedure that will synthesise a wide range of pheromones by this method.

The overall yield of (Z)-11-tetradecenal (**59**) is 3 %, compared with an 11 % yield for (Z)-9-tetradecenal (**70**). The alteration in the synthesis of the alkynol from the diol is more efficient than from propargyl alcohol.

The decarboxylation of the diacids were difficult to achieve on the long chain compounds. Decomposition would occur on heating in concentrated acid conditions. Citric acid was used as an alternative to reduce this decomposition. The diacid would leave a residual triplet at δ 3.43 in the ^{1}H NMR spectrum, the reaction therefore required longer reflux times to remove any starting material.

The reaction of the carboxylic acid with thionyl chloride also gave thermal decomposition. When all the thionyl chloride had been removed by distillation a black residue would remain. From this residue which the product had to be distilled. The distillation proved quite difficult due to the high molecular weights of the acid chloride compound. Even using the best

vacuum system available the distillation still required very high temperatures (>200 °C). The distillation of the long chain acid chlorides could perhaps be achieved by use of thin film evaporators, which are used on an industrial scale. However, on a laboratory scale their distillation was not possible without decomposition occurring. The acid chloride had to be of a high purity for the catalytic hydrogenation to proceed.

The procedure was not useful for the short chain aldehydes due to the problems encountered when introducing the diester functionality. The coupling of diethyl malonate with 1-bromo oct-3-yne would not give the desired product in a good enough yield to continue this method for the synthesis of short chained aldehyde pheromones.

An alternative method was the devised for the short chained Z-5 and Z-7 aldehydes. The new pathway would keep the original idea of catalytic hydrogenation but without using the double reduction methodology which was first thought of.

3.3 Mono-unsaturated aldehydes from simple lactones

A second procedure was developed to synthesise the mono-unsaturated aldehydes which was also achieved by reductive means. The main problems that came to light from the dual reduction synthesis were, the incorporation of the acid functionality, the high boiling point of the acid chloride effected both the purity of the product the progress of the reduction reaction. Introducing the acid at the beginning of the synthesis, and producing the aldehyde while the chain length was short where the aims.

The use of lactones as starting materials was thought to provide the answer to the synthesis for (Z)-5 and (Z)-7 alkenyl aldehyde pheromones. The aim was the synthesis of aldehyde intermediates, from which the full range of pheromones of different chain lengths could be produced. The first objective was to synthesis a series bromoaldehydes by reductive hydrogenation without reducing or affecting the bromide. When the aldehyde was produced it would be protected before continuing the synthesis.

The bromoacetal would be alkylated by the correct 1-alkynes, and the alkyne partially hydrogenated to give the (Z)- olefinic protected aldehyde. The protected pheromone could then be stored indefinitely, without any decomposition or oxidation occurring through time. The aldehyde could be easily deprotected when needed.

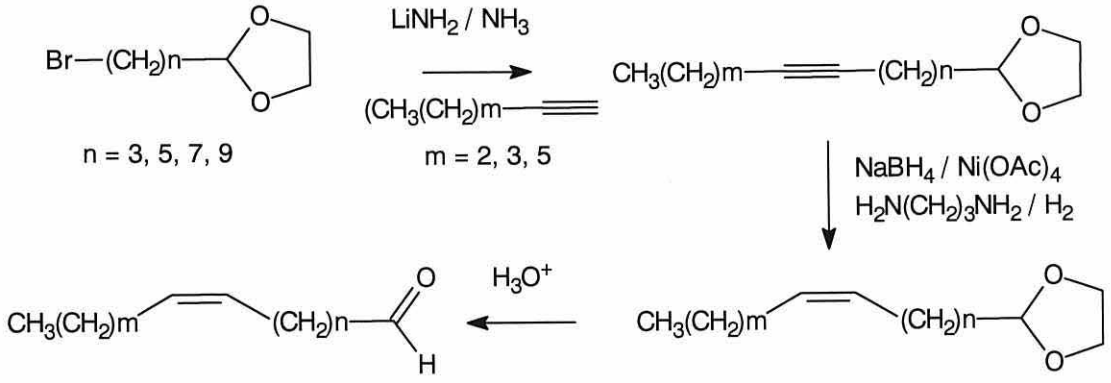


Figure 52

3.3.1 (Z)-5 and (Z)-7 Alkenals

γ-Butyrolactone and ε-caprolactone were the starting materials for six pheromones - (Z)-5-decenal (**77**), (Z)-5-dodecenal (**78**), (Z)-5-tetradecenal (**79**), (Z)-7-dodecenal (**80**), (Z)-7-tetradecenal (**81**) and (Z)-7-hexadecenal (**82**).

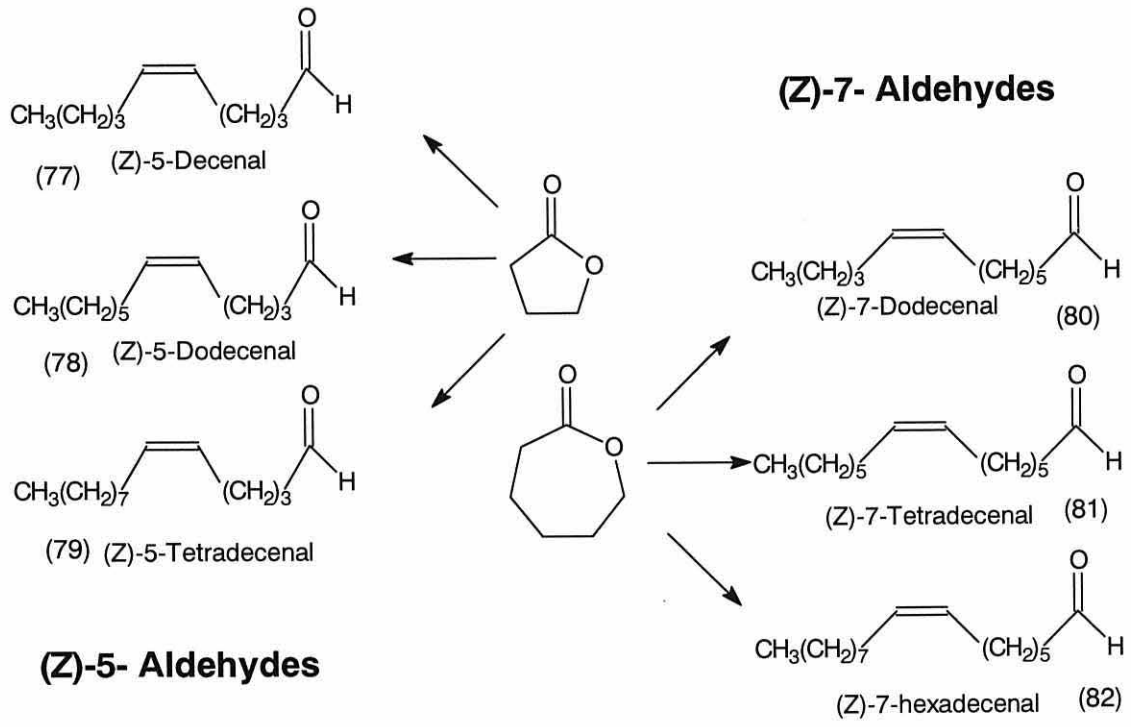


Figure 53

The lactones are very inexpensive, readily available and when ring opened, gave the required carboxylic acid functionality. The ring opening of γ-butyrolactone was achieved by reacting the lactone with 48 % hydrobromic acid and 98 % sulphuric acid for 1 hour at room temperature and a further 4 hours under reflux. The literature recommendations of 4 hrs reflux proved to be too long gave yields of approx. 50 % of 4-bromobutyric acid. The yield was increased to between 60 and 90 % by reduction of the reaction time. 4-Bromobutyric acid was easily extracted and distilled pure to give a white solid. The proton NMR spectrum showed that the methylene group beside the oxygen had shifted from δ 4.35 to δ 3.49, and the carbon NMR also corroborated the shift, showing that the carbon α- to oxygen had shifted from δ 68 to δ 32 for a carbon attached to the bromide, and the acid carbonyl δ 178.9. The infrared

spectrum was distinctive, the carboxylic acid, showing a deep broad OH peak at 3200 cm^{-1} and the carbonyl at 1712 cm^{-1}.

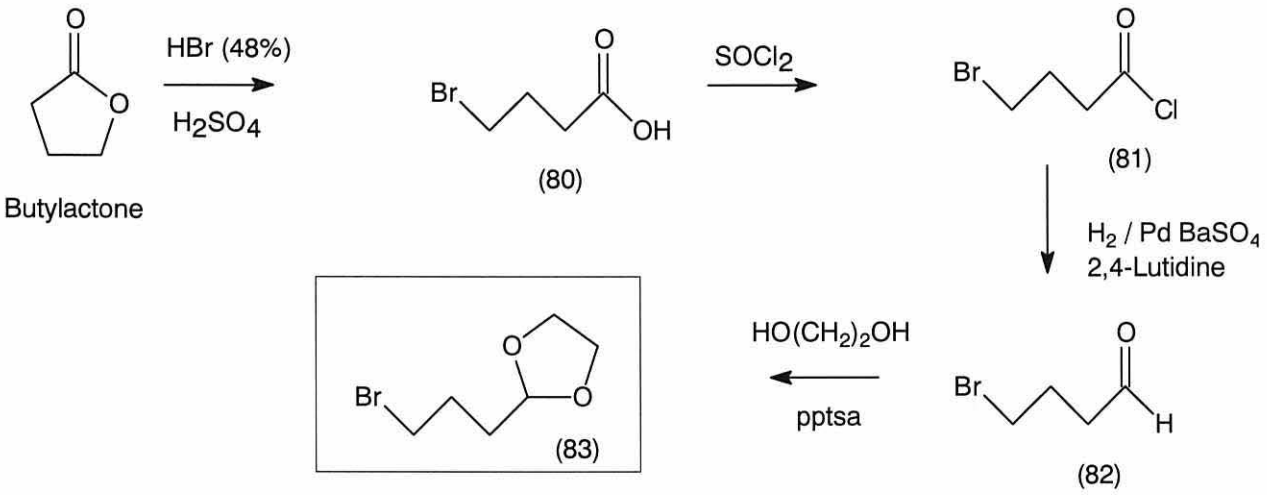


Figure 54

4-Bromobutyric was converted into the acid chloride (**81**) by gently refluxing the acid in thionyl chloride for 1 hr. The excess thionyl chloride was distilled off leaving the crude product in high yield of 90 %. 4-Bromobutyryl chloride was distilled pure giving a clear liquid. The proton NMR spectrum showed the methylene group adjacent to the carboxylic acid shift from a triplet at δ 2.58 to a triplet at δ 3.13. The carbon NMR spectrum showed the carbonyl of the acid chloride at δ 173.1, and in the infra red spectrum, the carbonyl appeared at 1794 cm^{-1}.

4-Bromobutyryl chloride (**81**) was reduced under a hydrogen atmosphere, using 5 % palladium on barium sulphate in THF, and 2,6-lutidine. The acid chloride reacted quickly at first, and the reaction slowed down as it neared completion. After 2 to 3 hours, hydrogen uptake ceased. The aldehyde (**82**) was isolated in 95 % yield and GLC gave a single peak. The infrared gave the carbonyl absorption at 1725 cm^{-1}. The proton NMR spectrum gave the aldehyde proton as a triplet (J 1.0 Hz) at δ 9.76, and the adjacent methylene as a doublet triplet (J 7.0, 1.0 Hz) at δ 2.63. In the carbon NMR spectrum, the aldehyde carbon appeared at δ 200.8.

The aldehyde was protected with 1,2-ethanediol, to give the dioxolane (**83**) (59 %). The peaks of the aldehyde had disappeared from the proton NMR spectrum. The tertiary proton gave a triplet (J 4.4 Hz) at δ 4.87 and the four protons of the dioxolane ring appeared as a multiplet at δ 3.88. The carbon NMR spectrum showed the carbons in the ring at δ 64.9 and δ 103.6.

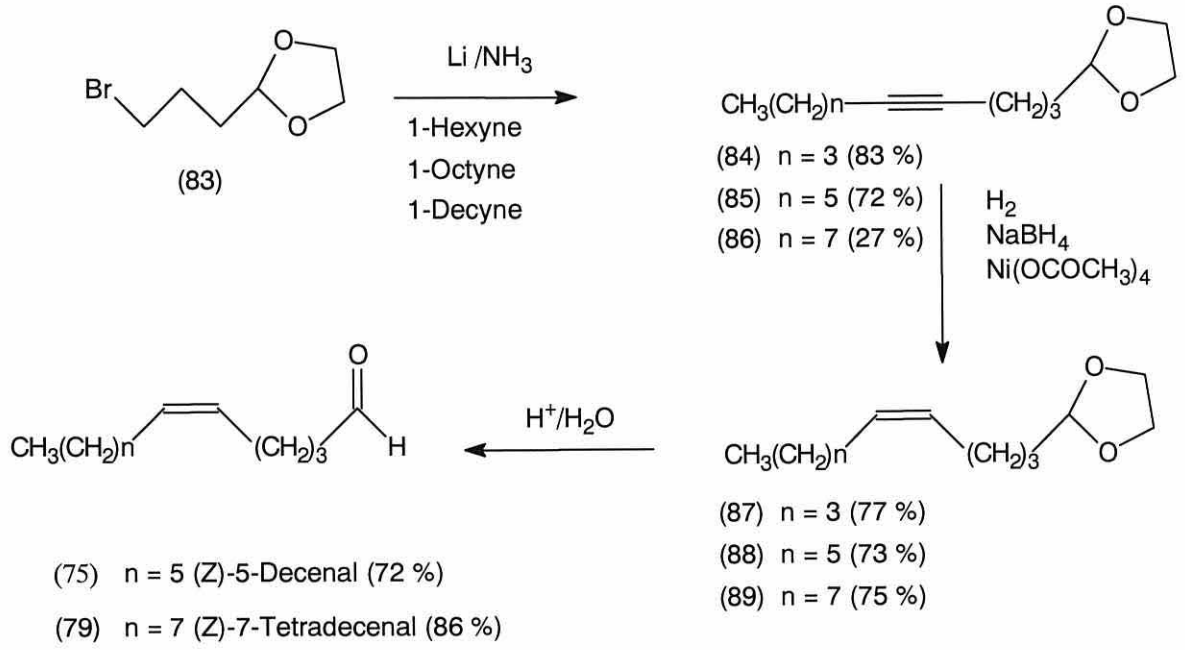


Figure 55

The intermediate compound 2-(3-bromopropyl)-1,3-dioxacyclopentane (**83**) was coupled to a range of 1-alkynes (1-hexyne, 1-octyne, and 1-decyne) using lithium amide in liquid ammonia. 1-Hexyne and 1-octyne coupled in good yields (**84**) 83 % and (**85**) 72 % respectfully. The procedure was much less successful when using 1-decyne. The yield of alkylation for (**86**) (27 %) was very low compared with the previous 1-alkynes. 1-Decyne is less soluble due to the length of the alkyl chain, and the anion was not able to react efficiently with the bromoacetal.

The alkynes were *cis* hydrogenated using the catalyst - nickel boride in a hydrogen atmosphere. Nickel boride was generated *in situ* from the addition of nickel acetate tetrahydrate and sodium borohydride in ethanol. The reduction was highly stereospecific giving 100 % *cis* double bond. The acetylenes was reduced in each case the alkyne in good yields with the aid of ethylendiamine as regulator. The infra red spectra showed a weak

absorption between 3003 – 3007 cm^{-1}. The ^{1}H NMR spectrum showed a complex multiplet at δ 5.37 with an integration of two protons, and the ^{13}C NMR spectrum showed two alkene signals at δ 129 and δ 130.

The deprotection of the acetals was easily achieved on refluxing in a water / acetone mixture with a catalytic quantity of pyridinium *para*-toluene sulphonic acid. After 48 hrs the acetal signals had disappeared, giving way to peaks denoting the aldehyde had reformed. The ^{1}H NMR spectrum showed a narrow triplet (J 1.7 Hz) at δ 9.77, coupling to a methylene group, and a doublet of triplets (J 1.7, 7.2 Hz) at δ 2.44. The ^{13}C NMR spectrum again showed a carbonyl signal at δ 202. Thus the range of (Z)-5 aldehyde pheromones were synthesised. The spectra of each pheromone was identical to those recorded in the literature.

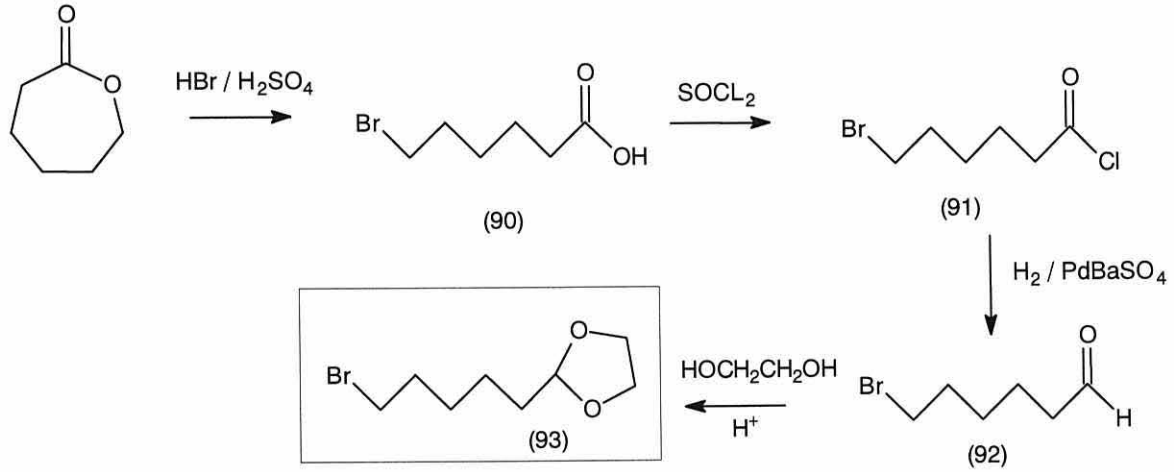


Figure 56

ε-Caprolactone was used as the starting material for synthesising the range of (Z)-7 aldehydes. The lactone was ring opened using 48 % aqueous hydrobromic acid to give 6-bromohexanoic acid in 91 5 yield. The ^{1}H NMR spectrum if this showed the methylene group next to the bromine as a triplet, which had shifted upfield from the corresponding signals in the lactone to δ 3.39, with a coupling constant of 6.7 Hz. The ^{13}C NMR spectrum showed six signals, the carboxylic acid carbon being at δ 179.8.

The acid was converted into the acid chloride (**91**) using thionyl chloride in 70 % yield. The ^{1}H NMR spectrum of this showed the signals for the methylene adjacent to the carbonyl had

shifted downfield to δ 2.91. The infrared spectrum gave the absorbance of the carbonyl as a strong peak at 1789 cm $^{-1}$, and the hydroxyl absorbance had disappeared. 6-Bromohexan-1-oyl chloride was distilled pure at 90 °C (3.5 mm Hg) and hydrogenated with palladium on barium sulphate to give 6-bromo hexanal (**92**) in 73 % yield. The aldehyde was then protected with ethylene glycol to give the acetal in good yield. The infra red spectrum of this showed that the carbonyl had disappeared.

The acetal was coupled in the same manner as before to give the correct chain length for a further three pheromones. The bromide was coupled with 1-hexyne, 1-octyne and 1-decyne. As with the previous coupling reactions, 1-hexyne and 1-octyne coupled well, but as with the (Z)-5 pheromones, 1-decyne gave a lower than expected yield.

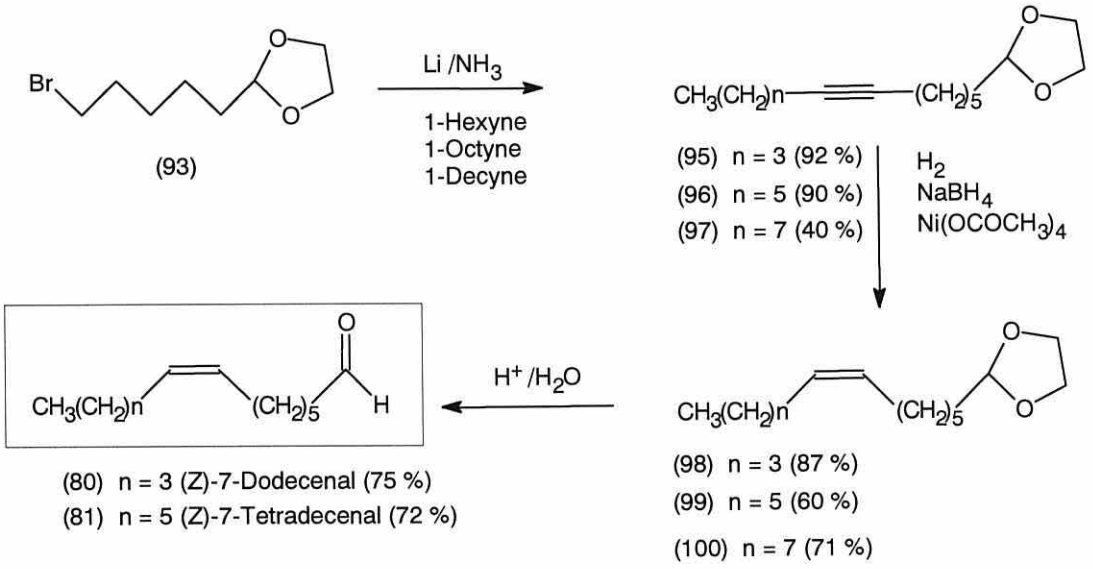


Figure 57

The partial reduction of the alkynes and deprotection gave the wide range of (Z)-5 and (Z)-7-aldehyde pheromones.

3.3.3 Conclusion

The procedure drawing from the lactones gave four (Z)-monounsaturated pheromones in an overall yield of 16 - 25 %. The reactions are simple and repeatable and could be achieved on a large scale, and would give very little waste products. This synthesis gives a more effective and cleaner route to the aldehyde pheromones at the (Z)-5 and (Z)-7 position. However the coupling step for the production of the two pheromones synthesised from 1-decyne ((Z)-5-tetradecenal and (Z)-7-hexadecenal) were obtained in lower than expected yield because of a lower solubility of the 1-decyne anion.

This procedure is more efficient than the double reduction, and the method is easily adaptable to produce a range of pheromones from one set of starting materials. The synthesis of the longer chained (Z-9, Z-11 and Z-12) pheromones must be possible using the same methodology and therefore give the full range of monounsaturated aldehydes from one adaptable pathway.

3.3.4 (Z)-9, (Z)-11 and (Z)-12-Alkenals

The synthesis of the short chained pheromones using the pathway from lactones was very successful. The overall yields to produce each pheromone was more than doubled. Also, only a small change to the procedure gives the opportunity to make a range of two or three products from one reaction pathway.

The next target was to try and produce the longer (Z)-9, (Z)-11, and (Z)-12 mono-unsaturated aldehyde pheromones, by a similar method and gain on the overall yield of the pathway compared with the double reduction route.

It was more difficult to obtain the lactone rings larger in size than seven, so the nearest alternative was to use diols and convert them into the equivalent bromo acid starting material. Octanediol and decanediol, and bromoundecanoic acid were used as starting materials. The diols were monobrominated with 48 % hydrobromic acid by continuous extraction with toluene for 16 to 18 hours. This gave the bromoalcohols (**100, 101**) in 90 % yield. The alcohol was oxidised easily with potassium permanganate. After this simple oxidation of the bromoalcohol, the synthesis is the same as that discussed above and gave good yields.

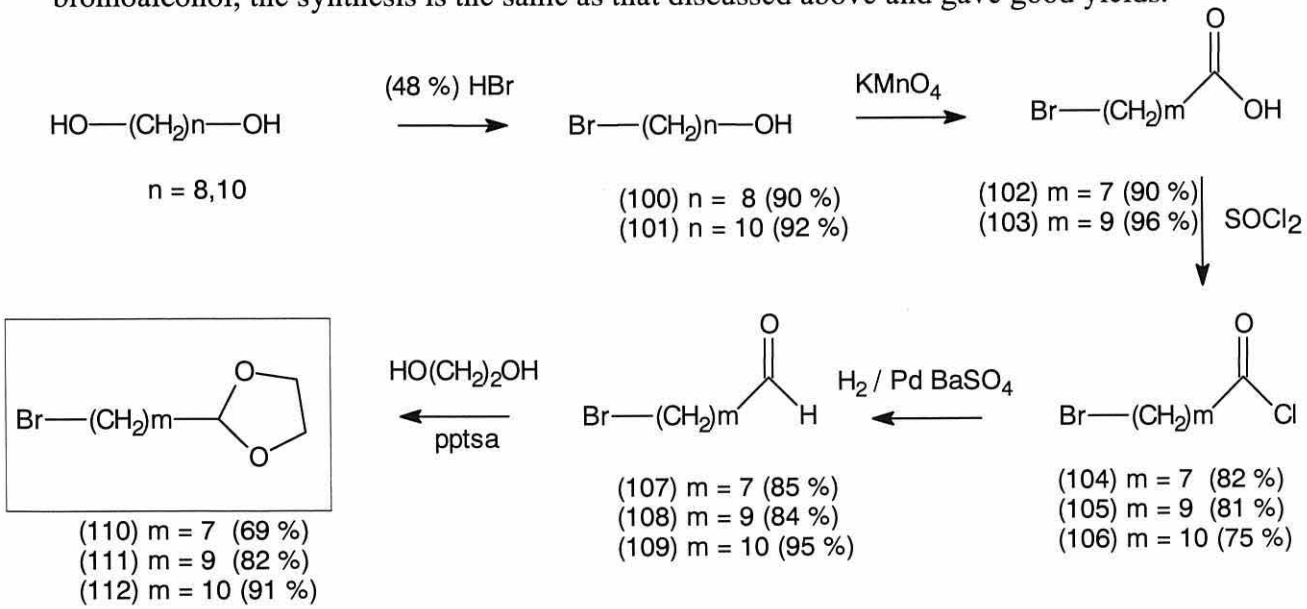


Figure 58

The bromoacetal was coupled to the appropriate 1-alkyne using Lithium amide. Semi-reduction followed by deprotection. This gave the (Z)-9, (Z)-11 and (Z)-12 aldehyde pheromones from a good yield in every step (**Fig. 59**).

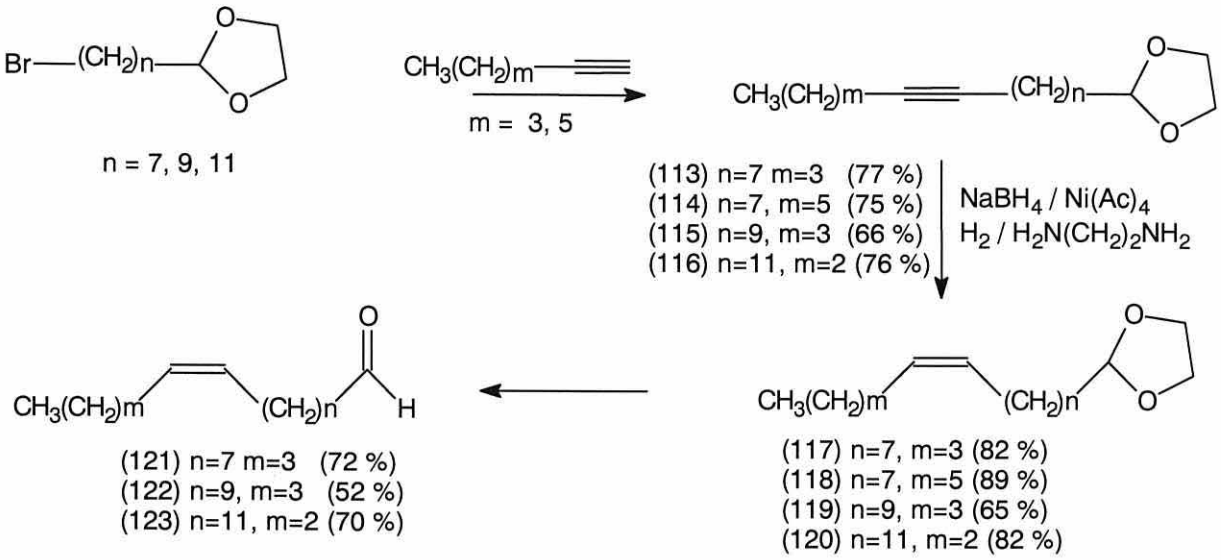


Figure 59

3.3.4 Conclusion and Further Work

The use of lactones seems to give an attractive synthesis for the shorter chained pheromones. The lactones are very inexpensive and are a convenient source for the carboxylic acid functionality. The ability to carry out the first four steps in the reaction scheme using standard equipment, with short reaction times, and easy purification by distillation give this synthesis a real possibility that the scale up reactions would prove successful. The second half of the reaction scheme from the bromoacetal supplies an adaptable route to at least three different products without changing procedures or equipment. The protected aldehyde may also be kept in storage indefinitely and be deprotected to the product on demand.

The (Z)-9, (Z)-11 and (Z)-12 pheromones are also easily produced from dialcohol starting materials using the same pathway and gave overall yields of between 11 and 28 %. This method means that a wide range of aldehyde pheromones can be produced from one

standard procedure. The whole procedure lends itself to perhaps an efficient and convenient process that replaces the need for heavy metal oxidation in the synthesis of aldehyde pheromones.

Future work could develop the process for *trans* pheromones. The *trans* alkene could be made by replacing the semi reduction of the alkyne with a step using solvated sodium in liquid ammonia to give the *trans* alkene (**Fig 60**).

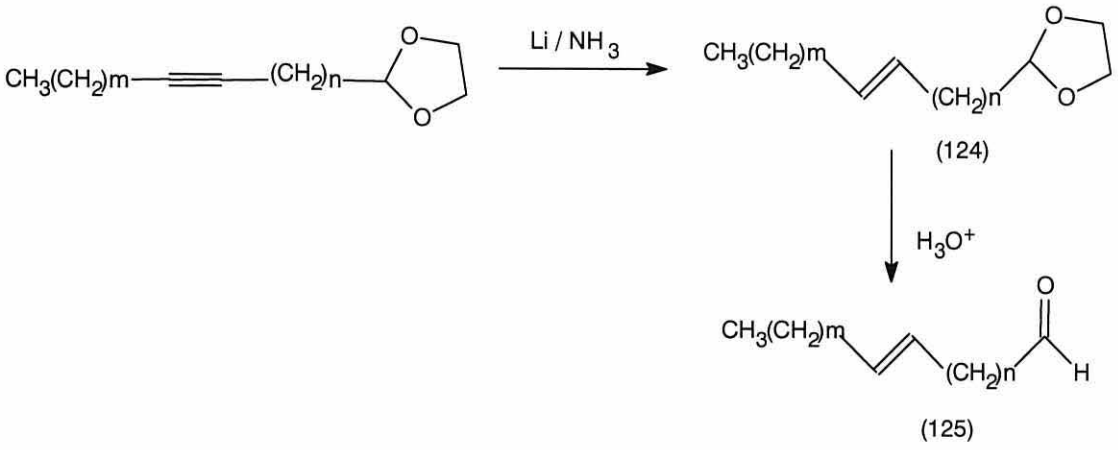


Figure 60

Chapter 4

4.1 Investigations into Dienic Aldehyde Pheromones

4.1.1 Introduction

The aim of this investigation was to attempt the synthesis of a range of dienic aldehyde pheromones with the intention of using the same ω–bromoaldehyde precursors as those used earlier the monoalkenal synthesis (**Section 3.3**). This would produce a comprehensive list of pheromones that could be easily synthesised without complex new processes and develop further the use of the bromoaldehydes synthesised from catalytic hydrogenation. The syntheses of five different types of dienic aldehydes were attempted (**Fig. 61**). These are examples of the four main classifications of dienic aldehyde pheromones: non-conjugated double bonds, conjugated *cis-trans*, skipped conjugated *cis-cis*, conjugated *cis-cis* and conjugated *trans-trans*.

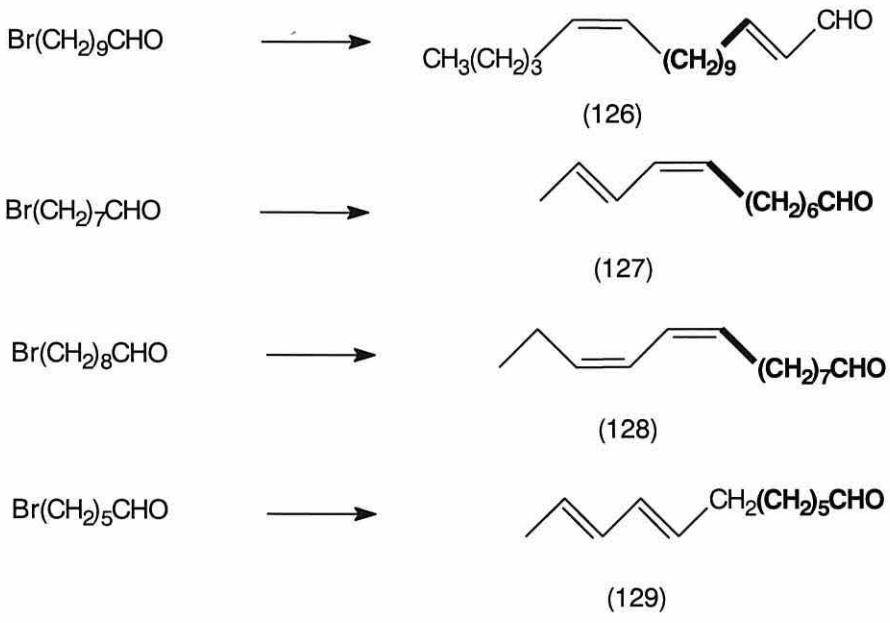


Figure 61

4.2 (E,Z)-2,13-Octadecadienal

4.2.1 Introduction

In 1985 Yamaoka *et al.* isolated and identified the pheromonal components from the female webbing clothes moth (*Tineola bisselliella*).[63] The pheromone is made up of a mixture of two aldehydes; (E)-2-octadecenal (**130**) (koiganal I) and (E,Z)-2,13-octadecadienal (**126**) koiganal II (**Fig. 62**).

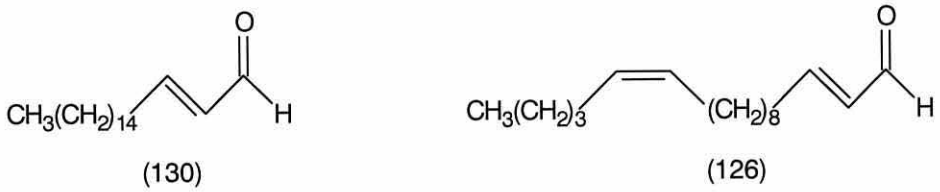


Figure 62

The larvae of the webbed clothes moth are responsible for the destruction of natural animal material used in garments and fabric industries, and especially fabrics in storage facilities, especially in museum exhibits and the storage of artefacts.

In 1996 K. Mori *et al*, synthesised the two components of the webbed clothes moth allowing the pheromone blend to be tested for biological activity.[64] Mori's synthesis (**Fig. 63 and 64**) of koiganal I and II used two PCC oxidations and a DIBAL reduction to give the products. The (E)-2-octadecanal was synthesised in four steps from hexadecanol. Oxidation of hexadecanol by PCC in dichloromethane afforded the aldehyde (**47**) in 86 % yield. The aldehyde was reacted with the stabilised phosphonate ylide, triethyl 3-phosphonopropionate, to form the *trans*-allylic ethyl ester (**131**) in 68 % yield. The full reduction of the ester functionality using DIBAL at -78 °C yielded the allylic alcohol (**132**) in 94 % yield. The alcohol was further oxidised by PCC to give the koiganal I (**130**) in 93 % yield.

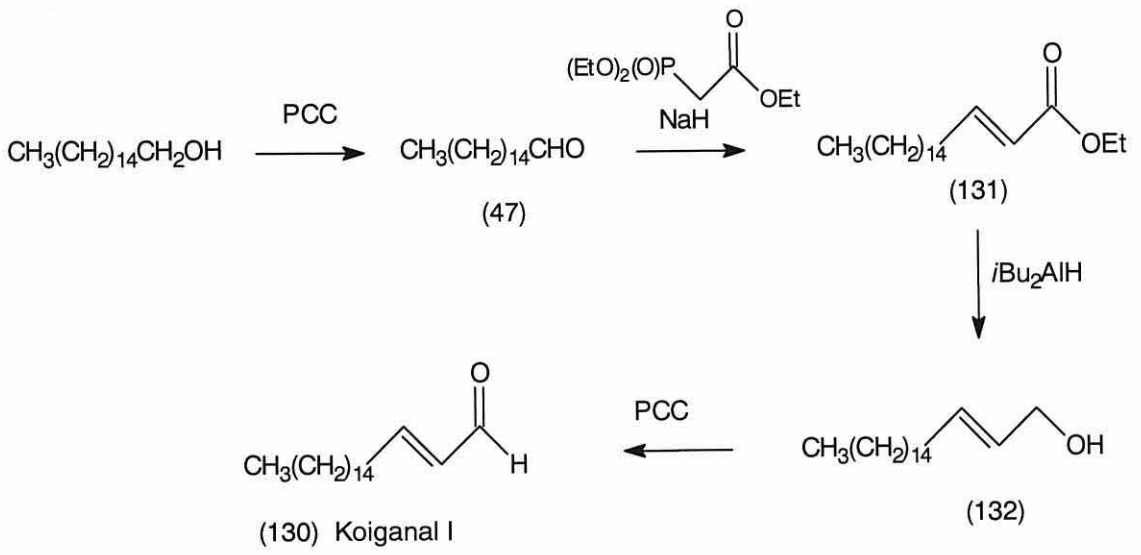


Figure 63

The same procedure was effected to produce (E,Z)-2,13-octadecadienal (**126**) from (Z)-11-hexadecenol (**133**) (**Fig. 64**). The *trans*-alkene was synthesised by a Wadsworth-Emmons reaction and the subsequent ester (**135**) was first reduced to (**136**) and then oxidised to the aldehyde product.

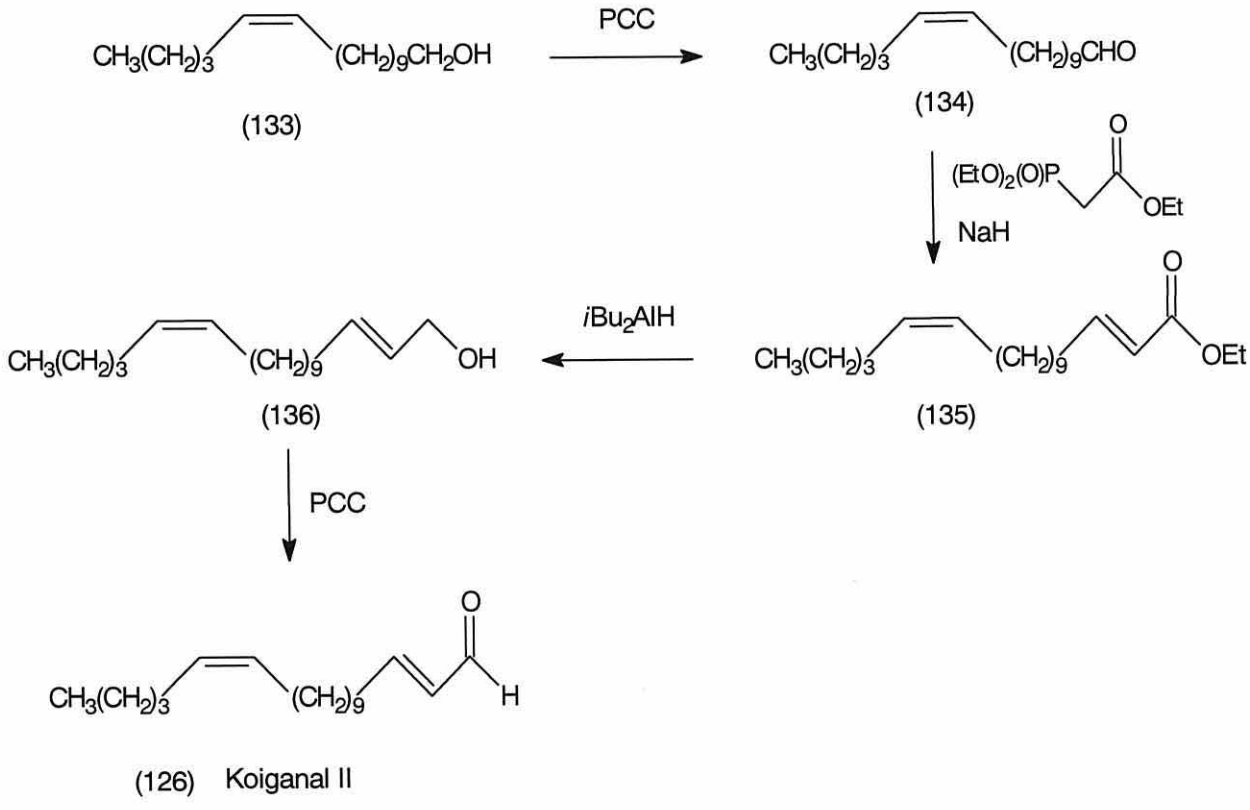


Figure 64

4.2.2 (E)-2-Octadecenal Synthesis

(E)-2-Octadecenal was synthesised from hexadecanal. Hexadecanal was produced by the catalytic hydrogenation of hexadecanoyl chloride as described in **Chapter 3**. The aldehyde was coupled with the nitrile phosphonate, diethyl cyanomethylphosphonate (**137**), using butyl lithium as a base. They reacted together in a Wadsworth-Emmons type reaction to give an α,β-unsaturated double bond. This gave the nitrile product, 2-octadecenonitrile (**138**) in 82 % yield.

The nitrile phosphonate is a convenient starting material, as it may be prepared easily and inexpensively from the Arbuzov rearrangement. The reaction requires the refluxing triethyl phosphite with chloroacetonitrile to give the phosphonate as product.[65]

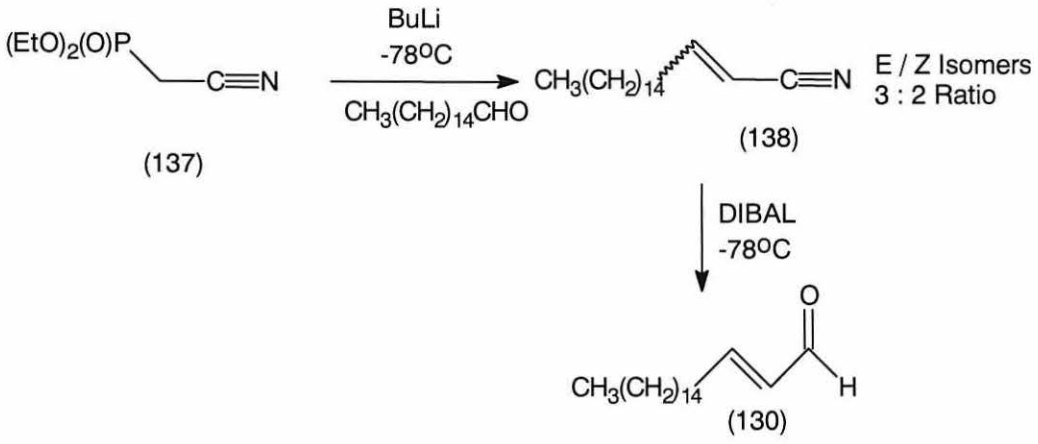


Figure 65

The electron withdrawing power of the nitrile group on the phosphonate was not strong enough for the reaction to be completely stereoselective. The reaction of hexadecanal and (**137**) resulted in a mixture of *cis* and *trans* isomers of (**138**), in a ratio was determined by G.C.. Analysis of the product proved that a 3:2 ratio in favour of the *trans* isomer was formed. The ^{1}H NMR spectrum gave peaks for both isomers, the methylene adjacent to the *trans* appeared as a double quartet at δ 2.20 (J 6.9 Hz) coupled to a single proton at δ 6.73 which showed double triplet which included a *trans* coupling of 16.2 Hz. The methylene adjacent to the *cis* olefin gave a smaller integration than the *trans* indicating order of the isomeric ratio.

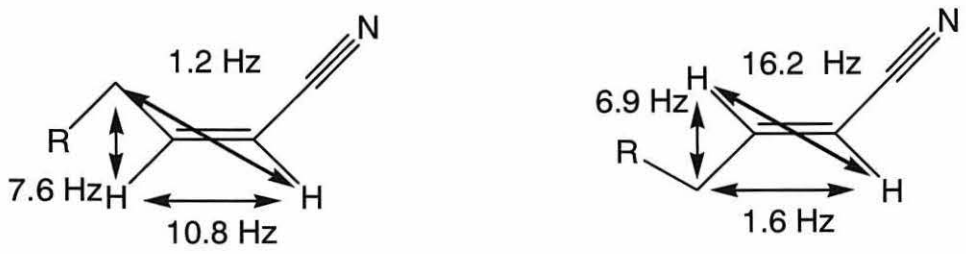


Figure 66

The *trans* olefin had a coupling constant of 16.2 Hz across the double bond and coupled to the adjacent methylene at δ 2.20 (6.9 Hz). The *cis* isomer showed a coupling constant of 10.8 Hz across the double bond and coupled to the adjacent methylene with a coupling constant of 7.6 Hz at δ 2.41 (**Fig. 66**).

In the final step 2-octadecenonitrile (**138**) was reduced using a metal hydride. The nitrile reduction was achieved in a rather disappointing yield of 53 % to give (**130**). The isomeric ratio of the nitrile proved not to affect the ultimate stereochemistry of the product. The reduction of the nitrile to the aldehyde using one equivalent of diisobutylaluminium hydride at -78 °C, isomerised the *cis* double bond, and converted the end product solely to the *trans* isomer. The reactivity of the nitrile may have been reduced due to the long aliphatic chain hindering the hydride reduction.

The yields of the Wadsworth-Emmons and the metal hydride reduction were not optimised, as the reaction conditions of both steps required very low temperatures of -78 °C. Such temperatures are not economical for an industrial synthesis and therefore warranted no further attention. Perhaps the use of industrial equipment would allow the Wadsworth-Emmons reaction to be achieved at temperatures of between 0 to –10 °C, and make the process more economical. However, this work is beyond the scope of this project.

4.2.3 (Z,E)-2,13-Octadecadienal Synthesis

A synthesis that avoided oxidation reactions and utilised the ω–bromoaldehyde intermediates used for the monounsaturated aldehydes was sought. The attempted synthesis of the target molecule (Z,E)-13,2-octadecadienal began with the strategy of using 10-bromodecanal, an intermediate from the synthesis of (Z)-11-hexadecenal (**Chapter 3**).

A series of test reactions were attempted to avoid PCC or equivalent metallic oxidations. Decanal was used first as an inexpensive model compound for this reaction procedure instead of 8-bromodecan-1-al.

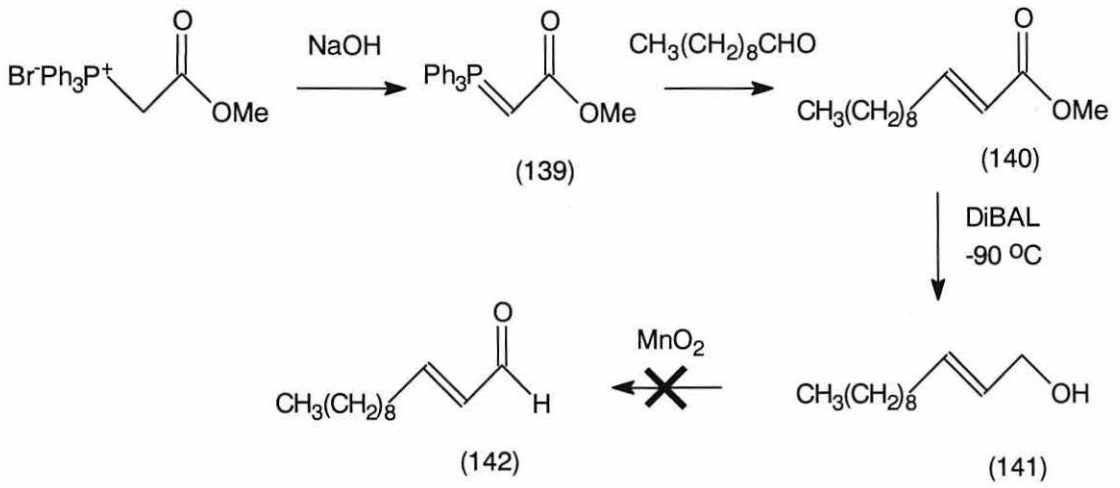


Figure 67

Decanal was reacted with the stabilised phosphorane ylide carbmethoxymethyl triphenylphosphorane (**139**) to form the *trans* methyl ester (**140**) in 92 % yield (**Fig. 67**). The ^{1}H NMR spectrum showed the expected signals for the *trans* double bond, a doublet of triplets at δ 6.97 and δ 5.82, with a coupling constant across the double bond of 15.5 Hz. The ^{13}C NMR gave olefinic signals at δ 120.7 and δ 149.8 and a carbonyl signal at δ 175.9. The attempted partial reduction of the ester with DIBAL at -90 °C to give the aldehyde was unsuccessful. The reduction caused the ester to over-reduce to the allylic alcohol (**141**). The ^{1}H NMR spectrum of the alcohol product showed two olefinic hydrogens at δ 5.66 and the

methylene between the olefin and the alcohol as a doublet at δ 4.08 (J 4.6 Hz). The carbonyl absorption in the IR spectra was removed and a broad OH band had appeared at 3331 cm^{-1}.

An alternative oxidation of allylic alcohols using activated manganese dioxide was tested. The alcohol was refluxed for three days with ten equivalents of MnO_2 but only achieved 50 % oxidation to the aldehyde, (E)-2-dodecenal (**142**). The ^1H NMR spectrum of (**142**) showed both the signals for the alcohol olefin, an alcohol methylene doublet and also for the proton of the aldehyde product, a doublet at δ 9.50 (J 7.9 Hz) which was coupled to a single proton double double triplet of the adjacent olefinic hydrogen at δ 6.15. This last signal was coupled across the double bond (J 15.5 Hz), to the aldehyde proton (J 7.9 Hz), and to the methylene adjacent to the double bond (J 1.5 Hz).

An alternative synthesis of (E,Z)-2,13-octadecadienal was proposed that would avoid the oxidative steps and also the use of low temperature reactions. **Figure 68** shows a retrosynthesis of koiganal II (**126**).

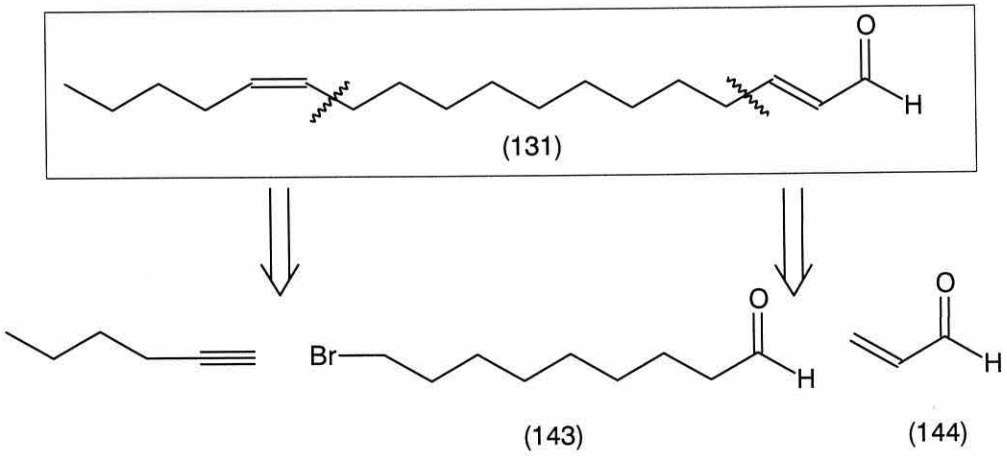


Figure 68

The key bromoalkanal, used in the synthesis of the monounsaturated aldehydes is also utilised here for the synthesis of Koiganal II. Nonanediol was converted into 9-bromononan-1-al (**143**) and forms the basis of the synthesis. Acrolein (**144**) is an inexpensive starting material. It can be easily synthesised from the readily available compound, glycerol.

The protonation of glycerol (**145**) by an acid catalyses the dehydration of the molecule *via* the secondary carbonium ion (**146**) results in the enol (**147**). Further acid catalysis eliminates a second water molecule, to give acrolein (**144**) as the product (**Fig 69**).

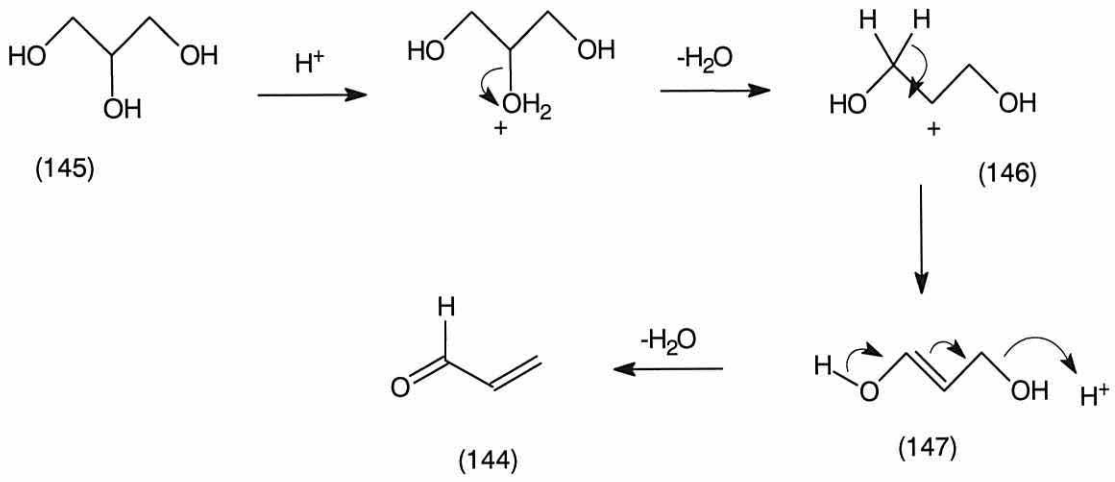


Figure 69

Following the work of Stowell *et al*, 2-(1,3-dioxan-2-yl)-ethyltriphenylphosponium bromide (**152**) was synthesised from acrolein in two steps.[66] The first step was the addition of bromide ion to the double bond of acrolein using HBr gas in a Michael type addition. The HBr gas was generated from the controlled addition of bromine to 1,2,3,4-tetrahydronaphalene. The HBr gas produced was bubbled through the reaction vessel for 6 hours. After this time 1,3-propanediol was added to protect the aldehyde functionality by producing a dioxolane ring. 2-(2-Bromoethyl)-1,3-dioxane (**151**) was refluxed with triphenylphosphine in cyclohexane for 24 hours to produce the phosphonium salt in 30 % yield.

The Wittig reaction using 2-(1,3-dioxolan-2-yl)-ethyltriphenylphosponium bromide (**150**) was attempted using hexanal, but the coupling reaction gave low yields of 30 % for (**148**), even though commercial Wittig salt was tested. The dioxolane was deprotected to give the aldehyde (E)-2 nonenal (**149**) in 57 %.

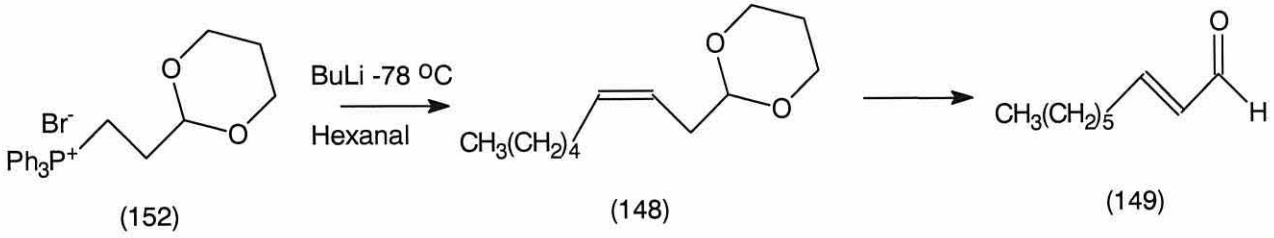


Figure 70

2-(1,3-Dioxolan-2-yl)-ethyltriphenylphosphonium bromide is very hygroscopic, retaining a water molecule in its structure. It is very important to dry the salt thoroughly before use. To achieve this, the compound was dissolved in dry benzene and the solvent azeotropically distilled using a rotary evaporator.

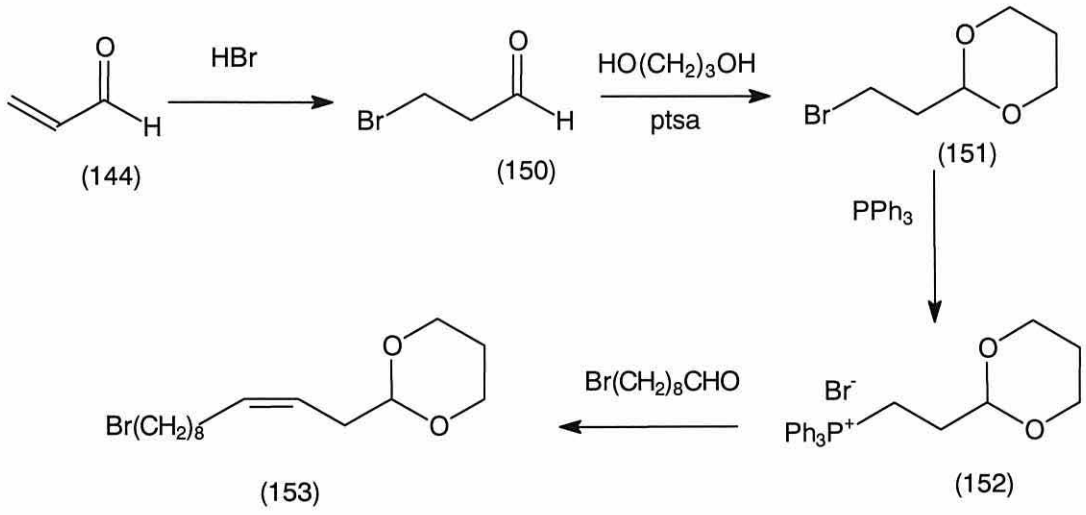


Figure 71

The carefully purified and dried Wittig salt (**152**) was coupled to the bromononanal, to give the product, 2-(11-bromoundec-2-enyl)-1,3-dioxane (**153**) in 60 % yield. The ^{1}H NMR spectrum of this showed the olefinic signal at δ 5.4 with an integration of two protons, and the ^{13}C NMR spectrum gave fourteen signals with the double bond carbons at δ 122.9 and δ 132.6. The mass spectrum gave the $[M-H]^{+}$ ion at 317/319.

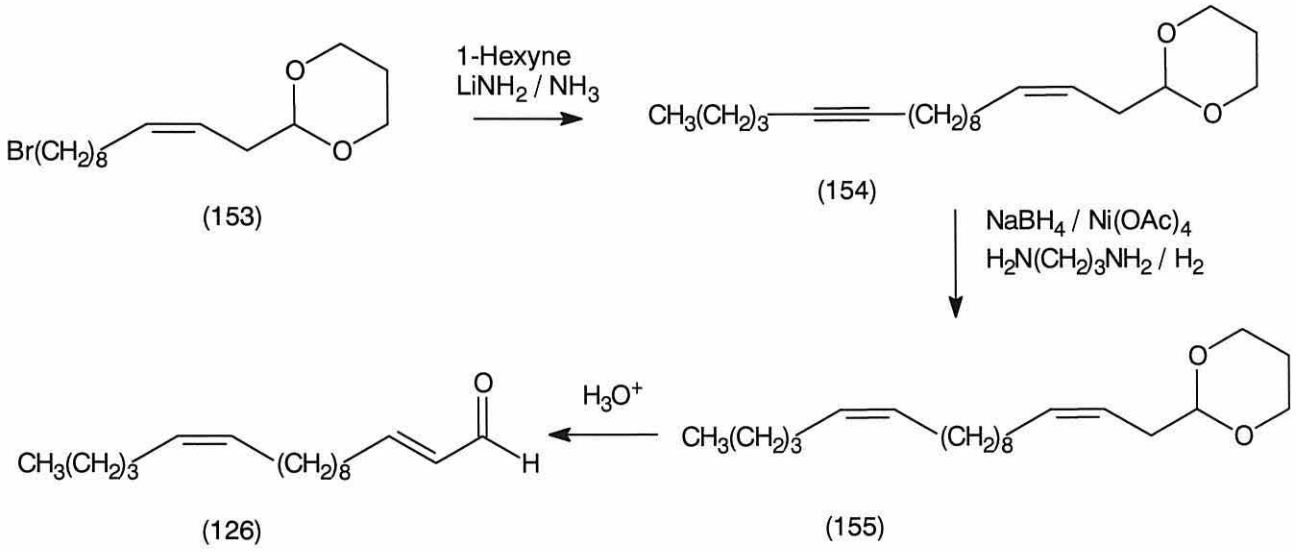


Figure 72

The bromide (**153**) was coupled to 1-hexyne using lithium amide in liquid ammonia in 77 % yield. The ^{1}H NMR spectrum of the product showed no bromo methylene triplet but the methyene group adjacent to the acetylene gave a four proton multiplet at δ 2.19, and a triplet appeared for the terminal methyl group at δ 0.86. The ^{13}C NMR spectrum signals for the acetylenic carbons overlap giving one signal at δ 80.1. The alkyne was partially hydrogenated using nickel (P-2) as catalyst gave the *cis* product 2-((Z,Z)-2,12-heptadecadienyl)-1,3-dioxolane (**155**).The reduction was achieved in 70 % yield. The ^{1}H NMR spectrum of product (**131**) gave four protons in the olefinic region and the methylene groups adjacent to the Z-13 alkene were shifted to δ 2.05.

The final step was the deprotection of the aldehyde. The acetal was refluxed in four molar hydrochloric acid with 3.5 equivalents of chromium (III) chloride. This isomerised the C-3 double bond from β to α to the aldehyde. When the double bond was brought into conjugation with the aldehyde it gave the correct *trans* stereochemistry. The deprotection gave a low yield of 26 % this was due to the difficulty in isolating the product. The aldehyde was steam distilled out of the reaction vessel, and this proved difficult to achieve on a small scale.

A more convenient synthesis of the 3-carbon Wittig reagent was attempted. The dioxolane ring was replaced with the an acyclic acetal protecting group.[67] The alternative synthesis also avoided the use of HBr gas. Instead it used 48 % aqueous hydrobromic acid as the source of bromide. The Wittig salt, (3,3-diisopropoxypropyl) triphenylphosphonium bromide (**157**), was synthesised in two steps in one reaction vessel.

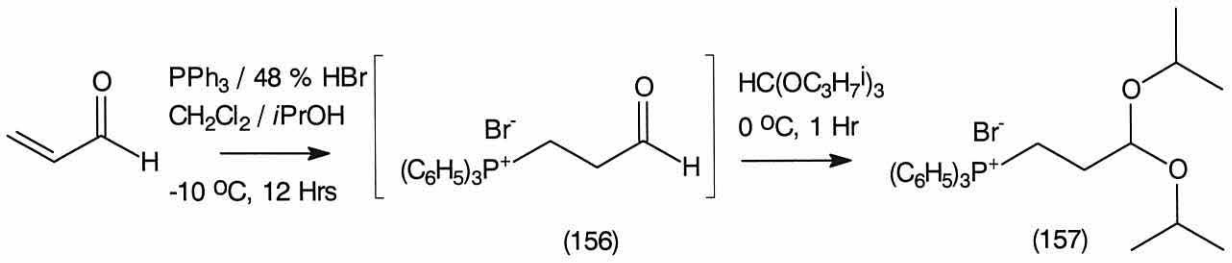


Figure 73

Triphenylphosphine and 48 % aq. HBr was reacted with acrolein in a Michael addition to give the aldehyde intermediate, (3-oxopropyl) triphenylphosphonium bromide (**156**). The acyclic

acetal was then formed on the addition of triisopropyl orthoformate to give the product (**157**) in 58 % yield. The phosphonium salt was recrystallised from CH_2Cl_2/ether/pentane (1:2:2) and the purified product was dried thoroughly before use.

The acyclic Wittig salt (**157**) also retains water in its structure. The salt had to be dried thoroughly before attempting any reaction. Microanalysis of (**157**) proved that one molecule of water per compound was absorbed by the salt. The calculated percentage of carbon and hydrogen for $C_{27}H_{34}O_2PBr.H_2O$ gave carbon 62.4 %, hydrogen 6.9 %, and the experimental: carbon 62.3 %, hydrogen 6.9 %. The salt was therefore dried twice by azeotropic distillation in anhydrous benzene immediately before use.

The ^1H NMR spectrum of the salt showed the isopropyl protecting group as a pair of doublets at δ 1.12 with 12 protons. These four methyl groups were coupled to a septet of two equivalent tertiary protons at δ 3.85. The single proton triplet (J 4.6 Hz) of the acetal was then shown at δ 4.04. The methylene group adjacent to the phosphine resonated as a multiplet at δ 3.68. The ^{13}C NMR spectrum showed the methyl groups of the two isopropyl groups overlap at δ 22.8 and δ 23.2 with the tertiary carbon at δ 69.8. The acetal carbon resonated further down field at δ 98.4.

The same route was then followed as in the previous synthesis of Koiganal II. The coupling of 9-bromononanal with (**143**) produced a double bond in the C-3 position giving (Z)-3-bromododecenal diisopropyl acetal (**158**) in 71 % yield. The proton NMR spectrum showed the signals of two alkene protons at δ 5.38. The bromomethylene group showed a triplet at δ 3.36 (J 6.8 Hz) coupled to the adjacent methylene pentet at δ 1.80, and the ^{13}C NMR spectrum gave eighteen signals including the olefin carbons at δ 124.3 and δ 131.9.

Coupling the bromide (**158**) with 1-hexyne gave the product (Z)-3-octadec-13-ynenal diisopropyl acetal (**159**). The ^1H NMR spectrum of this showed a large multiplet of the two methylene groups adjacent to the acetylene at δ 2.15. The spectral pattern of the bromide signals had disappeared. The ^{13}C NMR spectrum gave the overlapping alkyne signal at δ 80.1. Hydrogenation to give the *cis* alkene in the 13-position (**160**) without affecting the alkene in the 3-position gave a further two protons in the alkene region as a multiplet at δ 5.34. The two methylenes adjacent to the acetylene shift up field to δ 2.03. The carbon NMR spectrum

showed the olefinic C-3,4 carbons at δ 124.2 δ 132.1, and the C-13,14 carbons overlapping at δ 129.8. Deprotection of (**160**) isomerised the C-3 double bond, bringing it into conjugation with the aldehyde in a 32 % yield. The target molecule (**131**) was thus produced in four steps from the phosphoranes (**152**) and (**157**).

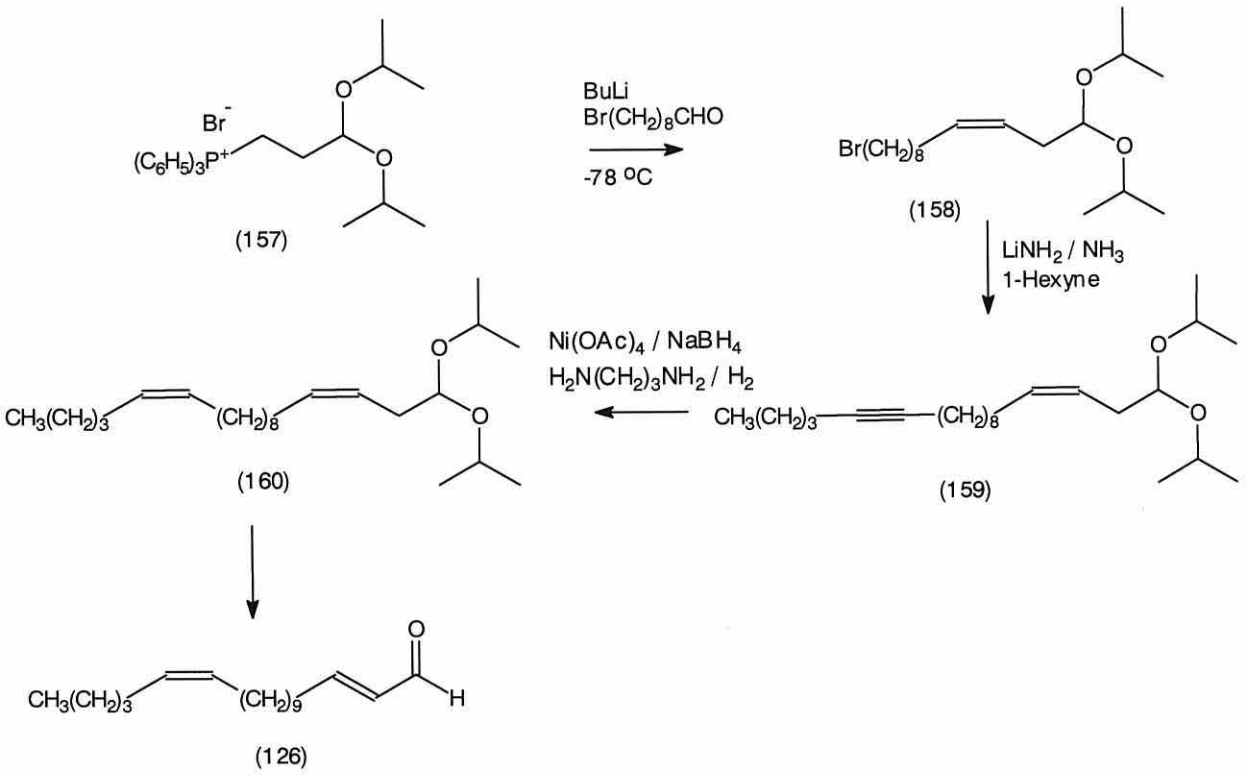


Figure 74

4.2.4 Conclusion and Future Work

Both the target molecules koiganal I and II were synthesised. They were synthesised using the techniques developed in **Chapter 3**.

The original synthesis of koiganal I was made on a small scale and used PCC in two oxidation steps in the pheromone synthesis. The method described here removes both oxidation steps with the reductive strategy of this thesis and provides an opportunity to produce the pheromone on a large scale in the future.

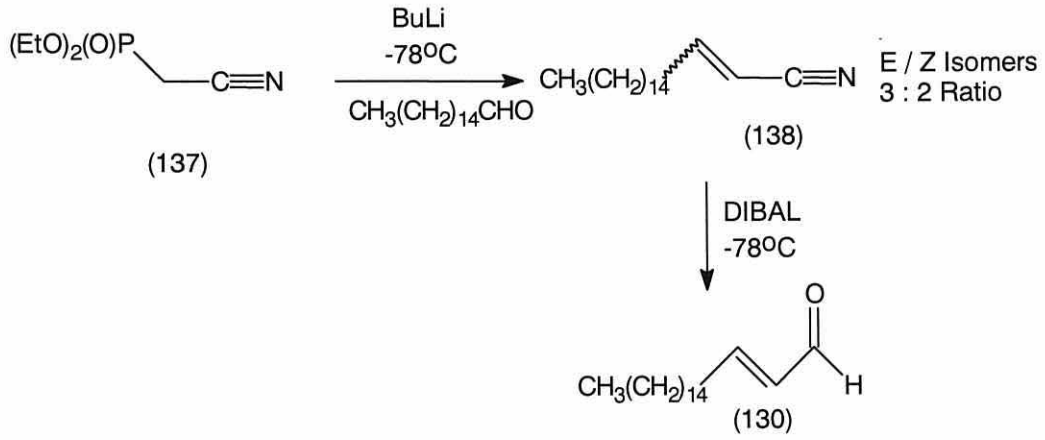


Figure 75

A catalytic hydrogenation of hexadeconyl chloride gave the aldehyde hexadecanal in 94 % yield. The subsequent Horner-Wadsworth coupling reaction and reduction of the cyano group gave an overall yield of 40 % for the synthesis of (Z)-2-octadecenal (**130**).

Koiganal II (**126**) was synthesised using the intermediate bromononanal. The aldehyde was coupled to a three carbon Wittig reagent. The Wittig salts proved to be very hydroscopic which lead to reduced yields. However, when dry the Wittig coupling between (**157**) and (**143**) was achieved in 71 % yield. The pheromone was synthesised in an overall yield of 13 %. This value was brought down due to the deprotection in the final step. The deprotection required the aldehyde product to de steam distilled from the reaction vessel, a technique not easily achieved on a small scale. It is more than likely that the yield of this step would improve when repeated on a larger scale.

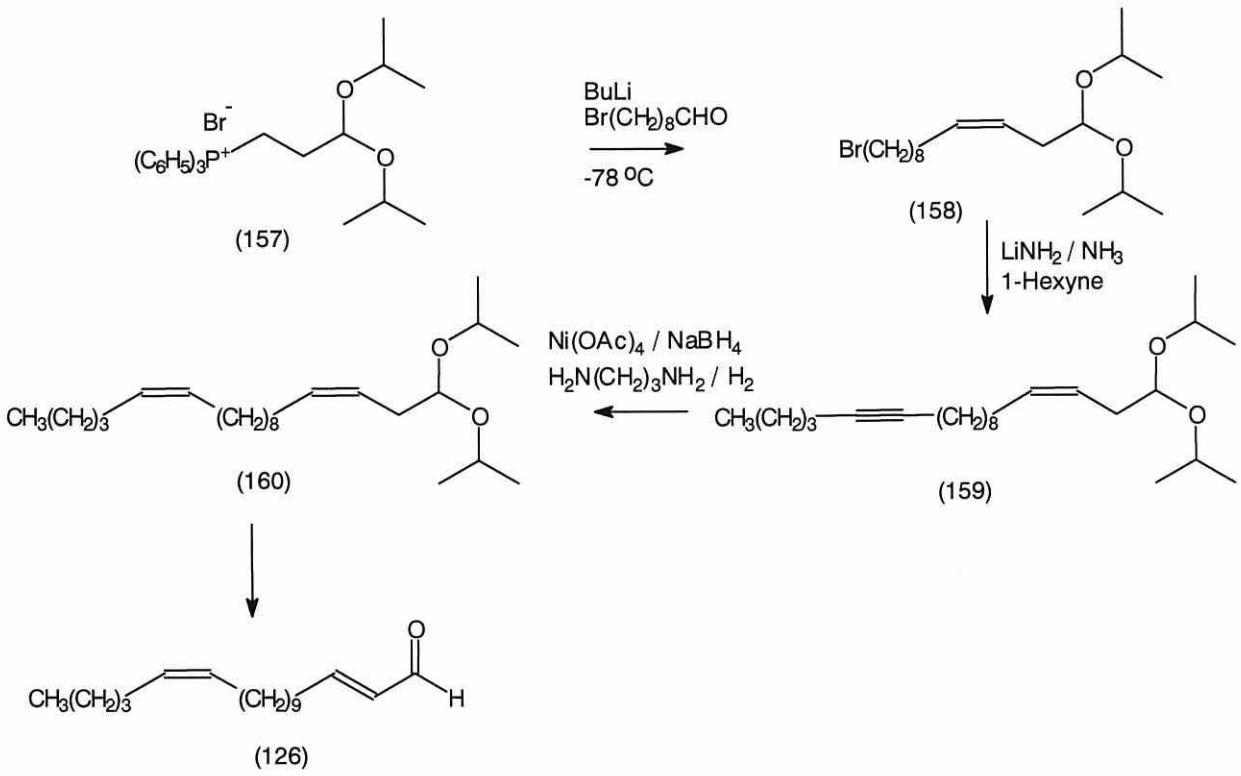


Figure 76

The replacement of the oxidative steps in the synthesis of koiganal I and II provide an opportunity to develop the production of these pheromones on a large scale. The starting materials are inexpensive, the reactions are comparatively clean and each step is achieved in good yields.

To deprotect the aldehyde so as not to isomerise the double bond would open a pathway to other pheromones. The product (Z,Z)-3,13-octadecadienal is a pheromone in its own right and it would be possible to reduce this aldehyde to the alcohol and also to form the acetate. This would give the full range of complementary pheromones which are structurally related.

Possible derivatives that could be synthesised from (Z,Z)-3,13-octadecadienal diisopropyl acetal (**160**) are listed below:

(E,Z)-3,13-octadecadienal
(E,Z)-3,13-octadecadienol
(E,Z)-3,13-octadecadienyl acetate
(E,Z)-2,13-octadecadienal
(E,Z)-2,13-octadecadienol
(E,Z)-2,13-octadecadienyl acetate

4.3 (Z,E) Conjugated Dienal Pheromones

4.3.1 Introduction

The synthesis of *cis-trans* conjugated dienal pheromones, using the bromoacetals as starting materials was attempted.

In 1978 Bestmann[68] synthesised (Z,E)-8,10-dodecadienyl acetate. The *trans* double bond was incorporated into the molecule by reacting crotonaldehyde with the ylide of 8-acetate octanyl-triphosphonium bromide. The unstable Wittig reaction was stereoselective to produce a *cis* double bond. The ylide of the Wittig salt was produced at –78 °C using the base sodium bis(trimethylsilyl)amide (NaHMDS). The Z,E configuration in the pheromone product was synthesised in one step in a yield of 49 %.

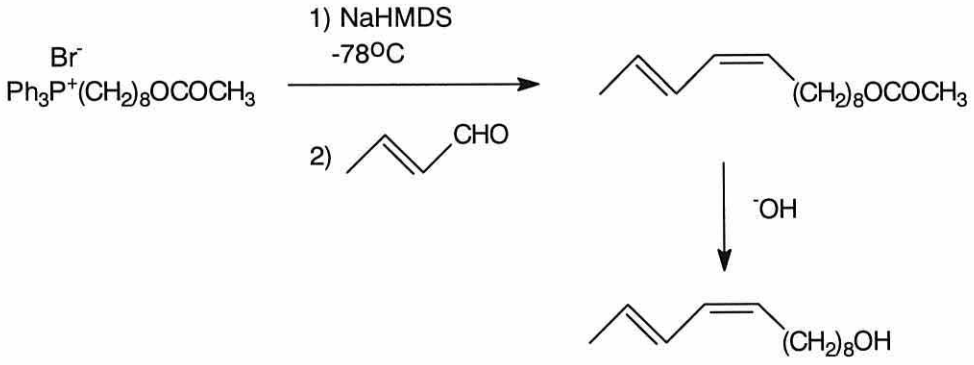


Figure 77

4.3.2 (Z,E)-8,10-Dodecadienal Synthesis

The synthesis of (Z,E)-8,10-dodecadienal was attempted using the same procedure as developed by Bestmann. The monounsaturated synthesis in Chapter 3 gave bromoacetal compounds which were used as starting material for the synthesis of (Z,E)-10-dodecadienal.

A test of the unstable Wittig reaction was attempted, reacting hexyltriphenylphosphonium bromide with crotonaldehyde to synthesis the (Z,E) diene functionality. The Wittig salt was deprotonated with sodium bis(trimethylsilyl)amide at –78 °C to give the yilde. The ylide reacted with the aldehyde at –78 °C give the *cis* alkene in 60 % yield.

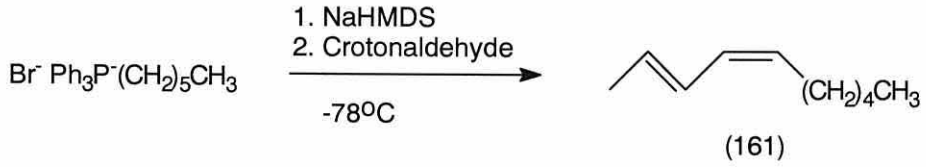


Figure 78

The Wittig salt of bromoheptanyl 1,3-dioxolane was synthesised on refluxing for 48 hours in toluene with triphenylphosphine. The ^{1}H NMR spectrum showed that the lines for the CH_2Br group, a triplet at 3.4 ppm had disappeared and was replaced with a two proton multiplet at 3.7 ppm. The spectra also showed that the acetal was partially deprotected. The ^{1}H NMR spectrum showed the appearance of a narrow triplet at 9.68 ppm with a proton integration denoting an approximate 10 % deprotection. The Wittig product was columned in methanol/dichloromethane 1:15 and dried by azeotropic distillation with benzene. However, deprotection still persisted. The Wittig reaction was still attempted, but the salt was partially insoluble in THF at low temperatures. Sodium bis(trimethylsilyl)amide was added to the reaction vessel and it did give an orange coloration in the reaction vessel which denoted the formation of an ylide. The crotonaldehyde was added, but the reaction did not give any of the desired products.

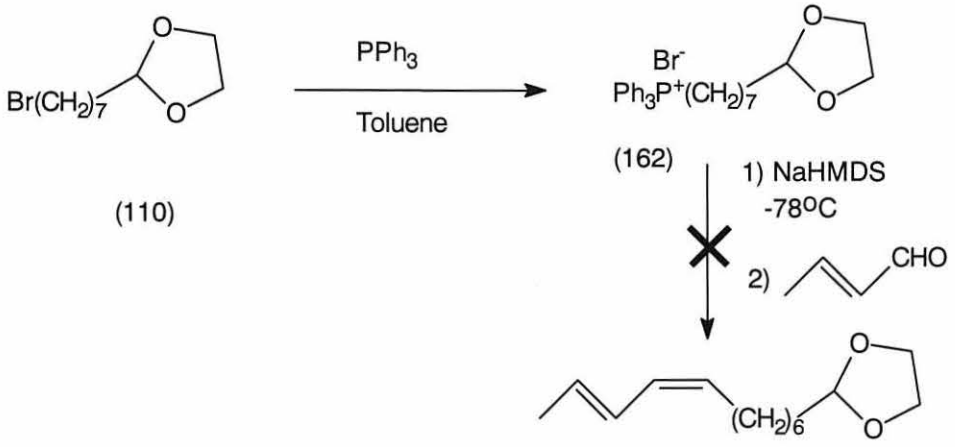


Figure 79

The dioxolane protecting group was slowly deprotecting in the slightly acidic conditions in the synthesis of the Wittig salt. The most obvious development was to replace the dioxolane group the more stable dioxane protecting group. The bromoaldehyde was protected with 1,3-propanediol in acid conditions using Dean-Stark apparatus, to give the bromoheptanyl 1,3-dioxane in 66 % yield. The product showed no signs of deprotection in NMR analysis. The dioxane Wittig salt proved to be more stable and gave a good CHN analysis.

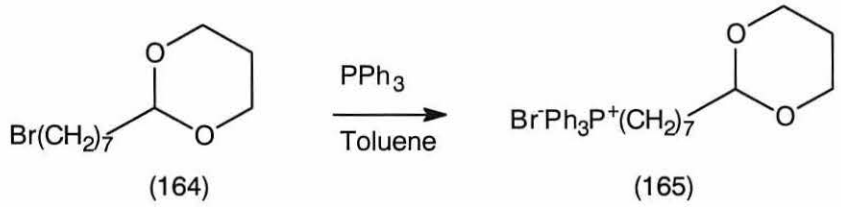


Figure 80

The Wittig reaction between 2-(heptanyl)-1,3-dioxolane triphenyl phosphonium bromide and crotonaldehyde was attempted at –78 °C (**Fig. 77**). The reaction produced the E,Z conjugation in 78 % yield.

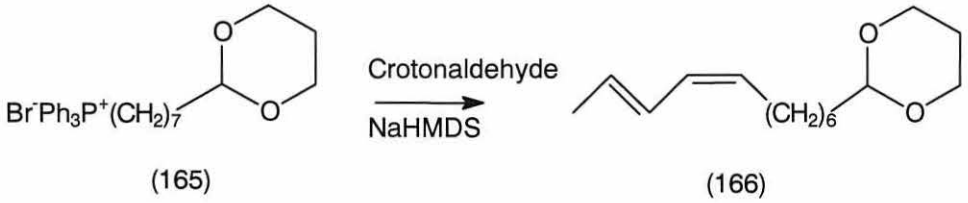


Figure 81

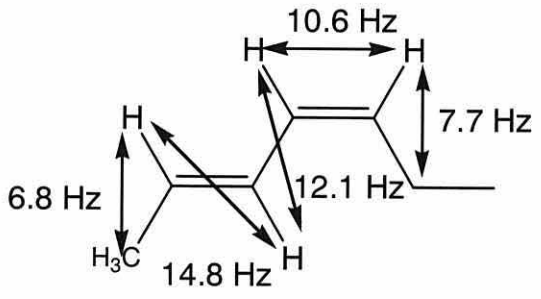


Figure 82

The ^{1}H NMR spectrum proved the stereochemistry of the Wittig product (**Fig. 82**). The terminal methyl produced a doublet at 1.78 ppm with a coupling constant of 6.8 Hz. This coupling constant also appeared in a signal at 5.68 ppm which showed a doublet quartet splitting, with coupling constants to the methyl (6.8 Hz) and across the *trans* double bond (14.8 Hz). This *trans* coupling constant also appeared in a double doublet at 6.32 ppm (14.8 Hz) and the coupling between the double bonds (12.1 Hz). The second double bond gave a *cis* coupling constant of 10.8 Hz.

The NaHMDS base used in the reaction was replaced with the cheaper base butyllithium. The reaction was repeated and coupled the dioxane Wittig with crotonaldehyde. The product was snyhtesised in 69 % yield, but the stereochemistry was reversed, giving a *trans-trans* conjugated system.

The lithium salt produced from butyllithium can effect the reaction. The presence of the lithium salt gave a 1:1 ratio of *trans* to *cis* isomers. The ratio was identified due to the shift in the position of the terminal methyl in ^{1}H NMR spectra. The methyl of the *cis* product resonating at δ 1.78 and the methyl of the *trans* product resonating slightly higher at δ 1.73.

At first appearance this was thought to be a disappointing result. However, the synthesis of *trans/trans* conjugated pheromones are often found in blends with the *cis/trans* conjugated pheromone blends. A reaction that could give a specific mixture of *trans/trans* to *cis/trans* isomers in one reaction step could possibly be of use in producing pre-mixed blends of pheromones.

The Wittig reaction was therefore repeated at different temperatures to see how the isomeric ratio altered. The results are recorded in **Table 5**.

Table 5 Results of the Effect of Base and Temperature on the Stereochemistry of the Wittig Reaction

Base	Temp. for addition of Base(°C)	Stirred Temp. (°C)	Temp. for addition of aldehyde (°C)	Overnight temp. (°C)	Yield (%)	ZE:EE Ratio
NaHMDS	-78	RT	-78	RT	78	100:0
	-78	RT	-78	-25	53	100:0
	RT	RT	-78	RT	55	100:0
	RT	RT	-30	RT	63	100:0
BuLi	-78	0	-78	RT	69	50:50
	-78	0	-78	0 for 4hrs-RT	56	60:40
	-78	-20	-78	-25	66	80:20

The control of the overnight temperature in the butyllithium reaction, affected the ratio. Reducing the temperature allowed a greater proportion of the product to be *cis/trans*. The reaction vessel had been allowed to warm to room temperature after the aldehyde had been added and this gave a 50:50 ratio of E/E to Z/E. The experiment was repeated, reducing the overnight temperature to 0 °C for 4 hours after the aldehyde had been added and then the reaction vessel was left to warm to rt overnight. This gave the Z/E configuration in 60 % of the product, with 40 % of the E/E isomer. The reaction was repeated at a lower temperature, to see how the temperature effected the stereoselectivity of the reaction. As the temperature decreased the ratio of *cis* to *trans* altered. The *cis* isomer was dominant but there was still a notable amount of *trans* product. The reaction vessel was kept at–25 °C after the aldehyde was added and this resulted in a ratio of 8:2 in favour of the Z/E isomer.

The presence of a lithium salt and higher temperatures, this favours the Z/E isomer.

As the percentage of Z/E isomer is controllable by the use of base and the variation of temperature, this might be of use in producing the E,E conjugated aldehyde pheromones and also producing a blends of Z,E and E,E directly instead of synthesising both and then combining them after.

The reaction was also repeated using the base sodium bis(trimethylsilyl)amide. The reaction was repeated to try to increase the temperature at which the Wittig occurs. Finally, the base was added at room temperature, and the aldehyde added at –30 °C to give a reasonable yield of 63 %, with no change in isomer ratios.

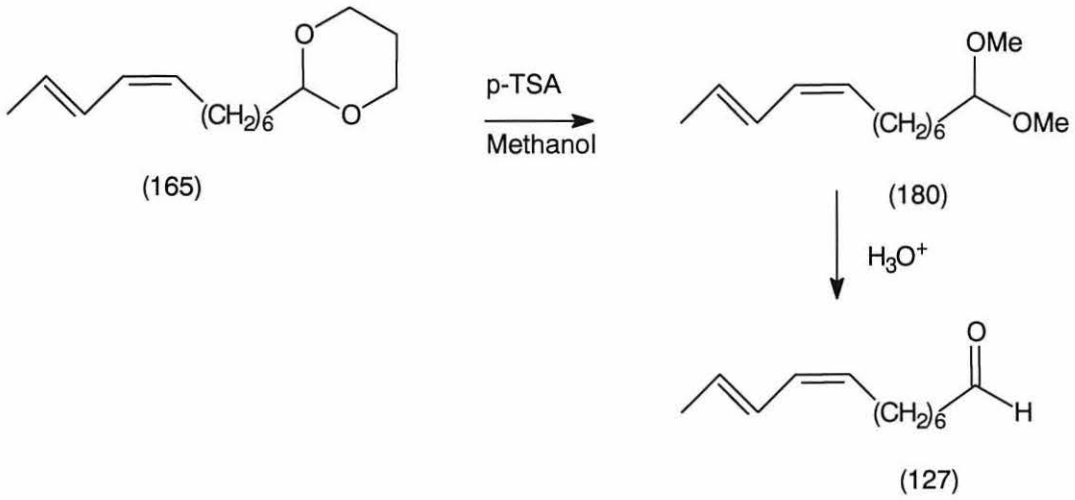


Figure 83

The protected aldehyde (**166**) was converted to a dimethyl acetal in 97 % yield. This allowed the aldehyde deprotected in mild conditions which left the *cis-trans* conjugated double bonds unaffected (**127**).

4.3.3 Conclusion and Further Work

The synthesis of (Z,E)-8,10-dodecadienal was successfully achieved with a synthesis that made use of ω-bromoaldehyde intermediate from the monounsaturated synthesis (Chapter 3). It was necessary to protect the aldehyde functionality with 1,3-propanediol, which gave the more resilient dioxane protecting group. The protected aldehyde could then withstand the conversion of the bromide to the Wittig salt. The unstable Wittig reaction could then proceed in good yields up to 80 %. Using sodium bis(trimethylsilyl)amide gave 100 % *cis* stereochemistry for the reaction. Unfortunately, increasing the temperature during the reaction only resulted in gaining lower yields.

Changing the base used in the experiments meant that the Wittig reaction gave a mixture of *cis* and *trans* isomers. Lowering the temperature of the reaction gave better control over the stereochemistry for the reaction. Perhaps the mixture of the isomers could be controlled so that this one reaction would produce either 100 % *trans-trans* or 100 % *cis-cis* product.

By selecting the base and varying the temperature, a wider range of pheromone products could be achieved from one reaction pathway.

The procedure for the synthesis of (Z,E)-8,10-dodecadienal should be adaptable for pheromones with the same conjugated system. The following conjugated *cis-trans* aldehyde pheromones are known and could be made by the same method:

(Z,E)-5,7-dodecadienal

(Z,E)-9,11-tetradecadienal

(Z,E)-9,11-hexadecadienal

(Z,E)-11,13-hexadecadienal

Figure 84 shows a retrosynthetic analysis of the remaining (Z,E) aldehyde pheromones. It gives the possible starting materials that would be used to achieve the synthesis of the full range of Z/E conjugated aldehyde pheromones.

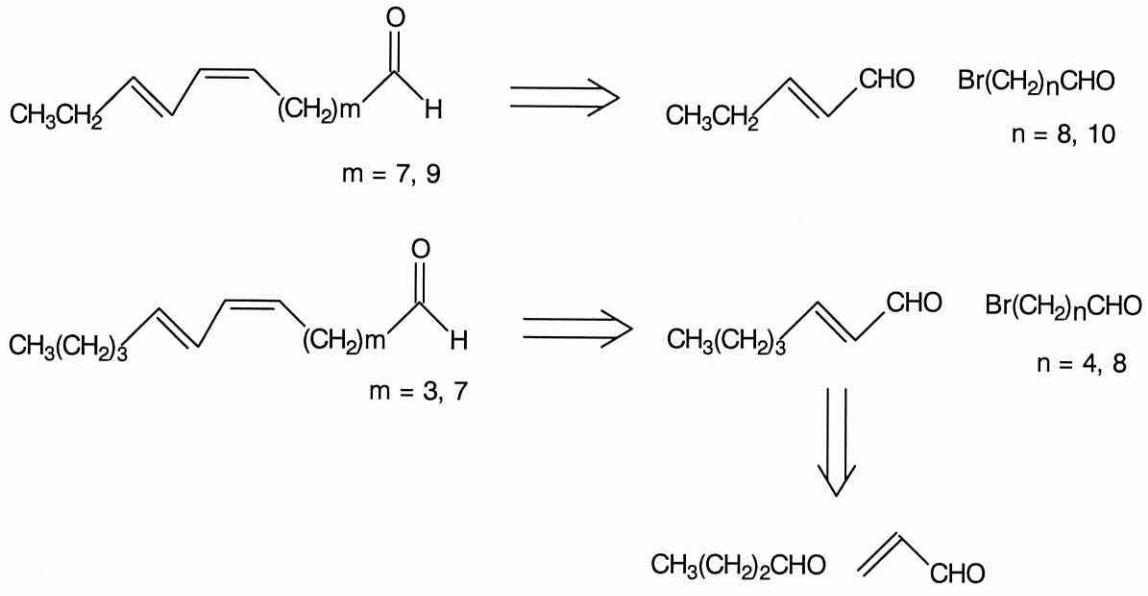


Figure 84

The (E)-2-aldehydes required here, could be produced by following the pathway to synthesis koiganal I (described earlier in this chapter).

4.4 (Z,Z) Conjugated Dienal Pheromones

4.4.1 Introduction

Routes to synthesis the Z,Z conjugated alcohol pheromones were reported by Bestmann in 1981.[69]

The first synthesis of the *cis-cis* conjugated pheromones used a Wittig to give the desired product. The synthesis used (Z)-2-aldehyde can easily isomerise to the *trans* form, giving E,Z as the major by-product.

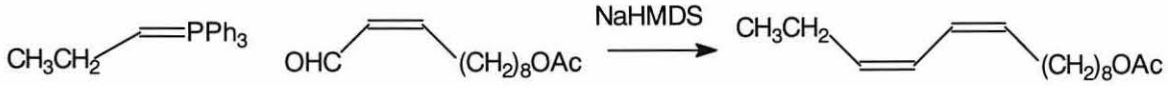


Figure 85

A second synthesis uses a Wittig to give the first *cis* double bond and the second is produced by the partial reduction of the triple bond using catecholborane in 66 % yield. [70]

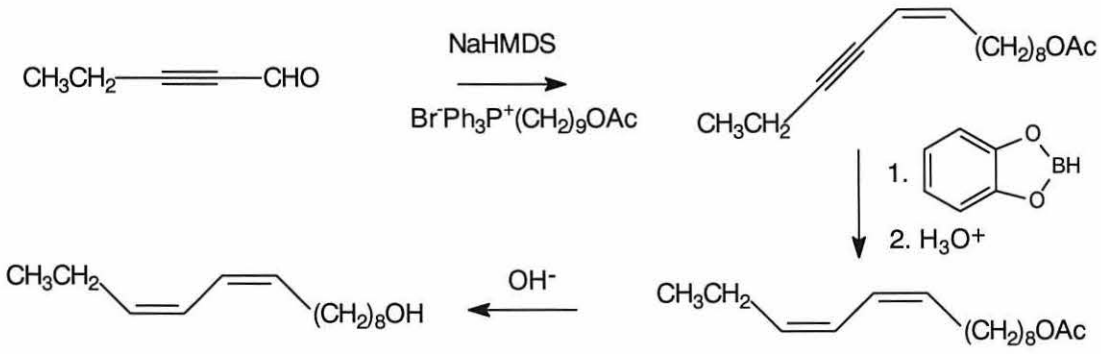
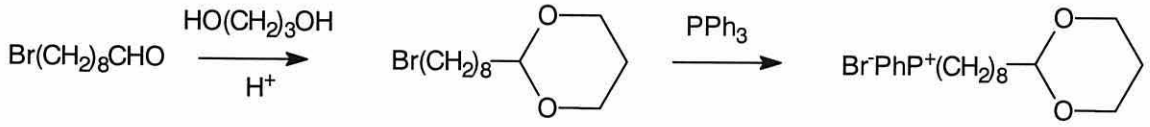


Figure 86

4.4.2 (Z,Z)-9,11-Tetradecadienal Synthesis

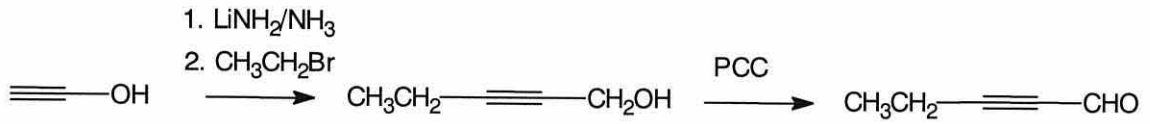
(Z,Z)-9,11-Tetradecadienal is one of six known conjugated cis-cis aldehyde pheromones. The synthesis of the *cis-cis* conjugated dienes followed a similar route to the to *cis/trans* conjugated pheromones (**4.3.2**). The Wittig salt of the bromodioxane was synthesised on reaction with triphenylphosphine in 63 % yield.



(143) (167) (168)

Figure 87

The aldehyde bromononanal (**143**) was protected with 1,3-propanediol to give the dioxane in 66 % yield. The dioxane (**167**) was then converted into 2-(octanyl)-1,3-dioxane-8-triphenylphosphonium bromide (**168**) on reflux with triphenylphosphine for 48 hrs in a yield of 63 %.



(169) (170)

Figure 88

Pent-2-ynal (**170**) was synthesised in two steps from propargyl alcohol (**Fig. 88**). First, the terminal acetylene was coupled with ethyl bromide using lithium amide in liquid ammonia. The product, pent-2-ynol (**169**), was then oxidised to the aldehyde in 56 % using PCC (PCC was used for convenience in the laboratory). This gave a simple ^{1}H NMR spectrum. The aldehyde proton was shown as a singlet at δ 9.16, the ethyl group as a three proton triplet at δ 1.22 and a two proton quartet at δ 2.42, with a coupling constant of 7.4 Hz between them.

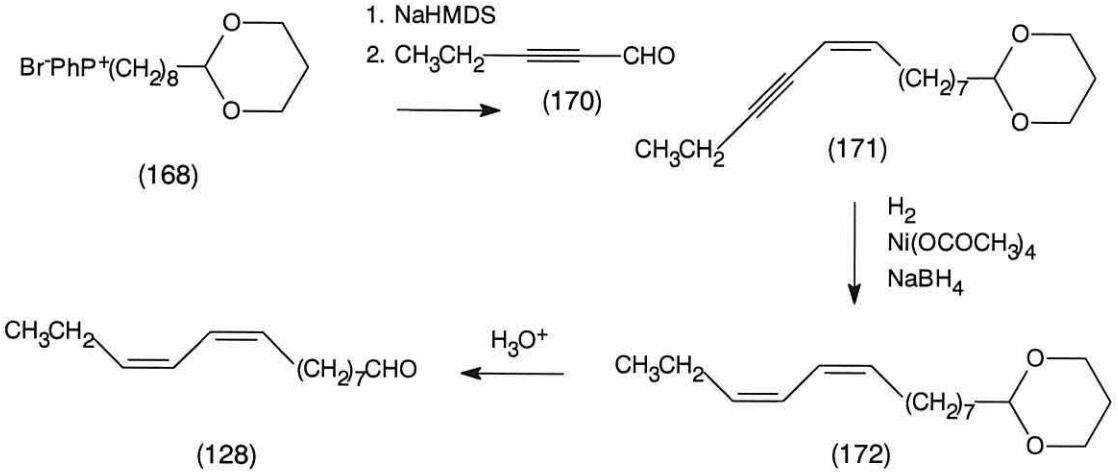


Figure 89

The two halves of the molecule were then reacted together. The ylide of the Wittig salt was produced by the addition of sodium bis(trimethylsilyl)amide at room temperature and the aldehyde was added after 1 hr at –78 °C. The reaction produced the *cis* product, 2-((Z)-8-tridecen-10-ynyl)-1,3-dioxane (**171**) but unfortunately the yield was quite low at 48 % which may possibly be increased on varying the reaction conditions. The ^{1}H NMR spectrum showed two protons in the olefinic region. A doublet of triplets appeared at δ 5.80 – the doublet giving the coupling constant across the *cis* double bond 10.3 Hz, and the triplet of 7.3 Hz to the alpha methylene group. The second proton at 4.43 was a narrow doublet of triplets with the long range coupling across the alkyne at 2.1 Hz. The ^{13}C NMR clarifies this, with two olefinic carbons, δ 109.2, δ 142.6 and the alkyne carbons at δ 77.5 and δ 96.2.

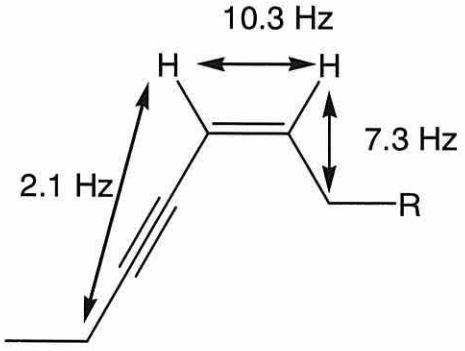


Figure 90

The alkyne was partially hydrogenated using nickel boride as catalyst to the *cis* product (**176**). The hydrogenation was achieved in a good yield of 83 %. The four protons appeared in two regions, with a doublet of doublets at δ 6.18 and a doublet of triplets at δ 5.39. The major coupling constant of 10.3 Hz was found in both regions, meaning that the hydrogenation did indeed lead to two *cis* conjugated double bonds, without any isomerisation. The ^{13}C NMR shows the four olefinic protons at δ 122.9, δ 123.4, δ 132.1 and δ 133.5.

4.4.3 Conclusion

The pheromone of (Z,Z)-9,11-tetradecadienal was synthesised as its propylene acetal in two steps from 2-(octanyl)-1,3-dioxane-8-triphenylphosphonium bromide (**168**).

The procedure was developed from the ω-bromo protected aldehyde made in the synthesis of monounsaturated aldehyde pheromones. The addition of two reaction steps the synthesis of the Wittig salt and its subsequent reaction allows for the production of possibly the full range of Z,Z aldehyde pheromones listed in the Appendix. It may be possible to synthesis the full range of pheromones by following the pathway described above. The Wittig reaction gave an unsatisfactory yield of 48 %. However, this yield should be able to be increased and give a method that maybe useful as a viable synthesis for *cis-cis* conjugated aldehyde pheromones. The deprotection of the aldehyde would follow the same procedure as used for the *cis-trans* aldehyde in Section 4.3.

4.5 (E,E) Conjugated Dienal Pheromones

4.5.1 Introduction

The synthesis of the sex pheromones of the Codling moth by the coupling of Grignard reagents using allylic halides was published by K. Mori in 1974.[71] (E,E)-8,10-Dodecadienol, was synthesised using 1,6-hexanediol and sorbic acid as starting materials. The diol was mono-brominated and the alcohol protected with DHP. Sorbic acid was reduced to sorbyl alcohol using $LiAlH_4$ and brominated to give sorbyl bromide. The Grignard of bromohexanol-THP was prepared and added to sorbyl bromide in THF-HMPA solution. When deprotected, gave the pheromone in 28 % yield.

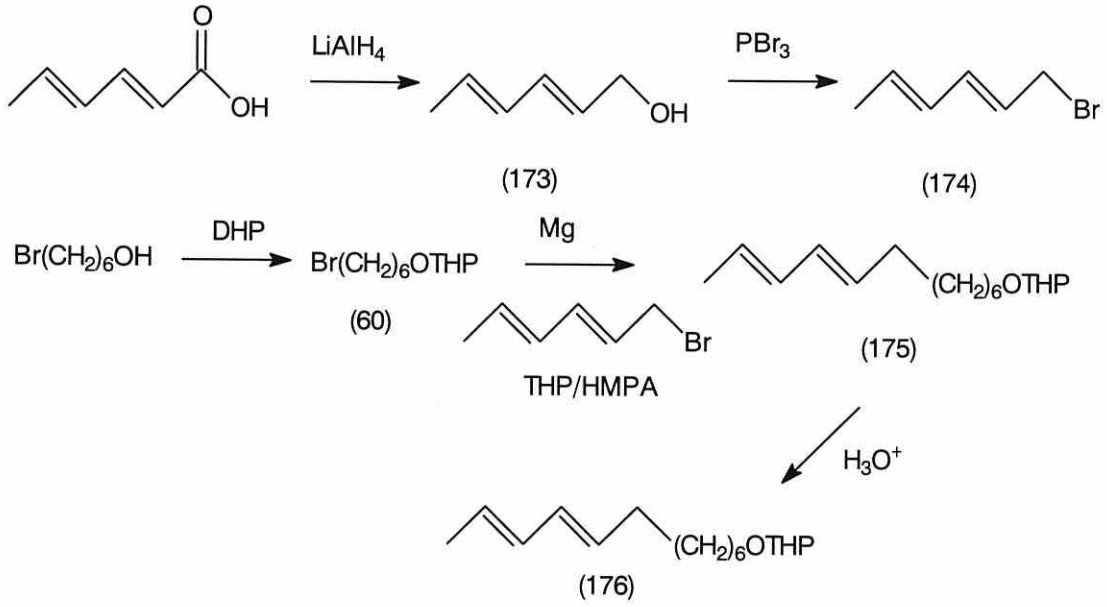


Figure 91

In 1978 Bestmann also synthesised (E,E)-8,10-dodecadienol (**176**) along with its acetate and aldehyde.[68] The procedure was similar, but avoided using HMPA as a solvent. The starting materials were the same, but instead of using sorbyl bromide, the sorbyl alcohol was converted to its acetate. Dilithium chlorocuprate was added to the Grignard reaction to soften the nucleophilic attack of the organometallic reagent. When deprotected, this gave the pheromone in 42 % yield. The aldehyde was synthesised on oxidation with PCC in 60 % yield.

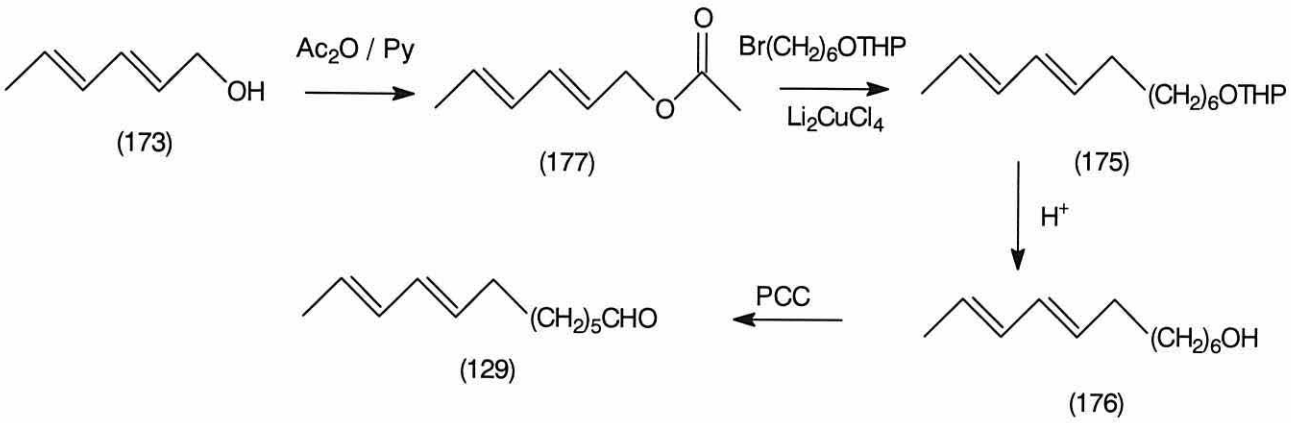


Figure 92

In 1987 the Bestmann's procedure was adapted to synthesise (E,E)-6,8-decadienal. 4-Bromobutyraldehyde diethyl acetal was coupled to sorbyl acetate in the presence of Li_2CuCl_4 in 62 % yield.[72]

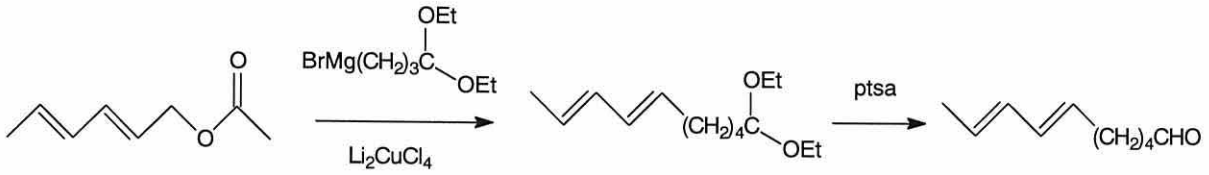


Figure 93

The synthesis of (E,E)-8,10-dodecadienal (**129**) was attempted from the precursor 2-(5-bromopentanyl)-1,3-dioxolane.

4.5.2 (E,E)-8,10-Dodecadienal

The first attempt to introduce a *trans-trans* conjugated functionality into a pheromone molecule was to use sorbyl bromide and couple it to a ω-bromoacetal. The retrosynthesis to the starting materials is shown in Fig 94. Sorbic acid was the starting material from which sorbyl bromide was made.

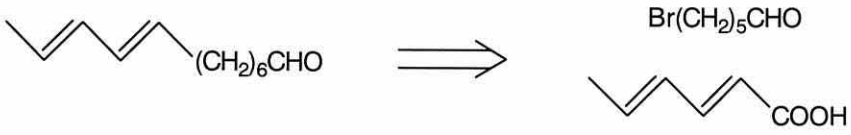


Figure 94

Sorbic acid is an inexpensive acid which contains the trans-trans double bonds in the correct position for the end of (E,E)-8,10-dodecadienal. Sorbic acid was easily reduced to the alcohol (E,E)-2,4-hexadien-1-ol (**173**) using lithium aluminium hydride in 91 % yield. The alcohol was converted to the 1-bromo (E,E)-2,4-hexadiene also in a good yield of 91 %. However, soon after the reaction, sorbyl bromide began decomposing, probably rearranged to its isomers (**182**) and (**183**) before decomposing (**Fig. 95**). This showed that the bromide was too unstable to work with. The alternative was the synthesis of the acetate from the alcohol.

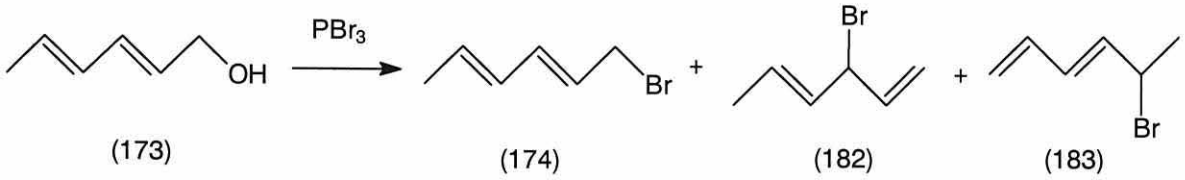
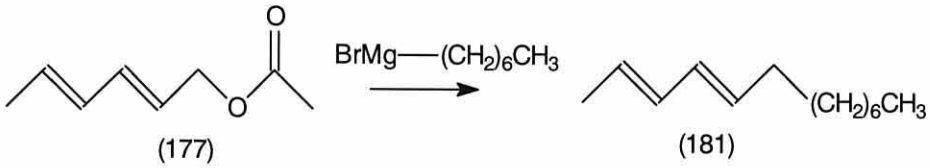


Figure 95

(E,E)-2,4-hexadien-1-ol (**173**) was reacted with triethylamine and acetyl chloride to produce the acetate in 90 % yield. The acetate proved to be much more stable and could survive some days at ambient temperature.

Figure 96

The Grignard coupling reaction was tested using sorbyl acetate and bromoheptane, replacing the bromoacetal. The Grignard of bromoheptane was produced on reaction with magnesium. The acetate reacted with the Grignard intermediate at low temperature in the presence of lithium chlorocuprate. (E,E)-2,4-tridecadiene was produced in a very good yield of 89 %.



(177) (181)

Figure 97

(E,E)-8,10-Dodecadienal was to be synthesised from the Grignard of ω-bromopentyl-1,3-dioxane with sorbyl acetate. The protected aldehyde was synthesised from 6-bromohexanoyl chloride by catalytic hydrogenation. The subsequent aldehyde was protected with 1,3-propanediol in case of any deprotection during the coupling reaction (**178**) was carefully reacted with magnesium to produce the Grignard. The Grignard was added to sorbyl acetate in the presence of dilithium chlorocuprate at low temperature just as in the test reaction. However, the reaction gave an unexpectedly low yield of 33 %. The results of the test reaction proved difficult to repeat when using (**178**). The protected aldehyde was not deprotected due to the low yield of the Grignard reaction.

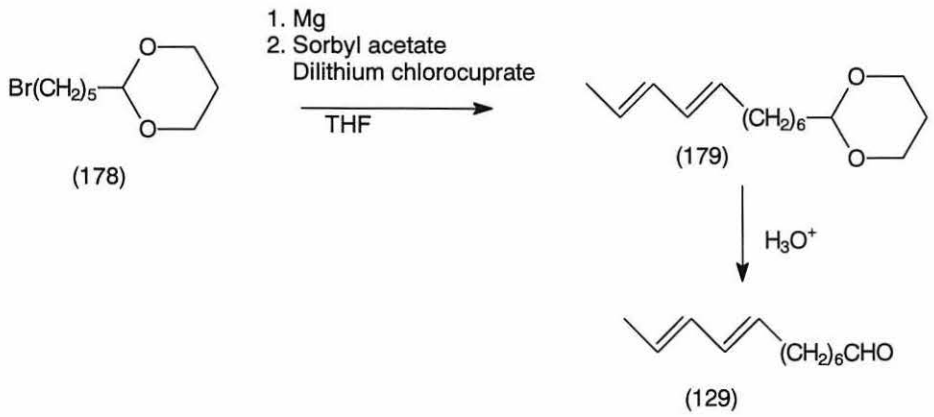


Figure 98

4.5.3 Conclusion and Further Work

The synthesis of *trans-trans* aldehydes needs further work to prove that the method would be successful. The proposed reaction pathway falls at the penultimate step of the Grignard coupling reaction. The reaction does work giving a low yield of 33 %. This must be increased for the procedure to be a viable method to these aldehyde pheromones.

Perhaps some factors in the reaction need to be altered in order to increase the yield. The formation of the Grignard may need extra time to form, or an increase in the equivalents of the reactants may be necessary. If successful then other *trans-trans* pheromones could be synthesised using this same pathway.

A general retrosynthesis of the *trans-trans* aldehydes given in **Fig. 99** to show the possible starting materials that could lead to the synthesis of all the pheromones in this range.

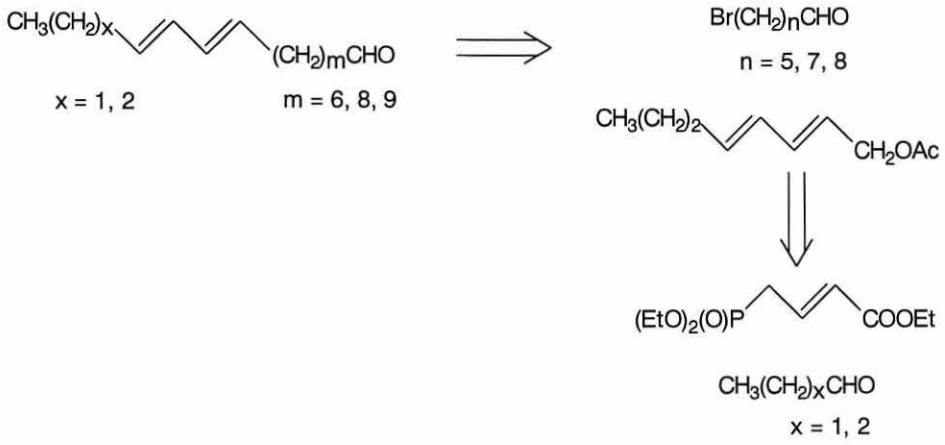


Figure 99

General Experimental Details

Reagents:

All reagents were obtained commercially and used without purification unless otherwise stated.

Solvents:

Solvents were purified when necessary using the methods suggested in "The Purification of Laboratory Chemicals" by D.D. Perrin, W.L.F. Armarego and D.R. Perrin. In particular, dicloromethane was distilled over calcium hydride, diethylether, tetrahydrofuran, and benzene were distilled over sodium wire. Ethanol was purified and dried by distillation from magnesium turnings containing iodine. Petrol refers to the fraction of petroleum spirit which boils between 40 and 60 °C.

Chromatography:

The purity of compounds were assessed by gas liquid chromatography or thin layer chromatography.

Thin layer chromatography was performed using Aldrich plates coated with silica gel 60 (F254). Compounds were visualised by examination under ultraviolet source or exposure to iodine vapour. Column chromatography was conducted using a Carlo Erba HRGC 5300 Mega series with a capillary column Perfin-Elmer Model F17 F.I.D., with nitrogen gas as a carrier. The gas liquid chromatography was carried out in the following conditions: 250 °C injection temperature, oven starting temperature 80°C, isothermal for one minute then ramped at 20°C to 200°C.

Analytical Methods:

Melting points were determined using a Gallenkamp apparatus and are uncorrected. Infrared spectra were obtained as liquid films on a Perkin-Elmer 1600 FTIR spectrometer. The GCMS were obtained using a Finnigan Mat 1020. Microanalyses were performed with a Calo-Erba Model 1106 CHN analyser. Some compounds have not had accurate mass measurements carried out on them due to decomposition whilst awaiting a quota on the EPSRC Mass Spectrometry service in Swansea.
Proton NMR spectra were recorded using a Bruker AC250 at 250 MHz. The carbon NMR spectra were also recorded using a Bruker AC250 at 62.9 MHz. All the samples were dissolved in $CDCl_3$ and run at room temperature.

Miscellaneous:

Reactions requiring anhydrous conditions were performed using oven dried glassware (250 °C) then were cooled under nitrogen and were carried out under a positive pressure of argon.

All yields are for purified compounds unless otherwise stated. Solids were purified by recrystallised, while oils were purified by chromatography or distillation. All new compounds were homogeneous by thin layer chromatography or gas liquid chromatography.

The term dried refers to the storage of a solution of he compound over anhydrous magnesium sulphate for at least one minute.

Kugelrohr distillations were carried out using a Buchi GKR 50. The term under reduced pressure refers to solvent removal on a Buchi rotary evaporator at vacuum pressure 14 mmHg at 30 to 60 °C or at *ca.* 1 mmHg at 25 °C to remove higher boiling solvents.

CHAPTER 5

Experimental

5.1 Saturated Aldehydes

Experiment 1

Dodecanal (45)

5 % Palladium on barium sulphate (0.13 g) was measured into a two necked flask. The flask was attached to a hydrogenator. Dry THF (15 ml) was injected through a septum into the flask. The contents was stirred vigorously, and the flask was evacuated using a water pump and filled with hydrogen. This procedure was repeated 3 times. The flask was left to equilibrate for 15 mins. 2,6-Lutidine (0.53 ml, 0.5 g, 4.5×10^{-3} mole, 1 mol. eq.) was injected, followed by dodecanoyl chloride (1.0 g, 4.5×10^{-3} mole, 1 mol. eq.). Hydrogen uptake began almost immediately. Absorption (90 ml) was complete in 2 hrs. The catalyst was removed by the filtration through silica with ether, the organic layer and was washed with water to remove the 2,6-lutidine salt. The organic solvents were dried with $MgSO_4$ and evaporated, to leave the product, dodecanal. This showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to those the literature.[45]

Yield:	0.7 g, 96 %.
^1H NMR:	δ 0.8 (3 H, t, J 6.9 Hz), 1.3 (16 H, m), 1.6 (2 H, p, J 7.3 Hz), 2.4 (2 H, dt, J 1.8, 7.3 Hz), 9.75 (1 H, t, J 1.8 Hz).
^{13}C NMR:	δ 14.0, 20.2, 20.3, 22.0, 29.1, 29.2, 29.3, 31.8, 43.9, 202.8.
$\nu_{(max)}$:	2925s, 2857s, 1727s, 1466, 1414, 1034w cm^{-1}.

Experiment 2

Tetradecanal (46)

The experimental procedure was followed as for experiment 1, but instead using myristoyl chloride (0.5 g, 2.0 $x10^{-3}$ mole), with 2,6-lutidine (0.23 ml, 0.27 g, 2.0 x 10^{-3} mole) and 5 % $Pd/BaSO_4$ (0.06 g). The product tetradecanal, a white semi-solid, which showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[73]

Yield: 0.35 g, 81 %.

^1H NMR: δ 0.87 (3 H, t, J 6.5 Hz), 1.25 (20 H, m), 1.62 (2 H, pent, J 7.2 Hz), 2.41 (2 H, dt, J 7.2, 1.8 Hz), 9.75 (1H, t, J 1.8 Hz).

^{13}C NMR: δ 14.1, 22.0, 22.6, 29.1, 29.3, 29.4, 29.5, 29.6, 31.8, 43.8, 202.8.

$\nu_{(max)}$: 2921s, 2712s, 1728s, 1466s, 1410m, 1377m, 1065m, 1032m cm^{-1}.

Experiment 3

Hexadecanal (47)

The experimental procedure was followed as for experiment 1, using palmitoyl chloride (5 g, 0.0182 mole), 2,6-lutidine (2.11 ml, 1.95 g, 0.0182 mole) and 5 % $Pd/BaSO_4$ (0.54 g). The product hexadecanal, a soft white solid, showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[73]

Yield: 4.6 g, 94 %.

^1H NMR: δ 0.82 (3 H, t, J 6.8 Hz), 1.25 (24 H, m), 1.62 (2H, pent, J 7.2 Hz), 2.42 (2 H, dt, J 7.2, 1.8 Hz), 9.65 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 14.08, 22.06, 22.66, 29.14, 29.33, 29.40, 29.56, 29.64, 29.84, 31.90, 43.89, 202.93.

$\nu_{(max)}$: 2910s, 2747m, 1710s, 1470s, 1410s, 1391s, 717s cm^{-1}.

Experiment 4

Octadecanal (48)

The experimental procedure was as for experiment 1, using stearoyl chloride (5 g, 0.0165 mole), 2,6-lutidine (1.91 ml, 1.76 g, 0.165 mole) and 5 % $Pd/BaSO_4$ (0.49 g). The product, octadecanal, was a white solid with a m.p. of 44 - 46 °C, and showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[45]

Yield: 4.18 g, 93 %.

^1H NMR: δ 0.89 (3 H, t, J 6.8 Hz), 1.26 (14 H, m), 1.63 (2 H, pent, J 7.2 Hz), 2.43 (2H, dt, J 1.85, 7.2 Hz), 9.77 (1H, t, J 1.85 Hz).

^{13}C NMR: δ 14.09, 22.07, 22.67, 29.15, 29.34, 29.41, 29.57, 29.66, 31.91, 43.89, 202.92.

$\nu_{(max)}$: 2920s, 2851s, 1727s, 1464m, 1071s, 911m cm^{-1}.

5.2 Monounsaturated Aldehydes by Double Reduction

Experiment 5

Dec-2-yn-1-ol (49)

Liquid ammonia (500 ml) was condensed into a 1 litre 3 necked flask using a liquid nitrogen/methylated spirits condenser. A mechanical stirrer was used as a means of agitation. Ferric nitrate (0.72 g, 1.7 x 10^{-3} mole, 0.0025 mol. eq.) was added and left for 10 mins. lithium wire (8.1 g, 1.17 mole, 2.2 mol. eq.) was cut to 0.5 cm pieces and added over 0.5 hr, and stirred for 0.5 hr. Propargyl alcohol (30.0 g, 0.53 mole, 1 mol. eq.) in dry ether (15 ml) was added dropwise over 0.5 hr. Followed by bromoheptane (85.0 g, 0.48 mole, 0.9 mol. eq.) in dry ether (50 ml), added dropwise over 0.5 hr. Stirring continued for 4 hrs after which the condenser was removed to allow the ammonia to evaporate overnight. This left a black sludge, which was acidified to pH 1with 10 % H_2SO_4 (350 ml). The product was extracted with ether (4 x 250 ml), washed with sat. aq. sodium bicarbonate (200 ml) and dried with

magnesium sulphate, and the solvents evaporated. The product was chromatographed on silica using the eluent petrol/ether (5:2), to give *dec-2-yn-1-ol*[74] as a colourless oil.

Yield: 47 g, 57 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.8 Hz), 1.28 (8 H, m), 1.5 (2 H, q, J 7.3 Hz), 1.92 (1 H, OH), 2.2 (2 H ,tt, J^1 6.8, J^2 2.8 Hz), 4.26 (2 H, t, J 2.0 Hz).

^{13}C NMR: δ 14.05, 18.7, 22.6, 28.59, 29.5, 31.7, 51.31, 78.2, 86.5.

$\nu_{(max)}$: 3332br, 2928 s, 2856 s, 2225w, 1465, 1137, 1015s cm^{-1}.

Experiment 6

Dec-9-yn-1-ol (50)

Lithium wire (12.2 g, 1.7 mole, 6 mol. eq.) was added to dry 1,3-diaminopropane (400 ml) and stirred for 0.5 hrs giving the reaction flask a blue colouration. The mixture was heated to 70 °C until the blue colour was discharged (1.5 hrs). The reaction vessel was cooled to room temperature, then potassium *t*-butoxide (136.8 g, 1.2 mole, 4 mol. eq.) was added and stirred for 20 mins. Dec-2-yn-1-ol (47 g, 0.258 mol, 1 mol. eq.) in dry ether, was added dropwise. The reaction mixture was stirred for 45 mins and then cooled to 0 °C before quenching. The flask was poured very carefully onto ice (1 kg) and the product was extracted with ether (3 x 200 ml). The solvent was dried with $MgSO_4$ and evaporated, to give the product *dec-9-yn-1-ol*[75] as a colourless oil.

Yield: 33.4 g, 71 %.

^{1}H NMR: δ 1.32 (6 H, m), 1.55 (4 H, m), 1.85 (1 H, OH), 1.93 (1 H, t, J 2.7 Hz), 3.6 (2 H, t, J 6.65 Hz).

^{13}C NMR: δ 18.3, 25.7, 28.4, 28.6, 29.0, 29.2, 32.7, 62.9, 68.1, 84.7.

$\nu_{(max)}$: 3311br, 2931s, 3116s, 1464s, 1055s cm^{-1}.

Experiment 7

Dodec-9-yn-1-ol (51)

Experiment 5 was repeated but using, liquid ammonia (500 ml), ferric nitrate (0.22 g, 5.4×10^{-4} mole, 0.0025 mol. eq.), dec-9-yn-1-ol (33 g, 0.2 mole, 1 mol. eq.) and bromoethane (52 g, 0.5 mole, 2.5 mol. eq.). The product was columned in petrol/ether (5:2) and the solvents were evaporated to give the *dodec-9-yn-1-ol*[76] as a colourless oil.

Yield: 28.7 g, 72.7 %.

^{1}H NMR: δ 1.13 (3 H, t, J 7.5 Hz), 1.4 (14 H, m), 1.7 (OH), 2.15 (4 H, dt, J^1 7.5, J^2 1.9 Hz), 3.65 (2 H, t, J 7.5 Hz).

^{13}C NMR: δ 12.3, 13.97, 18.6, 26.0, 28.4, 28.6, 28.7, 29.2, 29.6, 32.6, 62.7, 79.4, 81.5.

$\nu_{(max)}$: 3361br, 2930s, 2855s, 1460, 1058 cm^{-1}.

Experiment 8

1-Bromo-9-dodecyne (52)

Dodec-9-yn-1-ol (14 g, 0.057 mole, 1 mol. eq.) in dry ether (300 ml), was stirred with carbon tetrabromide (38.26 g, 0.11 mol, 1.3 mol. eq.) and triphenylphosphine (30.26 g, 0.115 mole, 1.3 mol. eq.) in an ice bath for 15 mins and then at room temperature for 3 hrs. The reaction was followed by TLC using petrol/ether (5:0.5). The product was separated from the reaction mixture by filtration through a bed of silica. Chromatography with silica eluting with petrol/ether (5:2) gave 1-bromo-9-dodecyne as a colourless oil.

Yield: 15.18 g, 80 %

^{1}H NMR: δ 1.13 (3 H, t, J 7.4 Hz), 1.34 (10 H, m), 1.87 (2 H, q, J 6.9 Hz), 2.16 (4 H, dt, J^1 7.4 Hz, J^2 2.0 Hz), 3.43 (2 H, t, J 6.9 Hz).

^{13}C NMR: δ 12.4, 14.4, 18.7, 28.4, 28.6, 28.7, 38.9, 29.0, 32.8, 34.0, 79.4, 81.6.

$\nu_{(max)}$: 2931s, 2854s, 2228w, 1460, 1436 cm^{-1}.

m/z: M^+: 244

Experiment 9

Optimisation of Diethylmalonate Coupling and Subsequent Decarboxylation.

Test 1

Sodium ethoxide was produced from super dry ethanol (50 ml), (absolute ethanol was refluxed for 30 mins with magnesium turnings before being distilled), and sodium pieces (0.61 g, 26.5 mole, 1 mol. eq.). The ethanol was added slowly to the sodium in a 2-necked round bottomed flask with condenser. This was cooled in an ice bath due to vigorous reaction. Diethyl malonate (4.24 g, 26.5 mmole, 1.1 mol. eq.) was added to the sodium ethoxide dropwise over 15 mins. The mixture was stirred for 10 mins before the addition of bromononane (5 g, 24 mmole, 1 mol. eq.). The flask was refluxed for 4 hrs. On cooling, the product was extracted from the ethanol by dilution with water (150 ml) and extracted with dichloromethane (3 x 50 ml). The solvents were dried and evaporated to leave *nonylmalonic acid diethyl ester*[77] as a colourless oil.

Yield: 5.6 g, 81 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.7 Hz), 1.27 (18 H, m), 1.87 (2 H, m), 3.31 (1 H, t, J 7.5 Hz), 4.19 (4 H, q, J 7.1 Hz).

$\nu_{(max)}$: 2926s, 2858s, 1732s, 1464s, 1368s cm^{-1}.

Test 2

Test 1, was repeated, changing the quantity of sodium.

Sodium (0.83 g, 36 mmole, 1.5 mol. eq.), diethyl malonate (4.24 g, 26.5 mmole, 1.1 mol. eq.), bromononane (5 g, 24 mmole, 1 mol. eq.).

Yield: 5.4 g, 78 %.

Test 3

Test 1 was repeated, changing the quantity of sodium.

Sodium (1.11 g, 48 mmol, 2 mol. eq.), diethyl malonate (4.24 g, 26.5 mmol, 1.1 mol. eq.), bromononane (5 g, 24 mmol, 1 eq.).

Yield: 4.5 g, 65 %.

Test 4

Test 1 was repeated, changing the quantity of sodium and using bromohexane instead of bromononane.

Sodium (0.76 g, 33 mmol, 1.1 equiv.), diethyl malonate (5.3g, 33 mmol, 1.1 equiv.) bromohexane (5 g, 30 mmol, 1 equiv.)

Yield: 6.1 g, 82 %.

Test 5

Test 1 was repeated, changing the quantity of sodium.

Sodium (1.04 g, 45.4 mmole, 1.5 mol. eq.), diethyl malonate (5.3 g, 33 mmol, 1.1 mole. eq.), bromohexane (5 g, 30 mmole, 1 equiv.).

Yield: 5.88 g, 79 %.

Test 6

Experiment test 1 above, was repeated, changing the quantity of sodium.

Sodium (1.11 g, 60.5 mmole, 2 mol. eq.), diethyl malonate (5.3 g, 33 mmole, 1.1 mol. eq.), bromohexane (5 g, 30.2 mmole, 1 mol. eq.)

Yield: 4.06 g, 55 %.

Decarboxylation

Nonylmalonic acid diethyl ester (14.0 g) was refluxed with potassium hydroxide (20 g) in water in (100 ml). The diacid was recovered from the reaction on acidification with sulphuric acid (10 %) and extracted with dichloromethane (2 x 20 ml). The solvent was extracted and dried with $MgSO_4$. The solvent was evaporated to give the product nonylmalonic acid.

Yield: 9.8 g, 87 %.

Nonylmalonic acid (1.0 g) was refluxed for 24 hrs at 100 °C in water (10 ml) in two acids at 3 different concentrations to find optimum reaction conditions. (See Table)

Citric acid (20 %), (40 %), (60 %).

Hydrochloric acid (5 %), (10 %), (20 %).

The mono acid was extracted with dichloromethane (3 x 30 ml), dried with $MgSO_4$ and evaporated to give undecanoic acid as a white solid, melting point 31 - 33 °C.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.27 (14 H, m), 1.64 (2 H, pent, J 7.3 Hz), 2.3 (2 H, t, J 7.3 Hz).

Table 6 Decarboxylation of nonylmalonic acid under different acidic conditions.

% Citric acid Concentration	w/w % Yield	% HCl Concentration	w/w % Yield
20%	95 %	5%	90 %
40 %	92 %	10%	95 %
60%	97 %	20 %	92 %

Experiment 10

Dodec-9-ynylmalonic acid diethyl ester (53)

Sodium ethoxide was produced from super dry ethanol (100 ml), (absolute ethanol was dried with magnesium turnings, refluxed for 30 mins. and then distilled), and sodium pieces (1.40 g, 0.6 mole, 1 mol. eq.). The sodium was added slowly to ethanol in a 2 necked round bottomed flask with condenser. This was cooled in an ice bath due to vigorous reaction. Diethyl malonate (12 ml, 0.75 mole, 1 mol. eq.) was added to the ethoxide dropwise over 15 mins. 1-Bromododec-10-yne (15.8 g, 0.06 mole, 1 mol. eq.) was then added over 15 mins. The mixture was refluxed for 2 hrs until the solution reached a neutral pH. The ethanol was removed by distillation on the rotary evaporation. The product was obtained by dilution with water (150 ml) and extraction with dichloromethane (3 x 50 ml). The solvents were dried and evaporated to leave *dodec-9-ynylmalonic acid diethyl ester*.

Yield:	14.25 g, 75 %.
^{1}H NMR:	δ 1.09 (3 H, t, J 7.2 Hz), 1.27 (6 H, t, J 7.5 Hz), 1.3 (12 H, m), 1.82 (2 H, dt, J 7.2 Hz), 2.16 (4 H, m), 3.31 (1 H, t, J 7.2 Hz), 4.19 (4 H, q, J 7.5 Hz).
^{13}C NMR:	δ 12.4, 14.05, 14.3, 18.7, 27.2, 28.6, 28.7, 28.9, 29.1, 29.2, 52.0, 61.2, 79.4, 81.6, 169.5.
$\nu_{(max)}$:	2924s, 1731s, 1736s 1464, 1369, cm^{-1}.
m/z:	M^{+}: 304

Experiment 11

Dodec-9-ynyl malonic acid (54)

Dodec-9-ynyl malonic acid diethyl ester (14.2 g, 0.04 mole) was added to a hot solution of 50 % aqueous potassium hydroxide (70 ml). The reaction mixture was gently refluxed for 3 hrs. The di-acid was acidified to pH 1 with 10 % H_2SO_4 and extracted with dichloromethane (3 x 200 ml), dried with $MgSO_4$ and rotary evaporated, to give the diacid with a melting point of 122- 124 °C.

Yield: 2.4 g, 82 %

^{1}H NMR: δ 1.0 (3 H, t, J 7.2 Hz), 1.4 (12 H, m), 1.95 (2 H, dt, J 7.5 Hz), 5 (4 H, m), 3.43 (1 H, t, J 7.5 Hz), 9.00 (2 H, OH).

^{13}C NMR: δ 12.4, 14.3, 18.7, 24.6, 28.8, 29.0, 29.1, 29.3, 33.9, 51.4, 75, 81.6, 174.6, 179.8.

$\nu_{(max)}$: 3020br, 2925s, 2825s, 2345w, 1698s cm^{-1}.

Experiment 12

11-Tetradecyn-1-oic Acid (55)

11-Tridecyne-1,1-dioic acid (2.40 g, 8.9 x 10^{-3} mole, 1 mol. eq.) was refluxed for 12 hrs. at 100 °C in aqueous citric acid (50 ml, 60 %). The mono-acid was extracted with dichloromethane (2 x 20 ml), dried with $MgSO_4$ and evaporated to give *11-tetradecyn-1-oic acid*[78] as a soft white solid.

Yield: 2.07 g, 86 %.

^{1}H NMR: δ 1.02 (3 H, t, J 7.2 Hz), 1.25 (14 H, m), 1.65(2 H, q, J 7.2 Hz), 2.1 (4 H, m), 2.35 (2 H, t, J 7.2 Hz).

Experiment 13

11-Tetradecyn-1-oyl Chloride (58)

11-Tetradecyn-1-oic acid (1.55 g, 6.92 x 10^{-3} mole, 1 mol. eq.) was added slowly to thionyl chloride (20 ml) and refluxed gently for 30 mins. The thionyl chloride was distilled off (76 °C) at atmospheric pressure, and the product was then distilled pure (b.p. 147 - 150 °C, 0.1 mm Hg).

Yield: 1.19 g, 71 %.

^{1}H NMR: δ 1.06 (3 H, t, J 7.2 Hz), 1.25 (14 H, m), 1.65 (2 H, pent, J 7.2 Hz), 2.09 (4 H, m), 2.8 (2 H, t, J 7.2 Hz).

^{13}C NMR: δ 12.4, 14.38, 18.7, 25.03, 28.7, 29.0, 29.07, 29.17, 47.09, 79.52, 81.66, 173.87.

$\nu_{(max)}$: 2973s, 2931s, 2855s, 1799s, 1460, 951 cm^{-1}.

Experiment 14

(Z)-3-Hexen-1-ol (57)

The experimental procedure was repeated as for Experiment 1, but using 5 % $Pd/BaSO_4$ (0.15 g), dry THF (15 ml), 2,6-lutidine (0.55 g, 5.14 x 10^{-3} mole), and quinoline (0.1 ml, 6.97 x 10^{-4} mole). Hex-3-yn-1-ol (0.5 g, 5.09 x 10^{-3} mole) was added dropwise to the stirred solution. Hydrogen (125 ml) was absorbed in 0.5 hr. (Z)-3-Hexen-1-ol showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature. [79]

Yield: 0.5 g, 98 %.

^1H NMR: δ 0.93 (3 H, t, J 7.3 Hz), 2.04 (2 H, p, 7.3 Hz), 2.28 (2 H, q, J 6.6 Hz), 3.60 (2 H, t, J 6.6 Hz), 5.26-5.63 (2 H, m).

^{13}C NMR: δ 13.95, 20.57, 24.24, 30.71, 61.95, 62.06.

$\nu_{(max)}$: 3429br, 3062w, 2973s, 2859s, 1593s, 1579s, 1453s, 1068s cm^{-1}.

Experiment 15

(Z)-11-Tetradecenal (59)

The experimental procedure was repeated as for Experiment 1, but using 5 % $Pd/BaSO_4$ (0.05 g), THF (15 ml), 2,6-lutidine (0.177 g, 1.65x10^{-3} mol, 1mol. eq.) and quinoline (0.05 g, 3.49 x 10^{-3} mol). Tetradec-11-yn-1-oyl chloride (0.4 g, 1.65 x 10^{-3} mol, 1 mol. eq.) was added dropwise. Hydrogen (40 ml) was absorbed in 4 hrs. The mixture was filtered through silica and the solvents were evaporated. The residue was columned with petrol/ether (5:2) and evaporated to give *(Z)-11-tetradecenal*[80] a colourless oil.

Yield: 0.1 g, 30 %.

^1H NMR: δ 0.95 (3 H, t, J 7.5 Hz), 1.29 (14 H, m), 1.63 (2 H, p, J 7.2 Hz), 2.02 (2 H, dq, J 5.7, 7.5 Hz), 2.41 (2 H, dt, J 1.87, 7.2 Hz), 5.33 (2 H, dt, J 5.7, 3.1 Hz), 9.76 (1 H, t, J 1.87 Hz).

^{13}C NMR: δ 14.4, 20.5, 22.0, 22.6, 27.0, 29.1, 29.2, 29.3, 29.7, 31.7, 129.2, 131.5, 202.9.

Experiment 16

1-Bromohexan-6-ol

Hexanediol (120 g, 1.01 moles) was dissolved in aqueous hydrobromic acid (48 %, 1 L). The solution was put into continuous extraction apparatus and toluene (1 L) was refluxed so as to cycle through the apparatus for 18 hrs. The toluene was evaporated, and *1-bromohexan-6-ol*[81] was purified by distillation (b.p. 58 °C, 0.05 mm Hg).

Yield:	165 g, 91 %.
^{1}H NMR:	δ 1.42 (4 H, m), 1.55 (2 H, Br, m), 1.79 (1 H, s, br), 2.88 (2 H, m), 3.48 (2 H, t, J 6.8 Hz), 3.63 (2 H, t, J 6.6 Hz).
^{13}C NMR:	δ 24.9, 27.9, 32.4, 32.7, 33.8, 62.6.
$\nu_{(max)}$:	3354br, 2931s, 2860s, 1460m, 1437m, 1260m, 1049s cm^{-1}.

Experiment 17

2-(6-Bromohexanyloxy)tetrahydropyran (60)

2,3-Dihydropyran (7.5 g, 0.088 mole, 1.3 mol. eq.) was added to an ice cooled solution of 1-bromohexan-6-ol (12.3 g, 0.067 mole, 1 mol. eq.) and pyridinium *p*-toluene sulphonic acid (1.7 g, 6.79 x 10^{-3} mole, 0.1 mol. eq.) in dry dichloromethane (60 ml). The mixture was stirred at ambient temperature for 18 hrs. The product mixture was washed with water, dried and the volatile solvents were evaporated to leave a brown oil. Chromatography with petrol/ether (5:2) gave *2-(6-bromohexanyloxy)tetrahydropyran*[82] as a colourless oil.

Yield:	18 g, 98 %.
^{1}H NMR:	δ 1.54 (14 H, m), 1.88 (2 H, pent, J 6.8 Hz), 3.37 (1 H, m), 3.42 (2 H, t, J 6.8 Hz), 3.42 (2 H, t, J 6.8 Hz), 3.51 (1 H, m), 3.74 (1 H, dt, J 9.6, 6.7 Hz) 4.81 (1 H, t, J 3.9 Hz).
^{13}C NMR:	δ 18.3, 25.7, 28.4, 28.7, 28.9, 29.0, 29.1, 32.7, 36.0, 68.0, 114.1.
$\nu_{(max)}$:	2837s, 2865s, 1453s, 1352s, 1135s, 1077s, 1033s cm^{-1}.

Experiment 18

2-(Dodec-7-ynyloxy)tetrahydropyran

The experimental procedure was repeated as for Experiment. 7, (6-bromohexanyloxy) tetrahydropyran (18.0 g, 0.065 mole, 1 mol. eq.), lithium amide (9.0 g, 0.39 mole, 6 mol. eq.) and 1-hexyne (6.47 g, 0.078 mole, 1.2 mol. eq.). The product showed one peak by g.l.c.. [83]

Yield: 14.2 g, 79 %

^{1}H NMR: δ 0.91 (3 H, t, J 7.1 Hz), 1.3-1.8 (18 H, m), 3.39 (4 H, m), 3.39 (1 H, dt, J 9.5, 6.5 Hz), 3.49 (1 H, m), 3.73 (1 H, dt, J 9.5, 6.5 Hz), 3.87 (1 H, m), 4.85 (1 H, t J 3.9 Hz).

$\nu_{(max)}$: 2933s, 2859s, 2361w, 1465m, 1352m,1136m, 1120m, 178m, 1033s cm^{-1}.

Experiment 19

Dodec-7-cyn-1-ol (61)

2-(Dodec-7-ynyloxy)tetrahydropyran (14 g, 0.507 mole, 1 mol. eq.) and *p*-toluenesulphonic acid (2.42g, 0.01 mole, 0.2 mol. eq.) were stirred in ethanol (100 ml) and refluxed gently for 24 hrs. On work up, water (100 ml) was added and the product extracted with dichloromethane (3 x 50 ml) The solvents were dried with $MgSO_4$ and evaporated to leave the crude product, which was columned on silica eluting with petrol/ether (5:2).

Yield: 8.2 g, 86 %.

^{1}H NMR: δ 1.1 (3 H, t, J 7.5 Hz), 1.4 (14 H, m), 1.7 (1 H, OH), 2.15 (4 H, dt, J 7.5, 1.9 Hz), 3.65 (2 H, t, J 7.5 Hz).

^{13}C NMR: δ 12.3, 13.9, 18.6, 26.1, 28.4, 28.6, 28.7, 29.2, 29.6, 32.6, 62.7, 79.4, 81.5.

$\nu_{(max)}$: 3361br, 2930s, 2855s, 1460m, 1058s cm^{-1}.

Experiment 20

1-Bromo dodec-7-yne (63)

Carbon tetrabromide (15.0 g, 0.066 mole, 1.5 mol. eq.) was dissolved in dry ether (120 ml) under an argon atmosphere. The reaction vessel was cooled to 0 °C and triphenylphosphine (17.3 g, 0.066 mole, 1.5 mol. eq.) was added which turned the mixture an opaque white colour. The mixture was stirred for 15 mins, then dodec-7-yn-1-ol (8.0 g, 0.044 mole, 1 mol. eq.) was added and the reaction was stirred for 1.5 hrs and then worked up by adding petrol (70 ml), and filtered through silica. The solvents were evaporated to give 1-bromododec-7-yne as a colourless oil.

Yield:	7.6 g, 70 %.
^{1}H NMR:	δ 1.13 (3 H, t, J 7.4 Hz), 1.34 (10 H, m), 1.87 (2 H, q, J 6.9 Hz), 2.16 (4 H, dt, J 7.4, 2.0 Hz), 3.43 (2 H, t, J 6.9 Hz).
^{13}C NMR:	δ 12.4, 14.37, 18.7, 28.38, 28.63, 28.7, 38.9, 29.0, 32.78, 34.0,79.4, 81.6.
$\nu_{(max)}$:	2931s, 2854s, 2228w, 1460, 1436 cm^{-1}.
m/z:	M^+: 244, M^+-Br: 165

Experiment 21

Dodec-7-ynyl malonic acid diethyl ester (64)

Sodium ethoxide was produced from super dry ethanol (50 ml), and sodium pieces (0.51 g, 0.022 mole, 1.1 mol. eq). The ethanol was added slowly to the sodium in a 2-necked round bottomed flask with condenser. This was cooled in an ice bath due to vigorous reaction. Diethyl malonate (3.92 g, 0.024 mole, 1.2 mol. eq.), was added to the sodium ethoxide dropwise over 15 mins. The flask was stirred for 10 mins before the addition of 1-bromo-dodec-7-yne (5.0 g, 0.0204 mole, 1 mol. eq.). The mixture was refluxed for 4 hrs. On cooling, the product was diluted with water (150 ml) and extracted with dichloromethane (3 x 50 ml). The solvents were dried and evaporated to leave the product *dodec-7-ynyl malonic acid diethyl ester.*

Yield: 4.1 g, 62 %.

^{1}H NMR: δ 0.91 (3 H, t, J 6.8 Hz), 1.44-1.24 (18 H, m), 1.91 (2 H, m), 2.14 (4 H, m), 3.31 (1 H, t, J 7.5 Hz), 4.21 (4 H, q, J 7.1 Hz).

^{13}C NMR: δ 13.6, 14.1, 18.4, 18.6, 21.9, 28.5, 28.6, 28.7, 28.9, 31.2, 52.0, 61.2, 79.9, 80.3, 169.5 (x 2).

$\nu_{(max)}$: 2928s, 2854s, 1734s, 1465s, 1368s, 1331s, 1177s, 1034s cm^{-1}.

Experiment 22

Tetradec-9-ynoic acid (66)

Dodec-7-ynyl malonic acid diethyl ester (4.1 g) was added to a hot solution of 50 % aqueous potassium hydroxide (70 ml). The reaction mixture was gently refluxed for 3 hrs. After cooling, ether (20 ml) was added and the aqueous layer was separated and acidified to pH 7. The di-acid (2.9 g) was refluxed for 12 hrs. at 100 °C in aqueous citric acid (50 ml, 60 %). *Tetradec-9-ynoic acid*[84] was extracted with dichloromethane (2 x 20 ml), dried with $MgSO_4$ and rotary evaporated.

Yield: 2.1 g, 73 %

^{1}H NMR: δ 0.89 (3 H, t, J 6.9 Hz), 1.30 (16 H, m), 2.15 (4 H, m), 2.36 (2 H, t, J 7.5 Hz).

^{13}C NMR: δ 13.59, 18.41, 18.69, 21.90, 24.62, 28.58, 28.73, 28.73, 29.04, 31.24, 33.96, 80.03, 80.25, 179.46.

$V_{(max)}$: 3000br, 2931s, 2856s, 2360w, 1706s, 1463m, 1434m, 1485m cm^{-1}.

Experiment 23

Tetradec-9-ynoyl chloride (67)

Tetradec-9-ynoic acid (2 g, 8.9 x 10^{-3} mole) was dissolved in thionyl chloride (25 ml) and gently refluxed for 0.5 hr. Thionyl chloride was then distilled off to leave a black liquid. The product was distilled out of this (b.p. 165-170 °C, 0.5 mm Hg). The product, tetradec-9-ynoyl chloride, was used directly in the next experiment as it easily decomposed in air back to the carboxylic acid.

Yield: 1.2 g, 55 %

^{1}H NMR: δ 0.91 (3 H, t, J 7.1 Hz), 1.34-1.46 (14 H, m), 1.72 (2 H, pent, J 7.3 Hz), 2.15 (4 H, m), 2.88 (2 H, t, J 7.3 Hz).

^{13}C NMR: δ 13.6, 18.4, 18.6, 21.9, 24.9, 28.3, 28.4, 28.5, 28.9, 31.2, 47.0, 79.8, 80.3, 173.7.

$\nu_{(max)}$: 2929s, 2856s, 2358w, 1799s, 1463s, 1403m, 954m cm^{-1}.

Experiment 24

(Z)-9-Tetradecenal (68)

The experimental procedure was as for experiment 1, but using 5 % Pd/$BaSO_4$ (0.15 g) in THF (10 ml), 2,6-lutidine (0.57 ml, 0.53 g, 4.95 x 10^{-3} mole). Tetradec-9-ynoyl chloride (1.2 g, 4.95 x 10^{-3} mole) was added dropwise. Hydrogen was absorbed over 5 hrs. After which the mixture was filtered through silica, and the solvents were evaporated. The residue was columned with petrol/ether (5:2) and reduced to give (Z)-9-tetradecenal[80] a colourless oil.

Yield: 0.83 g, 79 %

^{1}H NMR: δ 0.84 (3 H, t, J 6.8 Hz), 1.25 (12 H, m), 1.97 (2 H, m), 2.29 (4 H, m), 2.37 (2 H, dt, J 7.2, 1.8 Hz), 5.29 (2 H, m), 9.71 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 13.96, 24.64, 26.89, 27.11, 29.02, 29.11, 29.64, 32.24, 43.87, 129.72, 129.95, 179.91.

$\nu_{(max)}$: 2926s, 2854s, 1723s, 1459s cm^{-1}.

m/e: M^{+}: 210.

Experiment 25

Oct-2-ynyl malonic acid (73)

Experiment 21 was repeated but using bromooct-3-yne (4.3 g, 0.229 mole, 1 mol. eq.), sodium (0.55 g, 0.025 mole, 1.1 mol. eq.), diethyl malonate (4.03 g, 0.025 mole, 1.1 mol. eq.). This gave the product *oct-2-ynyl malonic acid.*

Yield: 0.2 g, 3 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.3 Hz), 1.26 (9 H, m), 2.12 (4 H, m), 3.56 (1 H, t, J 7.3 Hz), 4.21 (4 H, q, J 7.3 Hz).

m/z: $[M+H]^+$: 285.

Experiment 26

Octadec-9-ynoyl chloride (76)

Stearolic acid (0.61 g, 2.14 x 10^{-3} mole) was dissolved in thionyl chloride (20 ml) and stirred at ambient temperature for 1 hr. The thionyl chloride was distilled off and crude product was distilled pure (b.p. 180 °C, 0.05 mm Hg) to give *octadec-9-ynoyl chloride.*[85]

Yield: 0.62 g, 98 %.

^{1}H NMR: δ 0.84, 1.23 (20 H, m), 1.65 (2 H, m), 2.10 (4 H, m), 2.85 (2H, t, J 7.2 Hz).

^{13}C NMR: δ 14.11, 18.67, 18.74, 20.28, 22.66, 24.99, 28.32, 28.45, 28.58, 28.87, 28.94, 29.14, 29.22, 31.84, 47.07, 79.92, 80.45, 173.61.

$\nu_{(max)}$: 2926, 2855, 2364w, 1799s, 1464s, 1403m, 955s, 722s cm^{-1}.

Experiment 27

(Z)-9-Octadecenal (70)

Octadec-9-ynoyl chloride (0.5 g, 1.67 x 10^{-3} mole) was added to a stirred mixture of Pd/$BaSO_4$ (0.05 g), and 2,6-lutidine (0.2 ml, 0.18 g, 1.67 x 10^{-3} mole) in dry THF (10 ml), under a

hydrogen atmosphere for 4 hrs. The product was filtered through silica and washed with sat. aq. sodium bicarbonate solution (5 ml), then extracted with ether (2 x 10 ml), dried and the solvents evaporated to give *(Z)-9-octadecenal*[86] as a colourless liquid.

Yield: 0.4 g, 89 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.27 (20 H, m), 1.63 (2 H, m), 2.03 (4 H, m), 2.43 (2 H, dt, J 1.8, 7.2 Hz), 5.36 (2 H, m), 9.77 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 14.11, 18.74, 22.66, 24.62, 28.61, 28.76, 28.87, 28.95, 28.05, 29.15, 29.22, 31.84, 33.88, 129.67, 130.03, 202.92.

$\nu_{(max)}$: 3003m, 2923s, 2852s, 1728s, 1464s, 1036s cm^{-1}.

5.3 Monounsaturated Aldehydes from Lactones.

Experiment 28

4-Bromobutyric acid (80)

Hydrobromic acid (48%, 140 ml) and concentrated sulphuric acid (97 %, 34 ml) were poured carefully into a 500 ml three necked round bottomed flask. A mechanical stirrer, reflux condenser and dropping funnel were attached. The flask was cooled with an ice-salt bath and with stirring, and γ-butyrolactone (20 g, 0.232 mole) was added dropwise. The reaction mixture was allowed to reach room temperature, and stirred for 1 hr. The mixture was then gently refluxed for 1 hr. The flask contents was cooled and poured onto ice (300 g). The aqueous layer was extracted with ether (3 x 70 ml). The organic layer was then washed with saturated aq. sodium sulphate. The ether layer was dried with $MgSO_4$ and solvents evaporated to leave 4-bromobutyric acid. The product showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[87]

Yield: 23 g, 60 %.

^1H NMR: δ 2.19 (2 H, m), 2.58 (2 H, t, J 7.1 Hz), 3.49 (2 H, t, J 6.1 Hz).

^{13}C NMR: δ 27.3, 32.2, 32.4, 178.9.

$\nu_{(max)}$: 3200br, 2976s, 1712s, 1232s, 1130m cm^{-1}.

Experiment 28

4-Bromobutyryl chloride (81)

4-Bromobutyric acid (20 g, 0.119 mole) was dissolved in thionyl chloride (100 ml) and gently refluxed for 1 hr. The thionyl chloride was then distilled off at atmospheric pressure. This left a yellow liquid. The product was distilled out of the residue to give 4-bromobutyryl chloride as a clear liquid, (b.p. 73 °C, 1.4 mm Hg). The product showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[88]

Yield: 18.8 g, 85 %.

^{1}H NMR: δ 2.24 (2 H, pent, J 6.6 Hz), 3.13 (2 H, t, J 6.9 Hz), 3.46(2 H, t, J 6.3 Hz).

^{13}C NMR: δ 27.6, 31.2, 45.2, 173.1.

$\nu_{(max)}$: 2967w, 2918w, 1794s, 1437m 1401m, 1246m cm^{-1}.

Experiment 30

4-Bromobutan-1-al (82)

5 % Palladium on barium sulphate (2.70 g, 30 mg per 0.01 mole) in THF (30 ml), was stirred vigorously in a hydrogen atmosphere. The solution was stirred for 30 min. to adsorb hydrogen. The catalyst turned from a brown to a black colour. 2,4-Lutidine (6.23 ml, 5.77 g, 0.0539 mole, 1 mol. eq.) was injected into the vessel. ω-Bromobutyryl chloride (10 g, 0.0539 mole, 1 mol. eq.) was then injected dropwise over 10 min. Hydrogen uptake began almost immediately. When 0.75 mol. eq. of hydrogen had been absorbed, uptake stopped. The flask was removed and the contents diluted with ether and filtered through silica under vacuum to remove the catalyst. The ether was washed with water to remove the 2,6-lutidine salt. The ether was evaporated leaving the 4-bromobutan-1-al; further purification was unnecessary. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[89]

Yield: 7.8 g, 95 %.

^{1}H NMR: δ 2.13 (2 H, pent, J 6.8 Hz), 2.63 (2 H, dt, J 7.0, 1.0 Hz), 3.41 (2 H, t, J 6.4 Hz), 9.76 (1 H, t, J 1.0 Hz).

^{13}C NMR: δ 24.9, 32.8, 42.1, 200.8.

$\nu_{(max)}$: 2923s, 2851s, 1725s, 1437m, 1247m, 1044s cm^{-1}.

Experiment 31

2-(3-Bromopropyl)-1,3-dioxacyclopentane (83)

4-Bromobutan-1-al (7.8 g, 0.0516 mole, 1 mol. eq.) was added to a solution of benzene (100 ml), 1,2-ethanediol (9.6 g, 0.154 mole, 3 mol. eq.) and pyridinium *p*-toluene-4-sulphonic acid (1.29 g, 5.16 x 10^{-3} mole, 0.1 mol, eq.). A Dean-Stark apparatus was fitted and the reaction mixture was refluxed overnight (16 hrs) to separate the water. When the flask had cooled the

benzene was evaporated and the residue was washed with sat. aq. sodium bicarbonate solution (5 %) (50 ml). The product was extracted with dichloromethane (2 x 50 ml). The solvent was dried with $MgSO_4$ and rotary evaporated to give 2-(3-bromopropyl)-1,3-dioxacyclopentane. The product showed one peak by g.l.c. and gave an identical ^1H NMR spectrum to that in the literature.[90]

Yield: 5.74 g, 59 %.

^1H NMR: δ 1.79 (2 H, m), 1.98 (2 H, m), 3.43 (2 H, t, J 6.5 Hz), 3.88 (4 H, m), 4.87 (1 H, t, J 4.4 Hz).

^{13}C NMR: δ 27.1, 32.2, 33.6, 64.9 (x2), 103.6.

$\nu_{(max)}$: 2959s, 2883s, 1738s, 1438s, 1251s, 1129s cm^{-1}.

Experiment 32

2-(Non-4-ynyl)-1,3-dioxacyclopentane (84)

Liquid ammonia (20 ml) was condensed into a 50 ml 2-necked flask using a liquid nitrogen/methylated spirit condenser, protected by a soda lime guard. Lithium amide (0.35 g, 0.015 mole, 3 mol. eq.) was added over 0.5 hr, and stirred for 0.5 hr. 1-Hexyne (0.63 g, 7.69 x 10^{-3} mole, 1.5 mol. eq.) in dry ether (20 ml) was added dropwise over 0.5 hr. 2-(3-Bromopropyl)-1,3-dioxacyclopentane (1.0 g, 5.13 x 10^{-3} mole, 1 mol. eq.) in dry ether (50 ml) was added dropwise over 0.5 hr. The reaction was stirred for a further 5 hrs, after which the condenser was removed to allow the ammonia to evaporate overnight. This left a white sludge which was cooled in an ice-water bath, and acidified to pH 1 with dilute sulphuric acid (10 %, 40 ml). The product was extracted with ether (2 x 25 ml), washed with sat. aq. sodium bicarbonate and dried with magnesium sulphate, and the solvents evaporated to give *2-(5-decynyl)-1,3-dioxacyclopentane.* The product showed one peak by g.l.c..

Yield: 0.88 g, 83 %.

^1H NMR: δ 0.89 (3 H, t, J 7.0 Hz), 1.40 (4 H, m), 1.60 (2 H, m), 1.75 (2 H, m), 2.16 (4 H, m) 3.90 (4 H, m), 4.87 (1 H, t, J 4.5 Hz).

^{13}C NMR: δ 13.6, 18.4, 18.6, 21.9, 23.5, 31.2, 32.8, 64.8 (x2), 79.4, 80.7, 104.2.

$\nu_{(max)}$: 2956s, 2872s, 2230w, 1702m, 1458m, 1410m, 1143s cm^{-1}

m/z: M^+-H: 195.

Found: $[M-H]^+$: 195.1380 $C_{12}H_{20}O_2$ requires $[M-H]^+$: 195.1385.

Experiment 33

2-((Z)-4-Nonenyl)-1,3-dioxacyclopentane (87)

Nickel acetate tetrahydrate (0.11 g, 4.49 x 10^{-4} mole, 0.1 mol. eq.) in absolute alcohol (8 ml) was stirred under a hydrogen atmosphere for 5 mins. Sodium borohydride (0 017 g, 4.49 x 10^{-4} mol, 0.1 mol. eq.) was added in absolute ethanol (1 ml) and the reaction mixture was stirred for 20 mins. Ethylenediamine (0.75 ml, 0.67 g, 1.12 x 10^{-3} mole, 0.25 mol. eq.) was added followed by 2-(4-nonynyl)-1,3-dioxacyclopentane (0.88 g, 4.48 x 10^{-3} mole, 1 mol. eq.) in ethanol (1 ml). The reaction mixture was stirred under the hydrogen atmosphere until one molar equivalent of hydrogen was absorbed, in ca. 1.5 hrs. The product was washed with water (20 ml) and extracted with dichloromethane (2 x 10 ml) then the solvents were evaporated to give the product *2-((Z)-4-nonenyl)-1,3-dioxacyclopentane*. The product showed one peak by g.l.c..

Yield: 0.68 g, 77 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.8 Hz), 1.30 (4 H, m), 1.47 (2 H, m), 1.68 (2 H, m), 2.06 (4 H, m), 3.91 (4 H, m), 4.85 (1 H, t, J 4.6 Hz), 5.35 (2 H, m).

^{13}C NMR: δ 13.9, 22.3, 24.1, 26.9, 26.9, 31.89, 33.4, 64.8 (x2), 104.5, 129.1, 130.4.

$\nu_{(max)}$: 3003m, 2954s, 2871s, 1458m, 1404m, 1142m, 1030m cm^{-1}.

m/z: M^+-H: 197.

Found: $[M-H]^+$: 197.1554 $C_{12}H_{22}O_2$ requires, $[M-H]^+$: 197.1541.

Experiment 34

(Z)-5-Decenal (75)

2-((Z)-5-Nonenyl)-1,3-dioxacyclopentane (0.5 g, 2.52 x 10^{-3} mole) was dissolved in acetone (5 ml) and water (1 ml). *Para*-toluene-4-sulfonic acid (0.01 g) was added as catalyst. The solution was refluxed for 48 hrs, until the acetal had completely reacted. The product was extracted with dichloromethane (5 ml) and washed with sat. aq. sodium bicarbonate solution (5 ml). The aldehyde was dried and the solvent evaporated leaving (Z)-5-decenal. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[91]

Yield: 0.36 g, 72 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.8 Hz), 1.29 (6 H, m), 2.03 (4 H, m), 2.44 (2 H, dt, J 7.2, 1.7 Hz), 5.35 (2 H, m), 9.77 (1 H, t, J 1.7 Hz).

^{13}C NMR: δ 13.9, 22.3, 22.6, 26.4, 26.9, 31.8, 43.2, 128.1, 131.3, 202.6.

$\nu_{(max)}$: 3004m, 2956s, 2858s, 2716m, 1726s, 1459m, 1260m cm^{-1}.

Experiment 35

2(4-Undecynyl)-1,3-dioxacyclopentane (85)

The procedure was as for Experiment 32, but using 2-(3-bromopropyl)-1,3-dioxacyclopentane (4.2 g, 21.5 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.99 g, 4.3 x 10^{-2} mole, 2 mol. eq.) and 1-octyne (3.56g, 3.2 x 10^{-2} mole, 1.5 mol. eq.). The product, *2(4-undecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 3.5 g, 72 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.8 Hz), 1.40 (8 H, m), 1.62 (2 H, m), 1.77 (2 H, m), 2.11-2.24 (4 H, m) 3.82-4.00 (4 H, m), 4.88 (1 H, t, J 4.5 Hz).

^{13}C NMR: δ 14.04, 18.66, 18.72, 22.55, 23.58, 28.54, 29.08, 31.35, 32.89, 64.84 (x 2), 79.44, 80.78, 104.29.

$\nu_{(max)}$: 2928s, 2860s, 2348w, 1465s, 1040m cm^{-1}.

m/z: $[M-H]^+$: 223, M^+-C_3H_7: 181, M^+-C_5H_{11}: 153.

Found: $[M-H]^+$: 223.1698 $C_{14}H_{24}O_2$ requires $[M-H]^+$: 223.1698.

Experiment 36

2-((Z)-4-Undecenyl)-1,3-dioxacyclopentane (88)

The procedure was as for Experiment 33, but using 2-(4-undecynyl)-1,3-dioxacyclopentane (2.4 g, 10.7 x 10^{-3} mole, 1 mol. eq.), nickel tetraacetate (0.2 g, 1.07 x 10^{-3} mole, 0.1 mol. eq.), sodium borohydride (0.04 g, 1.07 x 10^{-3} mole, 0.1 mol. eq.) and ethylene diamine (0.18 ml, 0.16 g, 2.67 x 10^{-3} mole, 0.25 mol. eq.). The product, *2-((Z)-4-undecenyl)-1,3-dioxacyclopentane* showed one peak by g.l.c..

Yield: 1.76 g, 73 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.28 (8 H, m), 1.49 (2 H, m), 1.65 (2 H, m), 2.00-2.12 (4 H, m), 3.82-4.00 (4 H, m), 4.86 (1 H, t, J 4.6 Hz), 5.37 (2 H, m).

^{13}C NMR: δ 14.09, 22.64, 24.09, 27.00, 27.23, 28.98, 29.68, 31.76, 33.43, 64.83 (x 2), 104.57, 129.09, 130.52.

$\nu_{(max)}$: 3003s, 2924s, 2855s, 1459s, 1404m, 1141s, 1032m, 941m cm^{-1}.

m/e: M^+: 226, M^+-H: 225.

Found: M^+: 226.1941 $C_{14}H_{26}O_2$ requires M^+: 226.1932.

Experiment 37

2-(4-Tridecynyl)-1,3-dioxacyclopentane (86)

The procedure was as for Experiment 32, but using 2-(3-bromopropyl)-1,3-dioxacyclopentane (2 g, 10.2 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.47 g, 2.05 x 10^{-2} mole, 2 mol. eq.)and 1-decyne (2.13 g, 15.4 x 10^{-2} mole, 1.5 mol. eq.). The product *2-(4-tridecynyl)-1,3-dioxacyclopentane* showed one peak by g.l.c..

Yield: 0.65 g, 27 %.

^{1}H NMR: δ 0.88 (3 H, m), 1.27 (12 H, m), 1.46 (2 H, m), 1.60 (2 H, m), 2.09-2.23 (4 H, m), 3.81-3.99 (2 H, m), 4.87 (1 H, t, J 4.7 Hz).

^{13}C NMR: δ 14.11, 18.67, 18.73, 22.66, 23.59, 28.70, 28.88, 29.13, 29.21, 31.84, 32.89, 64.84 (x 2), 79.43, 80.79, 104.28.

ν_{max}): 2928s, 2856s, 2351w, 1465m, 1132m cm^{-1}.

m/z: M^+: 252.

Experiment 38

2-((Z)-4-Tridecenyl)-1,3-dioxacyclopentane (89)

The procedure was as for experiment 33, but using 2-(4-tridecynyl)-1,3-dioxacyclopentane (0.6 g, 2.38 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.06 g, 2.38 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.01 g, 2.38 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.034 g, 5.75 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-4-tridecenyl)-1,3-dioxacyclopentane,* showed one peak by g.l.c..

Yield: 0.46 g, 75 %.

^{1}H NMR: δ 0.83 (3 H, t, J 6.8 Hz), 1.22 (12 H, m), 1.43 (2 H, m), 1.61 (2 H, m), 1.95-2.05 (4 H, m), 3.77-3.95 (4 H, m), 4.81 (1 H, t, J 4.7 Hz), 5.24-5.38 (2 H, m).

^{13}C NMR: δ 14.08, 22.65, 24.08, 26.98, 27.21, 29.29 (x 2), 29.49, 29.70, 31.87, 33.41, 64.81 (x 2), 104.55, 129.07, 130.49.

$\nu_{(max)}$: 3007w, 2924s, 2854s, 1458m, 1141m, 1036w cm^{-1}.

m/z: M^+: 254, M^+-CH_3: 239, M^+-C_3H_7: 211.

Found: $[M-H]^+$: 253.2168 $C_{16}H_{30}O_2$ requires $[M-H]^+$: 253.2168.

Experiment 39

(Z)-5-Tetradecenal (79)

The procedure was as for Experiment 34. 2-((Z)-4-Tridecenyl)-1,3-dioxacyclopentane (0.42 g, 1.65 x 10^{-3} mole) was dissolved in acetone (5 ml) and water (1 ml). *P*-Toluene-4-sulfonic acid (0.01 g) was added as catalyst. The solution was refluxed for 48 hr when the acetal had completely reacted. The product was extracted with dichloromethane (5 ml) and washed with sat. aq. sodium bicarbonate solution (5 ml). The aldehyde was dried and the solvent evaporated leaving *(Z)-5-tetradecenal.*[92] The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature

Yield : 0.3 g, 86 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.28 (10 H, m), 2.04 (4 H, m), 2.44 (2 H, dt, J^1 7.3, J^2 1.7 Hz), 5.37 (2 H, m), 9.77 (1 H, t, J 1.7 Hz).

^{13}C NMR: δ 14.06, 22.05, 22.61, 24.62, 26.43, 27.23, 28.95, 29.34, 29.61, 31.73, 43.27, 128.16, 131.42, 202.59.

$\nu_{(max)}$: 3012m, 2927s, 2855s, 1724s, 1460m cm^{-1}.

Experiment 40

6-Bromohexanoic acid (90)

Hydrobromic acid (48 %, 140 ml) and concentrated sulphuric acid (97 %, 34 ml) were poured carefully into a 500 ml three necked round bottomed flask. A mechanical stirrer, reflux condenser and dropping funnel were attached. The flask was cooled with a ice-salt bath and with stirring, the ε-caprolactone (50 g, 0.438 mole) was added dropwise. The reaction mixture was allowed to reach room temperature, and stirred for 2 hrs. The mixture was then gently refluxed for 3 hrs. The flask contents was cooled and poured onto ice (300 g). The aqueous layer was extracted with ether (2 x 100 ml). The organic layer was then washed with saturated aq. sodium sulphate (100 ml). The ether layer was dried with $MgSO_4$ and solvents evaporated to leave the product of 6-bromohexanoic acid. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[93]

Yield: 93 g, 91 %.

^{1}H NMR: δ 1.47 (2 H, m), 1.64 (2 H, m), 1.86 (2 H, m), 2.35 (2 H, t, J 7.1 Hz), 3.39 (2 H, t, J 6.7 Hz).

^{13}C NMR: δ 23.75, 27.53, 32.33, 33.43, 33.83, 179.89.

$\nu_{(max)}$: 3200br, 2868s, 1686s, 1408s, 1259s, 1187s cm^{-1}.

Experiment 41

6-Bromohexan-1-oyl chloride (91)

6-Bromohexanoic acid (80 g, 0.41 mole) was dissolved in thionyl chloride (250 ml) and gently refluxed for 0.5 hr. The thionyl chloride was then distilled off. This left a black liquid. The product was distilled out of the black residue (b.p. 95 – 100 °C, atmospheric pressure). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[94]

Yield: 62 g, 70 %.

^{1}H NMR: δ 1.51 (2 H, m), 1.73 (2 H, m), 1.87 (2 H, m), 2.91 (2 H, t, J 7.1 Hz), 3.40 (2 H, t, J 6.6 Hz).

^{13}C NMR: δ 24.19, 26.93, 32.10, 33.22, 46.84, 173.57.

$\nu_{(max)}$: 2940s, 2865s, 1789s, 1459s, 1402s, 1251s, 949s cm^{-1}.

Experiment 42

6-Bromohexan-1-al (92)

5 % Palladium on barium sulphate (1.48 g, 30 mg per 0.01 mole) in THF (50 ml), was stirred vigorously in a hydrogen atmosphere. The catalyst turned from a brown to a black colour. 2,4-Lutidine (5.47 ml, 5.03 g, 0.047 mole, 1 mol. equiv.) was injected into the vessel. Then ω-bromohexan-1-oyl chloride (10 g, 0.047 mole, 1 mol. eq.) was injected dropwise over 10 min. Hydrogen uptake began almost immediately. When *ca.* 0.75 mol. equiv. had been absorbed, the flask was removed and the contents diluted with ether and filtered through silica under vacuum to remove the catalyst. The ether was washed with water to remove the 2,6-lutidine salt. The ether was evaporated leaving the 6-bromohexan-1-al; further purification was unnecessary. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[95]

Yield: 6.15 g, 73 %.

^{1}H NMR: δ 1.51 (2 H, m), 1.66 (2 H, m), 1.88 (2 H, m), 2.47 (2 H, dt, J 7.1, 1.0 Hz), 3.41 (2 H, t, J 6.7 Hz), 9.7 (1 H, t, J 1.0 Hz).

^{13}C NMR; δ 21.11, 27.58, 32.37, 33.37, 43.59, 202.19.

$\nu_{(max)}$: 2938s, 2863s, 1723s, 1034s cm^{-1}.

Experiment 43

2-(5-Bromopentyl)-1,3-dioxacyclopentane (93)

6-Bromohexan-1-al (11.2 g, 0.062 mole, 1 mol. eq.) was added to a solution of toluene (100 ml), 1,2-ethanediol (11.6 g, 0.18 mole, 3 mol. eq.) and pyridinium *para*-toluene-4-sulphonic acid (3.1 g, 0.012 mole, 0.2 mol, eq.). A Dean-Stark apparatus was fitted and the reaction mixture was refluxed overnight (16 hrs) to separate the water. When the flask had cooled the toluene was evaporated and the residue was washed with sodium bicarbonate solution (5 %) (50 ml). The product was extracted with dichloromethane (2 x 50 ml). The solvent was dried with $MgSO_4$ and rotary evaporated to give 2-(5-bromopentanyl)-1,3-dioxacyclopentane. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[96]

Yield: 13.3 g, 92 %.

^{1}H NMR: δ 1.39-1.50 (4 H, m), 1.59-1.67 (2 H, m), 1.77-1.86 (2 H, m), 3.37 (2 H, t, J 6.8 Hz), 3.77-3.98 (4 H, m), 4.81 (2 H, t, J 4.7 Hz).

^{13}C NMR: δ 23.13, 28.03, 32.66, 33.61, 33.71, 64.8 (x 2) 104.35.

$\nu_{(max)}$: 2944s, 2864s, 1129s, 1035m, 943m cm^{-1}.

Experiment 44

2-(6-Undecynyl)-1,3-dioxacyclopentane (95)

The procedure was as for Experiment 32, but using 2-(5-bromopentanyl)-1,3-dioxacyclopentane (2.0 g, 8.9 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.41 g, 17.9 x 10^{-3} mole, 2 mol. eq.) and 1-hexyne (1.10 g, 13.0 x 10^{-3} mole, 1.5 mol. eq.). The product, *2-(6-undecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 1.85 g, 92 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.9 Hz), 1.37-1.47 (10 H, m), 1.64 (2 H, m), 2.13 (4 H, m), 3.81-3.99 (4 H, m), 4.84 (1 H, t, J 4.7 Hz).

^{13}C NMR: δ 13.60 18.40, 18.63, 21.89, 23.59, 28.72, 29.03, 31.22, 33.78, 64.81 (x 2), 79.96, 80.26, 104.56.

$\nu_{(max)}$: 2932s, 2861s, 1465m, 1141s, 1038m, 734m cm^{-1}.

m/z: M^+: 224, M^+-C_3H_7: 181, M^+-C_4H_9: 167, M^+-C_6H_9: 143.

Found: $[M-H]^+$: 223.1701 $C_{14}H_{24}O_2$ requires $[M-H]^+$: 223.1698.

Experiment 45

2-((Z)-6-Undecenyl)-1,3-dioxacyclopentane (96)

The procedure was as for Experiment 33, but using 2-(6-undecynyl)-1,3-dioxacyclopentane (1.85 g, 8.25 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.20 g, 8.25 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.03 g, 8.25 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.14 ml, 0.12 g, 2.06 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-6-undecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 1.62 g, 87 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.9 Hz), 1.25-1.47 (10 H, m), 1.61-1.68 (2 H, m), 2.02 (4 H, m), 3.80-4.01 (4 H, m), 4.84 (1 H, t, J 4.8 Hz), 5.31-5.36 (2 H, m).

^{13}C NMR: δ 13.96, 22.30, 23.95, 26.87, 27.03, 29.17, 29.62, 31.91, 33.86, 64.78 (x 2), 104.62, 129.64, 129.95.

$\nu_{(max)}$: 3002s, 2927s, 2855s, 1464s, 1406m, 1141s, 1040m, 943m cm^{-1}.

m/z: M^+-C_2H_5: 197, M^+-C_3H_7: 183, M^+-C_4H_9: 169.

Found: $[M-H]^+$: 225.1855 $C_{14}H_{26}O_2$ requires $[M-H]^+$: 225.1855.

Experiment 46

(Z)-7-Dodecenal (80)

The procedure was as for Experiment 34. 2-((Z)-6-Undecenyl)-1,3-dioxacyclopentane (1.0 g, 4.44 x 10^{-3} mole) was dissolved in acetone (10 ml) and water (2 ml). *Para*-toluene-4-sulfonic acid (0.02 g) was added as catalyst. The solution was refluxed for 48 hr.[28]

Yield: 0.61 g, 75 %.

^{1}H NMR: δ 0.89 (3 H, t J 6.8 Hz), 1.26-1.37 (8 H, m), 1.64 (2 H, p, 7.2 Hz), 2.03 (4 H, m), 4.43 (2 H, dt, J 7.2, 1.8 Hz), 5.34 (2 H, m), 9.77 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 13.96, 21.95, 22.30, 26.89, 28.74, 29.31, 29.41, 31.89, 43.84, 129.38, 130.22, 202.91.

$\nu_{(max)}$: 3004m, 2927s, 2855s, 1726s, 1462m cm^{-1}.

Experiment 47

2-(6-Tridecynyl)-1,3-dioxacyclopentane (96)

The procedure was as for Experiment 32, but using 2-(5-bromopentanyl)-1,3-dioxacyclopentane (2 g, 8.9 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.41 g, 17.9 x 10^{-3} mole, 2 mol. eq.) and 1-octyne (1.48 g, 13.4 x 10^{-3} mole, 1.5 mol. eq.). The product, *2-(6-tridecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c.

Yield: 2.04 g, 90 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.9 Hz), 1.20-1.48 (12 H, m), 1.64 (2 H, m), 2.11 (4 H, m), 3.81-3.99 (4 H, m), 4.84 (1 H, t, J 4.7 Hz).

^{13}C NMR δ 14.04, 18.64, 18.73, 22.55, 23.60, 28.52, 28.73, 29.04, 29.09, 31.35, 33.79, 64.81 (x 2), 79.98, 80.33, 104.57.

$\nu_{(max)}$: 2931s, 2858s, 1465m, 1140m, 910s, 734s cm^{-1}.

m/z: M^+: 252, M^+-C_3H_7: 209, M+-C_5H_{11}: 181.

Found: $[M-H]^+$: 251.2008 $C_{16}H_{28}O_2$ requires $[M-H]^+$: 251.2011.

Experiment 48

2-((Z)-6-Tridecenyl)-1,3-dioxacyclopentane (98)

The procedure was as for Experiment 33, but using 2-(6-tridecynyl)-1,3-dioxacyclopentane (2.04 g, 8.09 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.20 g, 8.09 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.03 g, 8.09 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.13 ml, 0.12 g, 2.02 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-6-tridecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 1.22 g, 60 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.28-1.48 (14 H, m), 1.62-1.70 (2 H, m), 2.02 (4 H, m), 3.82-4.00 (4 H, m), 4.85 (1 H, t, J 4.8 Hz), 5.32-5.37 (2 H, m).

^{13}C NMR: δ 10.09, 22.64, 23.98, 27.06, 27.20, 28.87, 29.20, 29.64, 29.71, 31.76, 33.87, 64.80 (x 2), 104.64, 129.65, 130.03.

$\nu_{(max)}$: 3002m, 2925s, 2855s, 1465m, 1141s, 1038m, 943m cm^{-1}.

m/z: M^+: 254, M^+-CH_3: 239, M^+-C_2H_5: 223, M^+-C_3H_7: 211.

Found: $[M-H]^+$: 253.2170 $C_{16}H_{30}O_2$ requires $[M-H]^+$: 253.2168.

Experiment 49

(Z)-7-Tetradecenal (81)

The procedure was as for Experiment 34, but using 2-((Z)-6-tridecenyl-1,3-dioxacyclopentane (2.0 g, 7.87 x 10^{-3} mole) in acetone (10 ml) and water (2 ml). *p*-Toluene-4-sulfonic acid (0.02 g) was added as catalyst. The solution was refluxed for 48 hr when the acetal had completely reacted. The product was extracted with dichloromethane (5 ml) and washed with sat. aq. sodium bicarbonate solution (5 ml). The aldehyde was dried and the solvent was evaporated leaving (Z)-7-tetradecenal. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[97]

Yield: 1.2 g, 72 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.2 Hz), 1.29-1.37 (12 H, m), 1.64 (2 H, pent, J 7.2 Hz), 2.03 (4 H, m), 2.44 (2 H, dt, J^1 7.2, J^2 1.7 Hz), 5.30-5.40 (2 H, m), 9.77 (1 H, t, J 1.7 Hz).

^{13}C NMR: δ 14.09, 21.98, 22.64, 26.93, 27.22, 28.76, 28.97, 29.43, 29.69, 31.76, 43.87, 129.33, 130.29, 202.87.

$\nu_{(max)}$: 3004m, 2926s, 2855s, 1727s, 1460s, 1124m cm^{-1}.

m/z: $[M-H]^+$: 209, $[M-CHO]^+$: 180.

Experiment 50

2-(6-Pentadecynyl)-1,3-dioxacyclopentane (97)

The procedure was as for Experiment 32, but using 2-(5-bromopentanyl)-1,3-dioxacyclopentane (2 g, 8.9 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.41 g, 17.9 x 10^{-3} mole, 2 mol. eq.) and 1-decyne (1.85 g, 13.4 x 10^{-3} mole, 1.5 mol. eq.). The product *2-(6-pentadecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 0.84 g, 34 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.9 Hz), 1.21-1.48 (18 H, m), 1.63-1.66 (2 H, m), 2.13 (4 H, m), 3.82-4.00 (4 H, m), 4.85 (1 H, t, J 4.7 Hz)

^{13}C NMR: δ 14.11, 18.65, 18.74, 20.65, 23.61, 28.75, 28.87, 29.05, 29.13, 29.21 (x 2), 23.84. 33.80, 64.83 (x 2), 79.99, 80.36, 104.57

$\nu_{(max)}$: 2929s, 2857s, 2359w, 1465m, 1140s, 1039m, cm^{-1}

Experiment 51

2-((Z)-6-Pentadecenyl)-1,3-dioxacyclopentane

The procedure was as for Experiment 33, but using 2-(6-pentadecynyl)-1,3-dioxacyclopentane (0.84 g, 3.00 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.074 g, 3.0 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.01 g, 3.0 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.05 ml, 0.045 g, 7.5 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-6-pentadecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 0.6 g, 71 %.

^{1}H NMR: δ 0.83 (3 H, t, J 6.8 Hz), 1.28 (18 H, m), 1.41 (2 H, m), 1.60 (2 H, m), 1.97 (4 H, m), 3.76-3.95 (4 H, m), 4.79 (1 H, t, J 4.8 Hz), 5.27-5.35 (2 H, m).

^{13}C NMR: δ 14.09, 22.65, 23.97, 27.06, 27.19, 29.19 (x 2), 29.29, 29.49, 29.64, 29.74, 31.87, 33.86, 64.79 (x 2), 104.63, 129.63, 130.03.

$\nu_{(max)}$: 3002m, 2925s, 2854s, 1464m, 1141m, 1039m cm^{-1}.

m/z: M^{+}-$C_3H_5O_2$: 209, M^{+}-$C_4H_7O_2$: 195, M^{+}-$C_5H_9O_2$: 167.

5.4 Monounsaturated Aldehydes from Diols.

Experiment 52

8-Bromooctan-1-ol (100)

1,8-Octanediol (100 g, 0.685 mol) was dissolved in aqueous hydrobromic acid (48 %, 1 L). The solution was put into continuous extraction apparatus. Toluene (1 L) was continuously distilled through the HBr solution for 18 hrs. The toluene was evaporated, and the product purified by distillation, (b.p. 135 - 140 °C 0.5 mm Hg), yielding 8-bromooctan-1-ol. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[98]

Yield: 130.4 g, 90.6 %.

^{1}H NMR: δ 1.32-1.43 (8 H, m), 1.55 (2 H, pent, J 6.5 Hz), 1.85 (2 H, t, J 6.8 Hz), 3.40 (2 H, t, J 6.8 Hz), 3.63 (2H, t, J 6.5 Hz).

^{13}C NMR: δ 25.61, 28.06, 28.69, 29.19, 32.62, 32.75, 34.02, 62.91.

$\nu_{(max)}$: 3343br, 2928s, 2854s, 1463s, 1244m, 1055s cm^{-1}.

Experiment 53

8-Bromooctan-1-oic acid (102)

In a 2-necked flask (1 L) with mechanical stirrer, potassium permanganate (75 g, 0.47 mole, 5 mol. eq.) was dissolved in water (100 ml). The flask was cooled to 0 °C with an ice / water bath. Tetra-n-butyl ammonium bromide (4.6 g, 0.14 mole, 0.15 mol. eq.) was added and the solution. 8-Bromooctan-1-ol (20 g, 0.095 mole, 1 mol. eq.) in benzene (100 ml) was added dropwise from a addition funnel. Stirring continued at 0 °C for 1 hr, then the reaction mixture was stirred rapidly at room temp for 15 hrs. The flask was cooled to 0 °C with an ice /water bath and sat. aq. solution of sodium metabisulphate (150 g in 250 ml water) was added very slowly to quench the reaction. Dilute sulphuric acid (10 %, 100 ml) was added dropwise until pH 1 was attained. The colour changed from black to colourless. The products were extracted with ether (3 x 50 ml) and the solvents were dried and evaporated. This yielded

8-bromooctan-1-oic acid, a white solid at room temp. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[99]

Yield: 19.3 g, 90.5 %.

^{1}H NMR: δ 1.29-1.42 (6 H, m), 1.60 (2 H, pent, J 7.3 Hz), 1.81 (2 H, pent, J 6.8 Hz), 2.32 (2 H, t, J 7.3 Hz), 3.36 (2 H, t, J 6.8 Hz).

^{13}C NMR: δ 24.5, 27.9, 28.3, 28.8, 32.6, 33.9 (x2), 179.4.

$\nu_{(max)}$: 3000br, 2933s, 2856s, 1708s, 1412m,. 1242m cm^{-1}.

Experiment 54

8-Bromooctan-1-oyl Chloride (104)

8-Bromooctan-1-oic acid (20 g, 0.089 mole), was dissolved in thionyl chloride and stirred for 1 hr. The thionyl chloride was evaporated off under vacuum. The product 8-bromooctan-1-oyl chloride was distilled out of the residue giving a clear liquid (b.p. 140 °C, 0.4 mm Hg). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[100]

Yield: 17.8 g, 82 %.

^{1}H NMR: δ 1.51 (4 H, m), 1.73 (2 H, m), 1.87 (2 H, m), 2.91 (2 H, t, J 7.1 Hz), 3.40 (2 H, t, J 6.6 Hz).

^{13}C NMR: δ 24.87, 27.77, 28.17, 28.32, 32.53, 33.74, 46.96, 173.72.

$\nu_{(max)}$: 2934s, 2858s, 1799s, 1458m, 1402m cm^{-1}.

Experiment 55

8-Bromooctan-1-al (107)

The procedure was as for Experiment 30, but using 8-bromooctan-1-oyl chloride (5 g, 0.02 mole), 2,6-lutidine (2.4 ml, 2.22 g, 0.2 mole) and 5 % Pd/$BaSO_4$ (0.62 g). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[101]

Yield: 3.66 g, 85 %.

^{1}H NMR: δ 1.51 (6 H, m), 1.66 (2 H, pent, J 7.2 Hz), 1.86 (2 H, pent, J 6.8 Hz), 2.47 (2 H, t, J 7.2, 1.7 Hz), 3.41 (2 H, t, J 6.8 Hz), 9.77(1 H, t, J 1.7 Hz).

^{13}C NMR: δ 24.50, 27.91, 28.35, 28.80, 32.65, 33.85 (x 2), 202.21.

$\nu_{(max)}$: 2932s, 2857s, 1723s, 1579m, 1453m, 1039m cm^{-1}.

Experiment 56

2-(7-Bromoheptyl)-1,3-dioxacyclopentane (110)

The procedure was as for Experiment 31, but using 8-bromooctan-1-al (2.5 g, 0.012 mole, 1 mol. eq.), ethylene glycol (3.7 g 0.06 mole, 6 mol. eq.) and pyridinium *p*-toluene-4-sulphonic acid (1.5 g, 6.01 x 10^{-3} mole, 0.5 mol. eq.). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[101]

Yield: 2.1 g, 69 %.

^{1}H NMR: δ 1.41 (4 H, m), 1.65 (2 H, m), 1.83 (2 H, pent, J 6.8 Hz), 3.41 (2 H, t, J 6.8 Hz), 3.82-4.00 (4 H, m), 4.84 (1 H, t, J 4.8 Hz).

^{13}C NMR: δ 23.93, 28.02, 28.64, 28.76, 29.30, 32.76, 33.81, 64.82 (x 2), 104.59.

$\nu_{(max)}$: 2928s, 2857, 1463m, 1409m, 1127s, 1036s, 912m cm^{-1}.

Experiment 57

2-(8-Tridecynyl)-1,3-dioxacyclopentane (113)

The procedure was as for Experiment 32, but using 2-(7-bromoheptanyl)-1,3-dioxacyclopentane (0.89 g, 3.5 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.16 g, 7.09 x 10^{-3} mole, 2 mol. eq.) and 1-hexyne (0.44 g, 5.3 x 10^{-3} mole, 1.5 mol. eq.). The product, *2-(8-tridecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 0.7 g, 77 %.

^{1}H NMR: δ 0.90 (3 H, t, J 6.9 Hz), 1.32-1.45 (12 H, m), 1.64 (2 H, m), 2.14 (4 H, m), 3.81-4.00 (4 H, m), 4.84 (1 H, t, J 4.8 Hz).

^{13}C NMR: δ 13.61, 18.42, 18.71, 21.91, 24.03, 28.71, 29.04, 29.11, 29.42, 31.25, 33.87.

$\nu_{(max)}$: 2930s, 2860s, 1463m, 1141m, 910m cm^{-1}.

m/z: M^+: 252, M^+-C_3H_7: 209, M^+-C_4H_9: 195, M^+-$C_3H_5O_2$: 179.

Found: $[M-H]^+$: 251.2011 $C_{16}H_{28}O_2$ requires $[M-H]^+$: 251.2014.

Experiment 58

2-((Z)-8-Tridecenyl)-1,3-dioxacyclopentane (117)

The procedure was as for Experiment 33, but using 2-(8-tridecynyl)-1,3-dioxacyclopentane (0.7 g, 2.77 x 10^{-3} mole, 1 mol. eq.), nickel tetraacetate (0.07 g, 2.77 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.01 g, 2.77 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.05 ml, 0.04 g, 6.94 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-8-tridecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 0.54 g, 82 %.

^{1}H NMR: δ 0.90 (3 H, t, J 7.0 Hz), 1.31 (10 H, m), 1.63 (2 H, m), 2.02 (4 H, m), 3.81-4.02 (4 H, m), 4.84 (1 H, t, J 4.8 Hz), 5.35 (2 H, m).

^{13}C NMR: δ 13.99, 22.33, 24.08, 26.90, 27.15, 29.15, 29.42, 29.51, 29.72, 31.94, 33.89, 64.81 (x 2), 104.68, 129.83 (x 2).

$\nu_{(max)}$: 3005m, 2929s, 2857s, 1463m, 1140m, 1038m cm^{-1}.

m/z M^+: 254, M^+-C_4H_9: 197.

Found: $[M-H]^+$: 253.2163 $C_{16}H_{30}O_2$ requires $[M-H]^+$: 253.2168.

Experiment 59

(Z)-9-Tetradecen-1-al (121)

The procedure was as for Experiment 34, but using 2-((Z)-8-tridecenyl-1,3-dioxacyclopentane (0.5 g, 1.96 x 10^{-3} mole) was dissolved in acetone (5 ml) and water (1 ml). *p*-Toluene-4-sulfonic acid (0.01 g) was added as catalyst. The solution was refluxed for 48 hr, when the acetal had completely reacted. The product was extracted with dichloromethane (5 ml) and washed with sodium bicarbonate solution (5 ml). The organic layer was dried and the solvent evaporated leaving (Z)-9-tetradecenal.[102] The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.

Yield: 0.3 g, 72 %.

^{1}H NMR: δ 0.84 (3 H, t J 6.8 Hz), 1.25 (12 H, m), 1.97 (2 H, m), 2.29 (4 H, m), 2.37 (2 H, dt, J 7.2, 1.8 Hz), 5.29 (2 H, m), 9.71 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 13.96, 22.16, 24.64, 26.89, 27.11, 29.02, 29.11, 29.64, 32.24, 129.72, 129.95, 202.53.

$\nu_{(max)}$: 3011w, 2926s, 2855s, 1724s, 1460s cm^{-1}.

Experiment 60

2-(8-Pentadecynyl)-1,3-dioxacyclopentane (114)

The procedure was as for Experiment 32, but using 2-(7-bromoheptanyl)-1,3-dioxacyclopentane (3.0 g, 0.12 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.55 g, 0.02 x 10^{-3} mole, 2 mol. eq.) and 1-octyne (2.6 g, 0.02 x 10^{-3} mole, 1.5 mol. eq.). The product showed one peak by g.l.c..[24]

Yield: 2.5 g, 75 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.6 Hz), 1.36 (18 H, m), 1.65 (2 H, m), 2.14 (4 H, m), 3.82-4.00 (4 H, m), 4.85 (1 H, 4.78 Hz).

^{13}C NMR: δ 14.03, 18.38, 18.73, 22.56, 24.04, 28.44, 28.53, 28.72, 29.05, 29.11, 31.36, 33.87, 64.81 (x 2), 80.15, 80.30, 104.66.

$\nu_{(max)}$: 2931s, 2857s, 2249w, 1465m, 1139m, 1036m, 911m cm^{-1}.

m/z: M^+: 280, M^+-C_3H_7: 237, M^+-C_6H_{13}: 195.

Experiment 61

2-((Z)-8-Pentadecenyl)-1,3-dioxacyclopentane (118)

The procedure was as for Experiment 33, but using 2-(8-pentadecynyl)-1,3-dioxacyclopentane (2 g, 7.14 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.177 g, 7.14 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.027 g, 7.14 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.12 ml, 0.1 g, 17.8 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-8-pentadecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..[24]

Yield: 1.81 g, 89 %.

^{1}H NMR: δ 0.89 (3 H, t, J 6.7 Hz), 1.30 (18 H, m), 1.65 (2 H, m), 2.03 (4 H, m), 3.82-4.00 (4 H, m), 4.85 (1 H, 4.8 Hz), 5.35 (2 H, m).

^{13}C NMR: δ 14.09, 22.65, 23.92, 26.74, 28.53, 29.16, 29.32, 29.43, 29.52, 29.72, 31.77, 33.90, 64.81 (x 2), 104.68, 129.82, 129.92.

$\nu_{(max)}$: 3005m, 3926s, 2854s, 1456m, 1407m, 1141s, 1037m, 942m cm^{-1}.

m/z: M^+: 282, M^+-C_6H_{13}: 197.

Found: M^+: 282.2551 $C_{18}H_{34}O_2$ requires M^+: 282.2559.

Experiment 62

10-Bromodecan-1-ol (101)

The procedure was as for Experiment 31, but using 1,10-decanediol (78 g, 0.44 mole). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[103]

Yield : 97.7 g, 92 %.

^{1}H NMR: δ 1.32-1.43 (12 H, m), 1.55 (2 H, pent, J 6.5 Hz), 1.85 (2 H, t, J 6.8 Hz), 3.40 (2 H, t, J 6.8 Hz), 3.63 (2H, t, J 6.5 Hz).

^{13}C NMR: δ 20.27, 25.68, 28.11, 28.70, 29.32 (x 2), 32.75, 34.02, 63.04.

$\nu_{(max)}$: 3336br, 2924s, 2853s, 1464s, 1256m, 1056s cm^{-1}.

Experiment 63

10-Bromodecanoic acid (103)

The procedure was as for Experiment 53, but using 10-bromodecan-1-ol (22 g, 0.095 mole, 1 mol. eq.), potassium permanganate (60 g, 0.38 mole, 4 mol. eq.), tetra-n-butylammonium bromide (4.6 g, 0.014 mole, 0.15 mol. eq.). The product *10-Bromodecanoic acid* showed one peak by t.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[104]

Yield: 23 g, 96 %.

^{1}H NMR: δ 1.29-1.42 (10 H, m), 1.59 (2 H, pent, J 7.3 Hz), 1.80 (2 H, pent, J 6.8 Hz), 2.31 (2 H, t, J 7.3 Hz), 3.36 (2 H, t, J 6.8 Hz).

^{13}C NMR: δ 24.62, 28.08, 28.64, 28.95, 29.08, 29.16, 32.76, 32.76, 34.00, 34.08, 179.90.

$\nu_{(max)}$: 3000br, 2927s, 2854s, 1708, 1463m, 1410m, 1228m cm^{-1}.

Experiment 64

10-Bromodecanoyl Chloride (105)

The procedure was as for Experiment 29, but using 10-bromodecanoic acid (23 g, 0.91 mole). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[105]

Yield: 20 g, 81 %.

^{1}H NMR: δ 1.31 (10 H, m), 1.72 (2 H, pent, J 7.2 Hz), 1.86 (2 H, pent, J 6.8 Hz), 2.89 (2 H, t, J 7.2 Hz), 3.41 (2 H, t, J 6.8).

^{13}C NMR: δ 22.03, 28.11, 28.69, 29.09, 29.19, 29.26, 29.30, 32.78, 34.00, 202.93.

$\nu_{(max)}$: 2929s, 2854s, 1798s, 1463s, 1402m, 1254m, 952s cm^{-1}.

Experiment 65

10-Bromodecanal (108)

The procedure was as for Experiment 30, but using 10-bromodecanoyl chloride (5 g, 0.018 mole), 5 % Pd/$BaSO_4$ (0.55 g), 2,6-lutidine (2.16 ml, 1.98 g, 0.018 mole). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that the literature.[106]

Yield: 3.69 g, 84 %.

^{1}H NMR: δ 1.29 (10 H, m), 1.62 (2H, m), 1.85(2H, pent, J 6.8 Hz), 2.43 (2 H, dt, J^1 7.3, J^2 1.82 Hz), 3.41 (2 H, t, J 6.8 Hz), 9.76 (1 H, t, J 1.82 Hz).

^{13}C NMR: δ 20.30, 24.30, 28.12, 28.69, 29.11, 29.27, 32.78, 34.02, 43.88, 202.91.

$\nu_{(max)}$: 2927s, 2853s, 2716m, 1725s, 1580m, 1463s, 1254m, 1033m cm^{-1}.

Experiment 66

2-(9-Bromononyl)-1,3-dioxacyclopentane (111)

The procedure was as for Experiment 31, but using 10-bromodecan-1-al (3.69 g, 0.0157 mole, 1 mol. eq.), ethylene glycol (4.87 g 0.0785 mole, 4 mol. eq.) and pyridinium *para*-toluene-4-sulphonic acid (1.97 g, 0.0078 mole, 0.5 mol. eq.). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[107]

Yield: 3.62 g, 82 %.

^{1}H NMR: δ 1.29 (12 H, m), 1.65 (2 H, m), 1.85 (2H, pent, J 6.8 Hz), 3.41 (2 H, t, J 6.8 Hz), 3.82-4.00 (4 H, m), 4.85 (1 H, t, J 4.8 Hz).

^{13}C NMR: δ 24.06, 28.16, 28.73, 29.37, 29.46, 29.50, 32.82, 33.89, 33.89, 34.05, 64.82 (x2), 104.68.

$\nu_{(max)}$: 2926s, 2858s, 1465m, 1142m, 910m cm^{-1}.

Experiment 67

2-(10-Pentadecynyl)-1,3-dioxacyclopentane (115)

The procedure was as for Experiment 32, using 2-(9-bromononanyl)-1,3-dioxacyclopentane (3.0 g, 0.01 mole, 1 mol. eq.), lithium amide (0.41 g, 0.016 mole, 2 mol. eq.) and 1-hexyne (1.77 g, 0.16 mole, 2 mol. eq.). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[24]

Yield: 2.1 g, 66 %.

^{1}H NMR: δ 0.90 (3 H, t, J 7.0 Hz), 1.28-1.46 (18 H, m), 1.64 (2 H, m), 2.14 (4 H, m), 3.82-4.03 (4 H, m), 4.84 (1 H, t, J 4.8 Hz).

^{13}C NMR: δ 13.62, 18.42, 18.73, 21.91, 24.07, 28.83, 29.15, 29.51, 31.26, 33.89, 64.81 (x 2), 80.19 (x 2), 104.69.

$\nu_{(max)}$: 2929s, 2856s, 2250w, 1460m, 1139m, 910m cm^{-1}.

Experiment 68

2-((Z)-10-Pentadecenyl)-1,3-dioxacyclopentane (119)

The experimental procedure was as for Experiment 33, but using 2-(10-pentdecynyl)-1,3-dioxacyclopentane (1.5 g, 5.4 x 10^{-3} mole, 0.1 mol. eq.), nickel tetraacetate (0.13 g, 5.4 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.02 g, 5.4 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.045 ml, 0.41 g, 1.3 x 10^{-3} mole, 0.25 mol. eq.). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature,[24]

Yield: 0.98 g, 65 %.

^{1}H NMR: δ 0.91 (3 H, t, J 6.9 Hz), 1.28-1.45 (18 H, m), 1.65 (2 H, m), 2.02 (4 H, m), 3.83-4.01 (4 H, m), 4.85 (1 H, t, J 4.7 Hz).

^{13}C NMR: δ 13.99, 22.33, 24.09, 26.90, 27.18, 28.84, 29.29, 29.52, 29.76, 31.96, 33.91, 64.81 (x 2), 104.70, 129.83 (x 2).

$\nu_{(max)}$: 3005m, 3930s, 2855s, 1459m, 1407m, 1143m, 1040m cm^{-1}.

Experiment 69

(Z)-11-Hexadecenal (122)

The procedure was as for Experiment 34. 2-((Z)-10-Pentadecenyl)-1,3-dioxacyclopentane (0.90 g, 3.19 x 10^{-3} mole) was dissolved in acetone (5 ml) and water (1 ml). Para-toluene-4-sulfonic acid (0.01 g) was added as catalyst. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[108]

Yield: 0.41 g, 52 %.

^{1}H NMR: δ 0.95 (3 H, t, J 7.5 Hz), 1.29 (14 H, m), 1.63 (2H, p, J 7.2 Hz), 2.02 (2 H, dq, J^1 5.7, J^2 7.5 Hz), 2.41 (2 H, dt, J 1.87, J 7.2 Hz), 5.33 (2 H, dt, J^1 5.7, J^2 3.1 Hz), 9.76 (1H, t, J 1.87 Hz).

Experiment 70

11-Bromoundeconyl chloride (106)

The procedure was as for Experiment 29, using 11-bromoundecanoic acid (15 g, 0.056 mole). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[109]

Yield: 12 g, 75 %.

^{1}H NMR: δ 1.30 (12 H, m), 1.71 (2 H, pent, J 7.2 Hz), 1.86 (2 H, pent, J 6.8 Hz), 2.89 (2 H, t, J 7.2 Hz), 3.41 (2 H, t, J 6.8 Hz).

^{13}C NMR: δ 953s, 25.02, 28.11, 28.37, 28.67, 28.99, 29.17, 29.27, 32.78, 34.01, 47.09, 173.83.

$\nu_{(max)}$: 2929s, 2854s, 1799s, 1463m, 1402m, 1254m, cm^{-1}.

Experiment 71

11-Bromoundecan-1-al (109)

The procedure was as for Experiment 30, but using 11-bromoundeconyl chloride (5 g, 17.6 x 10^{-3} mole, 1 mol. eq.), 2,6-lutidine (2.05 ml, 1.89 g, 17.6 x 10^{-3} mole, 1 mol. eq.) and 5 % Pd/$BaSO_4$ (0.53 g). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[81]

Yield: 4.2 g, 95 %.

^{1}H NMR: δ 1.29 (12 H, m), 1.63 (2 H, m), 1.85 (2 H, pent, J 6.8 Hz), 2.43 (2 H, dt, J^1 1.8, J^2 5.7 Hz), 3.41 (2H, t, J 6.8 Hz), 9.77 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 2204, 38.12, 28.69, 28.80, 29.11, 29.27 (x 2), 32.78, 34.02, 43.88, 202, 94.

$\nu_{(max)}$: 2926s, 2853s, 1724s, 1463s, 1254s, 1036s cm^{-1}.

Experiment 72

2-(10-Bromodecyl)-1,3-dioxacyclopentane (112)

The procedure was as for Experiment 31, but using 11-bromoundecan-1-al (4.2 g, 16.8 x 10^{-3} mole. 1 mol. eq.), ethylene glycol (5.2 g, 0.084 mole, 5 mol. eq.) and pyridinium *p*-toluene-4-sulphonic acid (1.06 g, 0.042 mole, 0.5 mol. eq.). The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[110]

Yield: 4.5 g, 91 %.

^{1}H NMR: δ 1.29 (12 H, m), 1.65 (2H, m), 1.85 (2H, pent, J 6.8 Hz), 3.41 (2H, t, J 6.8 Hz), 3.82-3.98 (4H, m), 4.85, (1H, t, J 4.8 Hz).

^{13}C NMR: δ 24.06, 28.15, 28.73, 29.37 (x 2), 29.50 (x 2), 32.82, 33.89, 34.54, 64.82 (x 2), 104.68.

$\nu_{(max)}$: 2929s, 2860s, 2250w, 1465m, 1142m, 910m cm^{-1}.

Experiment 73

2-(11-Pentadecynyl)-1,3-dioxacyclopentane (116)

The procedure was as for Experiment 32, but using 2-(10-bromodecanyl)-1,3-dioxacyclopentane (3 g, 0.01 mole, 1 mol. eq.), lithium amide (0.48 g, 0.021 mole, 2 mol. eq.) and 1-pentyne (1.44 g, 0.021 mole, 2 mol. eq.). The product, *2-(11-pentadecynyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 2.2 g, 76 %.

^{1}H NMR: δ 0.97 (3 H, t, J 7.2 Hz), 1.28 (20 H, m), 1.64 (2 H, m), 2.14 (4 H, m), 3.82-4.00 (4 H, m), 4.85 (1H, t, J 4.7 Hz).

^{13}C NMR: δ 13.46, 18.73, 20.76, 22.54, 24.07, 28.83, 29.13 (x 2), 29.49 (x 2), 33.89, 64.8 (x 2), 80.2 (x 2), 104.7.

$\nu_{(max)}$: 2931s, 2857s, 2249w, 1465m, 1139m, 911m cm^{-1}.

m/z: M^+: 280.

Found: $[M-H]^+$: 279.2326 $C_{18}H_{32}O_2$ requires $[M-H]^+$: 279.2324.

Experiment 74

2-((Z)-11-Pentadecenyl)-1,3-dioxacyclopentane (120)

The procedure was as for Experiment 33, but using 2-(11-pentadecynyl)-1,3-dioxacyclopentane (2 g, 7.14 x 10^{-3} mole, 0.1 mol. eq.), nickel tetra-acetate (0.177 g, 7.14 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.027 g, 7.14 x 10^{-4} mole, 0.1 mol. eq.) and ethylene diamine (0.12 ml, 0.1 g, 17.8 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z)-11-Pentadecenyl)-1,3-dioxacyclopentane*, showed one peak by g.l.c..

Yield: 1.65 g, 82 %.

^{1}H NMR: δ 0.91 (3 H, t, J 7.2 Hz), 1.28 (18 H, m), 1.65 (2 H, m), 2.02 (4 H, m), 3.82-4.01 (4 H, m), 4.85 (1H, t, J 4.7 Hz), 5.36 (2 H, m).

^{13}C NMR: δ 13.80, 22.88, 24.09, 27.21, 29.29, 29.53, 29.76, 33.91, 64.81 (x 2), 104.7, 129.6, 130.09.

$\nu_{(max)}$: 3003m, 3924s, 2853s, 1464m, 1407m, 1141m, 1037m cm^{-1}.

m/z: M^+: 282, M^+-C_2H_5: 253, M^+-C_3H_7: 239.

Experiment 75

(Z)-12-Hexadecenal (123)

2-((Z)-11-Pentadecenyl)-1,3-dioxacyclopentane (1.0 g, 3.54 x 10^{-3} mole) was dissolved in acetone (15 ml) and water (1 ml), *p*-toluene sulphonic acid (0.01 g) was added and the reaction was refluxed for 48 hrs. Water (10 ml) and dichloromethane (20 ml) was added and the product was extracted. The organic solvent was dried with $MgSO_4$ and evaporated to leave the product, (Z)-12-hexadecenal, which compared well to the spectrum in the literature.[111]

Yield: 0.59 g, 70 %.

^{1}H NMR: δ 0.87 (3 H, t, J 7.3 Hz), 1.26 (16 H, m), 1.60 (2 H, m), 1.98 (4 H, m), 2.39 (2 H, dt, J 7.28, 1.7 Hz), 5.33 (2 H, m), 9.74 (1 H, t, J 1.7 Hz).

^{13}C NMR: δ 13.75, 22.03, 22.85, 27.16, 28.67, 29.11, 29.24, 29.30, 29.37, 29.48, 29.71, 33.92, 43.85, 129.57, 130.01, 202.95.

$\nu_{(max)}$: 3002w, 2924s, 2853s, 1727s, 1464m, 1409w, 1376w, 1143w cm^{-1}.

m/z: M^+: 238.

5.5 Di-unsaturated Aldehydes

Experiment 76

2-Octadecenonitrile (138)

Diethyl cyanomethylphosphonate (3.0 g, 0.0169 mole) dissolved in THF (50 ml) was cooled to –78 °C under an argon atmosphere. Butyllithium (18.6 ml, 0.9 M in hexane, 1.1 mol. eq.) was added dropwise. The ylide dropped out of solution at low temperature forming a white lump, but on warming to 0 °C it dissolved. The reaction mixture was stirred at 0 °C for 1 hr. Hexadecanal (4.3 g, 0.0169 mole) in THF (10 ml) was added dropwise at –70 °C. The mixture was warmed to room temperature and stirred overnight, then hydrolysed at –70 °C by the addition of water (10 ml) and warmed to rt. The product was extracted with ether (3 x 10 ml). The combined organic extracts were washed with water (10 ml), dried with $MgSO_4$ and concentrated to give *2-octadecenonitrile* in a 1:1.2 mixture of *cis* and *trans* isomers.

Yield: 3.42 g, 82 %

^{1}H NMR: δ 0.88 (6 H, t, J 6.8 Hz) 1.26 (52 H, m).
δ (*trans* isomer) 2.20 (2 H, dq, J 6.9, 1.5 Hz), 5.33 (1 H, dt, J 16.4, 1.5 Hz), 6.73 (1 H, dt J 16.2, 6.9 Hz).
δ (*cis* isomer) 2.41 (2 H, dq, J 7.6, 1.2 Hz), 5.32 (1 H, dt, J 10.8, 1.2 Hz), 6.49 (1 H, dt, J 10.8, 7.6 Hz).

^{13}C NMR: δ 14.10, 22.68, 27.91, 28.23, 28.96, 29.28, 29.35, 29.46, 29.66, 31.91, 33.32, 99.39, 99.60 (*trans* and *cis* CN), 155.28, 156.19.

$\nu_{(max)}$: 3005w, 2927s, 2854s, 2221s,1632m, 1463m, 1438m, 1454m, 968m cm^{-1}.

m/z: $[M+H]^+$: 264, M^+-CH_3: 248, M^+-C_2H_5: 234, M^+-C_3H_7: 220

Experiment 77

(E)-2-Octadecenal (130)

2-Octadecenonitrile (3.2 g, 0.012 mole, 1 mol. eq.) in dry dichloromethane (20 ml) was cooled to -70 °C under an argon atmosphere. Diisobutylaluminium hydride (12.16 ml, 0.012 mole, 1 mol. eq.), was added slowly and stirred for 3 hrs. The mixture was warmed to 0 °C for 15 mins before cooling to -60 °C and quenching with sat. ammonium chloride solution (10 ml) and warming to rt. The product was extracted with ether (3 x 10 ml) and washed with brine (10 ml) and water (10 ml). The organic layer was dried and concentrated. The mixture was columned with petrol/ether (5:2) to give *(E)-2-octadecenal*[64] as a white solid (m.p. 45 - 50 °C).

Yield: 1.7 g, 53 %

^{1}H NMR: δ 1.25-1.49 (14 H, m), 1.79 (2 H, pent, J 6.8 Hz), 2.30 (2 H, dq, J 6.8, J 1.4 Hz), 3.34 (2 H, t, J 6.8 Hz), 6.07 (1 H, ddt, 15.0, 7.9, 1.4 Hz), 6.80 (1 H, dt, 15.5, 6.8 Hz), 9.46 (1 H, d, J 7.9 Hz).

^{13}C NMR: δ 27.80, 28.12, 28.70, 29.09, 29.27 (x 2), 29.34, 32.70, 32.78, 34.02, 132.97, 158.99, 194.15.

$\nu_{(max)}$: 2925s, 2854s, 1690s, 1461m, 1121m, 1060m, cm^{-1}.

CHN: $C_{18}H_{34}O$ (266.26) Calcd: C 81.16, H 12.86, found: C 81.13, H 12.14

Experiment 78

(E)-2-Dodecenoic acid methyl ester (140)

A 2 molar solution of sodium hydroxide (100 ml) was added to carbomethoxymethyl triphenylphosphonium bromide (5.0 g, 0.0119 mole, 1 mol. eq.) at 0 °C and stirred well for 15 mins. The stabilised ylide was filtered under vacuum and washed with water and petrol and dried under vacuum overnight. The ylide (4 g, 0.0119 mole, 1 mol. eq.) was dissolved in toluene (30 ml) and decanal (1.86 g, 0.119 mole. 1 mol. eq.) was added and the mixture refluxed overnight. The solvent was evaporated and the product columned in petrol/ether (5:1) to give *(E)-2-dodecenoic acid methyl ester*[112] as a colourless oil.

Yield: 2.0 g, 92 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.8 Hz), 1.26-1.32 (14 H, m), 2.21 (2 H, dq, J 6.9, 1.5 Hz), 3.81 (3 H, s), 5.82 (1 H, dt, J 15.5, 1.5 Hz), 6.97 (1 H, dt, J 15.5, 6.9 Hz).

^{13}C NMR: δ 14.07, 20.27, 22.63, 27.98, 29.25, 29.35, 29.45, 31.85, 32.19, 63.72, 120.74, 149.87, 175.95.

Experiment 79

(Z)-2-Dodecenol (141)

(Z)-2-Dodecenoic acid methyl ester (2 g 0.01 mole) in dry dichloromethane in an argon atmosphere was cooled to -90 °C. Diisobutylaluminium hydride (10.7 ml, 0.0107 mole) was added slowly dropwise. The reaction was kept at low temperature and monitored by G.C. for 2 hrs. The reaction was then quenched with sat. ammonium chloride solution (5 ml) and warmed to rt. The product was then extracted with ether (2 x 10 ml), and the solvents dried and evaporated to leave *(E)-2-dodecenol*[113] as a colourless oil. No aldehyde product was observed.

Yield: 1.8 g, 91 %.

^{1}H NMR: δ 0.87 (3 H, t, 6.8 Hz), 1.29 (14 H, m), 2.04 (2 H, m), 4.08 (2 H, d, 4.6 Hz), 5.66 (2 H, m).

^{13}C NMR: δ 14.07, 22.65, 29.13, 29.30, 29.48, 29.54, 29.83, 31.87, 32.19, 32.41. 63.76, 128.76, 133.53.

$\nu_{(max)}$: 3331br, 2919s, 1456s, 1377m, 1091m,1007m cm^{-1}.

Experiment 80

(E)-2-Dodecenal (142)

(E)-2-Dodecenol (0.14 g, 7.6 x 10^{-4} mole) was added to laboratory prepared activated manganese dioxide (0.66 g, 7.6 x 10^{-3} mole, 10 mol. eq.) in dry dichloromethane (10 ml). The mixture was refluxed for 48 hrs. The MnO_2 was filtered off and the solvent concentrated and gave a mixture of alcohol starting material and aldehyde product.

Experiment 81

2-(2-Bromoethyl)-1,3-dioxane (151)

Hydrogen bromide was generated by the addition of bromine (50.0 g) to tetralin (300 ml). The HBr gas that was produced was passed through three traps, the first containing tetralin the other two being empty in case of suck back. An excess HBr gas was bubbled into a 500 ml round bottomed flask, containing acrolein (14.0 g) in dichloromethane (300 ml) and which was stirred at room temperature. Free HBr was removed on bubbling nitrogen through the flask for 20 min. 1,3-Propanediol (19.0 g) and pyridinium *p*-toluene sulphonic acid (0.25 g) were added and stirred overnight. The acid was neutralised with sat. aq. sodium bicarbonate, and washed with water. The solvent was dried and evaporated and *2-(2-bromoethyl)-1,3-dioxane*[114] was distilled as a pure liquid (44 °C, 0.9 mm Hg).

Yield: 15.3 g, 30 %.

^{1}H NMR: δ 1.38 (1 H, dpent, J^1 13.5, J^2 1.3 Hz), 2.05 (1 H, m), 2.16 (2 H, dt, J 5.0, 6.7 Hz) 3.49 (2 H, t, J 6.8 Hz), 3.82 (2 H, dt, J 2.3, J 12.3 Hz), 4.12 (2 H, dd, J 1.2, 5.0 Hz), 4.74 (1 H, t, J 5.0 Hz).

^{13}C NMR: δ 25.6, 27.7, 38.0, 66.7 (x 2), 100.0.

$\nu_{(max)}$: 2968s, 2925m, 2854s, 1430s, 137s, 1240s, 1143s, 1092s, 1010s cm^{-1}.

Experiment 82

2-(1,3-Dioxan-2-yl)-ethyltriphenylphosphonium bromide (152)

Triphenylphosphine (30.1 g, 0.115 mole, 1.5 mol. eq.) was added to 2-(2-bromoethyl)-1,3-dioxane (15.0 g, 0.076 mole, 1 mol. eq.) in cyclohexane (80 ml). The mixture was stirred and refluxed for 24 hrs. A white solid precipitated which was filtered and washed with ether and petrol (100 ml). The solid was dried under vacuum overnight giving the Wittig *salt 2-(1,3-dioxan-2-yl)-ethyltriphenylphosphonium bromide* as a white solid with a melting point of 95 – 102 °C.

Yield: 10.4 g, 30 %.

^{1}H NMR: δ 1.27 (1 H, broad d, J 13 Hz), 1.85 (3 H, m), 2.32 (2 H, br, H_2O), 3.74 (2 H, m), 3.80 (2 H, dt, J 1.9, 13 Hz), 3.95 (2 H, dd, J 5.0, 11.4 Hz), 4.98 (1 H, t, J 4.7 Hz).

^{13}C NMR: δ 17.25, 18.1, 25.5, 27.85, 66.7, 99.2, 117.1, 130.6, 1334, 133.6, 135.1, 135.2.

Experiment 83

2-((Z)-2-Octenyl)-1,3-dioxane (148)

2-(1,3-Dioxan-2-yl)-ethyl triphenylphosphonium bromide (2.0 g) was dissolved in dry THF (50 ml) at room temperature. Sodium bis(trimethylsilyl)amide (5.6 ml, 1M in THF) was added, giving an orange colour and the mixture was stirred at rt for 30 mins. Hexanal (0.57 g) in THF (2 ml) was added slowly and the reaction mixture was stirred for 2 hrs. Pouring onto water (5 ml) quenched the reaction and the product was then extracted with ether (2 x 20 ml). The solvent was dried and evaporated. The residue was purified using column chromatography eluting with petrol/ether (5:2) to give *2-((Z)-2-octenyl)-1,3-dioxane.*[115]

Yield: 0.27 g, 31 %.

^{1}H NMR: δ 0.88 (3 H, t, J 6.5 Hz), 1.30 (6 H, m), 2.04 (2 H, m), 2.38 (2 H, t, J 5.45 Hz), 3.77 (2 H, dt, J 12.3, 22.3 Hz), 4.12 (2 H, dd, J 10.6, 4.9 Hz), 4.54 (1 H, t, J 5.28 Hz), 5.3-5.5 (2 H, m).

^{13}C NMR: δ 14.05, 22.53, 25.72, 27.37, 29.18, 31.48, 33.43, 66.97 (x2), 102.00, 122.82, 132.77.

Experiment 84

E-2-Nonenal (149)

Chromium (III) chloride (1.17 g) in 4 molar hydrochloric acid (50 ml) was added to 2-(2-octenyl)-1,3-dioxane (0.25 g). The mixture was refluxed for 1 hr and the reaction mixture steam-distilled to remove the product. The distillate was extracted with ether, dried with magnesium sulphate and the solvent evaporated, to leave *(E)-2-nonenal.*[116]

Yield: 0.1 g, 57 %.

^{1}H NMR: δ 0.87 (3 H, t, J 6.7 Hz), 1.31 (6 H, m), 1.50 (2 H, m), 2.35 (2 H, m), 6.12 (1 H, ddt, J 15.6, 7.9, 1.5 Hz), 6.86 (1 H, dt, J 15.6, J 6.8 Hz), 9.50 (1 H, d, J 7.9 Hz).

^{13}C NMR: δ 14.03, 22.52, 27.79, 28.80, 31.23, 32.74, 132.96, 159.15, 195.21.

$\nu_{(max)}$: 2957m, 2929s, 2857m, 1687s, 1466w, 1144w, 908s, 733s cm^{-1}.

m/z: $[M-H]^+$: 139.

Experiment 85

9-Bromononan-1-ol

1,9-Nonanediol (25 g) was dissolved in 48 % aqueous HBr (100 ml). Toluene (250 ml) was refluxed through the solution by continuous extraction for 18 hrs. The toluene was evaporated to give *9-bromononan-1-ol*[15] as a colourless oil.

Yield: 38 g, 91 %.

^{1}H NMR: δ 1.31 (8 H, m), 1.54 (2 H, m), 1.85 (2 H, m), 1.85 (2 H, pent, J 6.8 Hz), 3.41 (2 H, t, J 6.8 Hz), 3.64 (2 H, t, J 6.5 Hz).

^{13}C NMR: δ 25.68, 28.12, 28.67, 29.29, 29.37, 32.72, 32.78, 34.05, 62.98.

$\nu_{(max)}$: 3363br, 2926s, 2854s, 1464s, 1370s, 1264s, 1056s cm^{-1}.

Experiment 86

9-Bromononan-1-al

1-Bromononan-1-ol (8 g, 0.15 mole, 1 mol. eq.) was added to pyridinium chlorochromate (15 g, 0.172 mole, 2 mol. eq.) which was dissolved in dry dichloromethane (100 ml). The flask was stirred at room temperature under argon for 1 hr, and heated to reflux for 1 hr. The reaction mixture turned a dark brown colour and was of a tar like consistency. It was diluted with ether (100 ml) and filtered through a silica pad under vacuum. The solvent was evaporated leaving a yellow oil. The oil was purified by column chromatography, using petrol/ether (5:2). This gave 9-bromononan-1-al[117] as a colourless oil.

Yield: 6.13 g, 77 %

^{1}H NMR: δ 1.33 (8 H, m), 1.64 (2 H, m), 1.86 (2 H, pent, J 6.8 Hz), 2.44 (2 H, dt, J 7.2, J 1.5 Hz), 3.41 (2 H, t, J 6.8 Hz), 9.77 (1 H, t, 1.5 Hz).

^{13}C NMR: δ 21.98, 28.05, 28.52, 29.01, 29.14, 32.72, 33.95, 43.85, 202.87.

$\nu_{(max)}$: 2929s, 2855s, 2718m, 1724s, 1463m, 1251m cm^{-1}.

Experiment 87

2-(11-Bromoundec-2-enyl)-1,3-dioxane (153)

2-(1,3-Dioxan-2-yl)-ethyltriphenylphosphonium bromide (5.0 g, 1.09 x 10^{-2} mole, 1 mol. eq.), was dried twice by azeotropic distillation of dry benzene on a rotary evaporator. The phosphonium salt was dissolved in THF (20 ml), and cooled to -40 °C. A 1.6 M. solution of butyllithium in hexane (13 ml, 1.2 mol. eq.) was added. The ylide was allowed to form over 1 hr at 0 °C, then cooled to –78 °C and bromononanal (3.62 g, 1.6 x 10^{-2} mole, 1.5 mol. eq.). in THF (15 ml) was added slowly. The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with the addition of sat. aq. ammonium chloride (5 ml) at 0 °C and the product extracted with ether (3 x 10 ml). The organic extracts were washed with brine solution (5 ml) and dried with magnesium sulphate. The solvents were evaporated and the viscous brown liquid was chromatographed using petrol/ether (5:0.5) as eluent. This gave *2-(11-bromoundec-2-enyl)-1,3-dioxane* as a clear liquid.

Yield: 1.7 g, 30 %.

^{1}H NMR: δ 1.59 (10 H, m), 1.86 (2 H, pent, J 6.8 Hz), 2.38 (2 H, m), 3.41 (2 H, t, J 6.8 Hz), 3.77 (2 H, dt, J 12.3, 2.1 Hz), 4.12 (2 H, dd, J 10.6, 5.0 Hz), 4.55 (1 H, t, J 5.3 Hz), 5.4-5.5 (2 H, m).

^{13}C NMR: δ 25.71, 27.36, 28.13, 28.70, 29.11, 29.26, 29.42, 32.81, 33.44, 34.01, 66.96 (x 2), 101.96, 122.92, 132.61.

$\nu_{(max)}$: 3015m, 2924s, 2852s, 1463m, 1428m, 1376m, 1239m, 1140s, 1014s cm^{-1}.

m/z: M^+: 318/320.

Found: $[M+H]^+$: 319.1268 $C_{15}H_{27}O_2Br$ requires $[M+H]^+$: 319.1272.

Experiment 88

2-(Heptadec-2-en-12-ynyl)-1,3-dioxane (154)

The procedure was as for Experiment 32, but using (11-bromoundec-2-enyl)-1,3-dioxane (1.7 g, 5.3 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.24 g, 0.01 mole, 2 mol. eq.) and 1-hexyne (0.87 g, 0.01 mole, 2 mol. eq.). The product, *2-(heptadec-2-en-12-ynyl)-1,3-dioxane*, was obtained as a colourless oil.

Yield: 1.2 g, 77 %.

^{1}H NMR: δ 0.96 (3 H, J 7.1 Hz), 1.34-1.54 (16 H, m), 2.10 (2 H, m), 2.19 (4 H, m), 2.42 (2 H, m), 3.82 (2 H, dt, J 12.4, 2.2 Hz), 4.16 (2 H, dd, J 10.6, 5.0 Hz), 4.59 (1 H, t, J 5.2 Hz), 5.4-5.5 (2 H, m).

^{13}C NMR: δ 13.62, 18.43, 18.74, 21.91, 25.72, 27.40, 28.83, 29.11, 29.29, 29.40, 29.49, 31.26, 33.44, 66.96 (x 2), 80.18 (x 2), 101.98, 122.85, 132.72.

$\nu_{(max)}$: 3017m, 2928s, 2854s, 1465s, 1376s, 1239s, 1140s, 1081s, 1015s cm^{-1}.

m/z: M^+: 320.

Found: $[M+H]^+$: 321.2792 $C_{21}H_{36}O_2$ requires $[M+H]^+$: 321.2793.

Experiment 89

2-(Heptadeca-2,12-dienyl)-1,3-dioxolane (155)

The procedure was as for Experiment 33, but using 2-(heptadec-2-en-12-ynyl) 1,3-dioxane (0.77 g, 2.4 x 10^{-3} mole, 0.1 mol. eq.), nickel tetraacetate (0.06 g, 2.4 x 10^{-4} mole, 0.1 mol. eq.), sodium borohyride (0.01 g, 2.4 x 10^{-3} mole, 0.1 mol. eq.) and ethylenediamine (0.06 ml, 6.01 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-(heptadeca-2,12-dienyl)-1,3-dioxolane*, was obtained as a colourless oil.

Yield: 0.54 g, 70 %.

^{1}H NMR: δ 0.9 (3 H, t, J 6.8 Hz), 1.31 (18 H, m), 2.05 (6 H, m), 2.37 (2 H, m), 3.77 (2 H, dt, J 12.4, 2.1 Hz), 4.12 (2 H, dd, J 10.7, J 4,9 Hz), 4.54 (1 H, t, J 5.2 Hz), 5.29-5.55 (4 H, m).

^{13}C NMR: δ 13.99, 22.33, 25.71, 26.89, 27.18, 27.40, 29.27, 29.49, 29.75, 31.95, 33.43, 66.96 (x 2), 101.99, 122.82, 129.84, 132.75.

$\nu_{(max)}$: 3073w, 3004m, 2932s, 2851s, 1465s, 1376s, 1239s, 1138s, 1081s, 1015s cm^{-1}.

m/z: M^+: 322.

Found: M^+: 322.2864 $C_{21}H_{38}O_2$ requires M^+: 322.2872.

Experiment 90

(E,Z)-2,13-Octadecadienal (126)

Chromium (III) chloride (0.76 g) in 4 M hydrochloric acid (20 ml) was added to 2-(heptadeca-2,12-dienyl)-1,3-dioxane (0.32 g). The mixture was refluxed for 1 hr and the reaction mixture steam-distilled. The distillate was refluxed for a further 30 mins, before being steam distilled out of the reaction vessel. The product was extracted from the water with ether (2 x 5 ml), and the solvent layer dried and evaporated to give the product *(E,Z)-2,13-octadecadienal*[64] as a colourless oil.

Yield: 0.07 g, 26 %.

^{1}H NMR: δ 0.89 (3 H, t, J 7.0 Hz), 1.32 (20 H, m), 2.00 (4 H, m), 2.34 (2 H, m), 5.34 (2 H, m), 6.11 (1 H, ddt, J 15.8, 7.9, 1.4 Hz), 6.84 (1 H, dt, J 15.8, 6.8 Hz), 9.49 (1 H, d, J 7.9 Hz).

^{13}C NMR: δ 13.97, 22.32, 26.89, 28.78, 29.12, 29.28, 29.44, 29.72, 31.94, 32.71, 129.82, 132.95, 159.00, 194.10.

$\nu_{(max)}$: 3002m, 2926s, 2854s, 1694s, 1464m, 1132m, 974m cm^{-1}.

Experiment 91

(3,3-Diisopropoxypropyl) triphenylphosphonium bromide (157)

A solution of acrolein (3.6 ml, 3.0 g, 0.055 mole) in dichloromethane (60 ml) was added very slowly over a period of 4 hrs to a stirred mixture of triphenylphosphine (13.1 g, 0.05 mole), 48 % hydrobromic acid (7.2 ml, 0.06 mole), dichloromethane (10 ml) and 2-propanol (10 ml), at -10 °C. The reaction was stirred for a further 12 hrs at this temperature. On completion of this reaction, the flask was warmed to room temperature and excess water was removed by decantation. The flask was cooled to 0 °C when triisopropyl orthoformate (45 ml, 43.0 g, 0.2 mole) was added quickly and stirred for 30 mins after which triethylamine (30 ml) was added. The mixture was concentrated on a rotary evaporator. Dry benzene (20 ml) was added to induce crystallisation of the phosphonium salt overnight. The crystals were washed with pentane and dried *in vacuo*, before being recrystallised from CH_2Cl_2/ether/pentane (1:2:2). *(3,3-Diisopropoxypropyl) triphenylphosphonium bromide*[118] was stored *in vacuo* for 48 hrs.

Yield: 14.1 g, 58 %.

^{1}H NMR: δ 1.11 (12 H, d, J 6 Hz), 1.85 (2 H, m), 3.62-3.78 (2 H, m), 3.85 (2 H, sept, 2 H, J 6.0 Hz), 5.04 (1 H, J 4.6 Hz), 7.62-7.78 (15 H, m).

^{13}C NMR: δ 18.6, 22.8, 23.2, 69.8, 98.4, 118.9, 128.3, 130.3, 130.5, 133.6, 133.7, 135.0.

CHN: $C_{27}H_{34}O_2PBr.H_2O$ (519.46): Calcd.: C 62.43, H 6.99. Found: C 62.34, H 6.91.

Experiment 92

(Z)-3-Bromododecenal diisopropyl acetal (158)

(3,3-Diisopropoxypropyl) triphenylphosphonium bromide (3.1 g, 6.58 x 10^{-3} mole, 1 mol. eq.) was dried twice by azeotropic distillation of dry benzene on a rotary evaporator. The phosphonium salt was dissolved in THF (20 ml), and cooled to - 40 °C. A 1.6 M. solution of butyllithium in hexane (14 ml, 1.2 mol. eq.) was added. The ylide was allowed to form over 1 hr at 0 °C, then cooled to -78 °C and bromononanal (1.75 g, 7.89 x 10^{-3} mole, 1.2 mol. eq.) in THF (8 ml) was added slowly. The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with the addition of sat. aq. ammonium chloride (5 ml) at 0 °C and the product extracted with ether (3 x 10 ml). The organic extracts were washed with brine solution (5 ml) and dried with magnesium sulphate. The solvents were evaporated to leave a viscous brown liquid. The residue was chromatographed on silica eluting with petrol/ether (5:0.5) to give the product *(Z)-3-bromododecenal diisopropyl acetal* as a colourless oil.

Yield:	1.7 g, 71 %.
^{1}H NMR:	δ 1.10 (6 H, d, J 6.1 Hz), 1.15 (6 H, d, J 6.1 Hz), 1.25 (10 H, m), 1.80 (2 H, pent, J 6.8 Hz), 2.01 (2 H, m), 2.29 (2 H, m), 3.36 (2 H, t, J 6.8 Hz), 3.82 (2 H, sept, 6.1 Hz), 4.49 (1 H, t, J 5.7 Hz), 5.31-5.44 (2 H, m).
^{13}C NMR:	δ 22.5, 23.3, 27.4, 28.1, 28.5, 28.6, 28.7, 28.9, 29.1, 29.3, 29.4, 32.7, 33.7, 33.9, 67.7, 100.0, 124.3, 131.9.
$\nu_{(max)}$:	2967s, 2927s, 2856s, 1460m, 1374m, 1174m, 11274 s, 1029s cm^{-1}.
m/z:	$[M-H]^+$: 361/363.

Experiment 93

Octadec-13-yn-(Z)-3-enal diisopropyl acetal (159)

The procedure was as for Experiment 32, but using (1.68 g, 4.62 x 10^{-3} mole, 1 mol. eq.), lithium amide (0.16 g, 5.55 x 10^{-3} mole, 1.5 mol. eq.) and 1-hexyne (0.56 g, 5.55 x 10^{-3} mole, 1.5 mol. eq.).

Yield: 1.3 g, 82 %.

^{1}H NMR: δ 0.88 (1 H, t, J 6.9 Hz), 1.15 (6 H, d, J 6.1 Hz), 1.20 (6 H, d, J 6.1 Hz), 1.30 (16 H, m), 2.05 (2 H, m) 2.15 (4 H, m), 3.87 (2 H, sept, J 6.1 Hz), 4.54 (1 H, t, J 5.6 Hz), 5.45 (2 H, m).

^{13}C NMR: δ 13.61, 18.4, 18.7, 21.9, 22.5, 23.3, 27.4, 28.1, 28.8, 29.1, 2934, 29.5, 33.07, 67.7, 80.15, 100.0, 124.2, 132.0.

Experiment 94

(Z,Z)-3,13-Octadecadienal diisopropyl acetal (160)

The procedure was as for Experiment 33, but using (0.75 g, 2.06 x 10^{-3} mole, 0.1 mol. eq.), nickel tetraacetate (0.05 g, 2.06 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.08 g, 2.06 x 10^{-4} mole, 0.1 mol. eq.) and ethylenediamine (0.035 ml, 5.15 x 10^{-4} mole, 0.25 mol. eq.).

Yield: 0.54 g, 71 %.

^{1}H NMR: δ 0.91 (3 H, t, J Hz), 1.15 (6 H, d, J 6.1 Hz), 1.19 (6 H, d, J 6.1 Hz), 1.29 (16 H, m), 2.03 (6 H, m), 2.35 (2 H, m), 3.88 (2 H, sept, J 6.1 Hz), 4.54 (1 H, t, J 5.7 Hz), 5.37 (4 H, m).

^{13}C NMR: δ 133.9, 22.33, 22.54, 23.3, 26.9, 27.1, 27.5, 29.3, 29.5, 29.7, 31.9, 67.7, 100.0, 124.2, 129.8, 132.1

$\nu_{(max)}$: 3004m, 2967s, 2925s, 2854s, 1465m, 1378m, 1127s, 1021s cm^{-1}.

m/z: $[M+H]^+$: 367.

Experiment 95

(E,Z)-2,13-Octadecadienal (126)

The procedure was as for Experiment 84, but using (Z,Z)-3,13-octadecadienal diisopropyl acetal (0.3 g, 8.19 x 10^{-4} mole, 1 mol. eq.) and chromium (III) chloride (0.76 g, 2.8 x 10^{-3} moles, 3.5 mol. eq.).

Yield: 0.07 g, 32 %.

Experiment 96

(E,Z)-2,4-Decadiene (161)

Hexanyl triphenylphosphonium bromide (1.0 g, 2.26 x 10^{-3} mole) was dissolved in dry THF (20 ml) under an argon atmosphere. The reaction vessel was cooled to -78 °C and sodium bis(trimethylsilyl)amide (2.2 ml, 1 M in THF) was added dropwise. The flask was allowed to warm to room temperature for 30 mins and before being cooled to -78 °C for the addition of crotonaldehyde (0.17 g, 2.49 x 10^{-3} mole, 1.1 mol. eq.). The reaction mixture was stirred overnight at rt. For work up the flask was cooled to -50 °C and sat. aq. ammonium chloride (10 ml) was added. The product was extracted with ether (2 x 10 ml). The extractions were collected, dried and the solvent evaporated and the resulting oil flash columned through a pad of silica using 5:2 petrol/ether to leave the product *(E,Z)-2,4-decadiene.*[119]

Yield: 0.2 g, 58 %.

^{1}H NMR: δ 0.94 (3 H, t, J 6.86 Hz), 1.83 (2 H, d, J 6.9 Hz), 183 (2 H, q, J 6.6 Hz), 5.32 (1 H, dt, J 10.6, 6.6 Hz), 5.74 (1 H, dq, J 14.8, 6.9 Hz), 5.99 (1 H, dd, J 10.6, 11.0 Hz), 6.39 (1 H, dd, 14.8, 11.0 Hz).

^{13}C NMR: δ 14.06, 18.25, 22.59, 27.59, 27.65, 28.92, 29.69, 31.72, 127.025, 128.37, 128.89, 129.91.

Experiment 97

2-(7-Heptyl)-1,3-dioxolane-7-triphenylphosphonium bromide (162)

Triphenylphosphine (3.1 g, 0.115 mole) was dissolved in toluene (30 ml) and 2-(7-bromoheptyl)-1,2-dioxolane (2.9 g, 0.115 mole) was added. The mixture was stirred vigorously under reflux for 48 hrs. The toluene was decanted and evaporated and columned with methanol and dichloromethane.

Partial deprotection was apparent from a occurred triplet at 9.68 ppm in the ^{1}H NMR spectrum which effected the CHN accuracy.

Yield: 3.5 g, 60 %.

^{1}H NMR: δ 1.43 (2 H, m), 1.63 (10 H, m), 3.76 (2 H, m), 3.82-3.97 (4 H, m), 4.81 (1 H, t, J 4.6 Hz), 7.70-7.89 (15 H, m), 9.68 (0.1 H, t).

^{13}C NMR: δ 22.22, 22.42, 23.01, 23.38, 29.97, 30.13, 33.09, 64.71, 104.12, 117.52, 118.88, 130.35, 130.55, 133.49, 133.655, 134.99.

CHN: C_{28} $H_{34}O_2PBr.H_2O$ (531.46): calcd. C 63.28, H 6.83 found C 62.18 H 6.85.

Experiment 98

Attempted Wittig reaction with 2-(7-Heptyl)-1,3-dioxolane-7-triphenylphosphonium Bromide. (163)

2-(7-Heptyl)-1,3-dioxolane-7-triphenylphosphonium bromide (3 g 5.6 mole, 1 mol. eq.) in THF (40 ml) was cooled to –78 °C and the base sodium bis(trimethylsilyl)amide (5.65 ml, 1 M in THF) was added. The flask was stirred at rt for 1 hr before being cooled to –78 °C for the addition of crotonaldehyde (0.8 g, 0.0113 mole, 2 mol. eq.). The mixture was then stirred at rt overnight. The flask was cooled to 0 °C and ammonium chloride (10 ml) was added. The product was extracted with ether (3 x 20 ml). The extractions were collected, dried and the solvent evaporated and the resulting oil flash columned through a patch of silica using 5:2 petrol/ether. The resulting oil was analysed by proton NMR and no aliphatic peaks were observed.

Experiment 99

2-(7-Bromoheptanyl)-1,3-dioxane (164)

Bromooctanal (7.3 g), 1,3-propanediol (10.0 g, 4 mol. eq.), *p*-toluene sulphonic acid (0.34 g) in benzene (70 ml) were refluxed in a Dean-Stark apparatus overnight. The mixture was cooled and a saturated aqeous solution of sodium bicarbonate (10 ml) was added and the product extracted with dichloromethane (2 x 20 ml). The organic layer was dried with $MgSO_4$ and concentrated. The product was columned in petrol/ether (5:2).

Yield: 6.3 g, 66 %.

^{1}H NMR: δ 1.33 (10 H, m), 1.57 (2 H, m), 1.85 (2 H, m), 3.40 (2 H, t, J 6.8 Hz), 3.77 (2 H, dt, J 12.4, 1.6 Hz), 4.10 (2 H, dd, J 11.6, 4.9 Hz), 4.50 (1 H, t, J 5.1 Hz).

^{13}C NMR: δ 23.8, 25.8, 28.0, 28.6, 29.2, 32.76, 32.9, 33.9, 35.1, 66.8, 102.3.

$\nu_{(max)}$: 2928s, 2852s, 1466m, 1376m, 1240s, 1144s, 999s cm^{-1}.

m/z: M^+: 265.

Experiment 100

2-(Heptanyl)-1,3-dioxane-7-triphenylphosphonium bromide (165)

Triphenylphosphine (9.3 g, 0.0356 mole, 1.5 mol. eq.), was dissolved in dry toluene (70 ml) 2-(7-bromoheptanyl)-1,3-dioxane (6.3g, 0.0237 mole, 1 mol. eq.) was added and the mixture was refluxed for 48 hrs. The toluene was evaporated and the product, *2-(heptanyl)-1,3-dioxane-7-triphenylphosphonium bromide* was washed with pentane and dried thoroughly, to give a thick viscous oil.

Yield: 10.7 g, 91 %.

^{1}H NMR: δ 1.20 (6 H, m), 1.45 (2 H, m), 1.59 (4 H, m), 3.69 (4 H, m), 4.03 (2 H, dd, J^1 11.6, J^2 4.8 Hz), 4.43 (1 H, t, J 5.0 Hz), 7.64-7.85 (15 H, m).

^{13}C NMR: δ 22.3, 22.5, 23.1, 23.7, 25.7, 28.8, 28.9, 30.0, 34.9, 66.8, 102.2, 117.5, 118.9, 130.4, 130.6, 133.5, 133.6, 135.0, 135.0.

CHN: $C_{29}H_{36}O_2PBr.H_2O$ (545.49): Calcd: C 63.97, H 7.00. Found: C 63.93; H 7.05.

Experiment 101

2-((Z,E)-7,9-Undecadienyl)-1,3-dioxane (166)

2-(Heptanyl)-1,3-dioxane-7-triphenylphosphonium bromide (3 g, $6.04x10^{-3}$ mole) was dissolved in THF (30 ml). Sodium bistrimethylsilylamide (6.04 ml, 1 M) was added dropwise at –78 °C. The ylide turned orange and the reaction vessel was allowed to warm to rt. for1 hr, after which the vessel was cooled again to –78 °C for the addition of crotonaldehyde (0.99 ml, 0.84 g, 0.012 mole, 2 mol. eq.) in THF (4 ml). The reaction mixture was allowed to warm to rt and stirred overnight. The flask was cooled to 0 °C and sat. aq. ammonium chloride (10 ml)

was added. The product was extracted with ether (3 x 20 ml). The extractions were collected, dried and the solvent evaporated. The resulting oil was flash columned through silica with 5:2 petrol/ether to leave the product 2-((Z,E)-7,9-undecadienyl)-1,3-dioxane.

Yield: 1.22 g, 78 %.

^{1}H NMR: δ 1.33 (10 H, m), 1.56 (2 H, m), 1.78 (3 H, d, J 6.8 Hz), 2.07 (2 H, m), 3.75 (2 H, dt, 12.4, 2.3 Hz), 4.10 (2 H, dd, J 10.6, 5.0 Hz), 4.51 (1 H, t, J 5.1 Hz), 5.30 (1 H, dt, J 10.6, 7.7 Hz), 5.68 (1 H, dq, J 14.8, 6.8 Hz), 5.93 (1 H, dd, J 10.8, 12.1 Hz), 6.32 (1 H, dd, J 14.8, 12.1 Hz).

^{13}C NMR: δ 18.2, 23.9, 25.8, 27.6, 29.1, 29.3, 29.5, 35.2, 66.8, 102.4, 127.0, 128.4, 128.9, 129.8.

$\nu_{(max)}$: 3017m, 2926s, 2852s, 1675m, 1458m, 1376m, 1145s, 999s cm^{-1}.

m/e: M^+: 238.

Found: $[M-H]^+$: 237.1852 $C_{15}H_{26}O_2$ requires $[M-H]^+$: 237.1855.

Reaction repeated with addition of base at –78 °C, aldehyde at –78 °C and stirred overnight at –25 °C.

Yield: 53 %.

Reaction repeated with addition of base at RT, aldehyde at –78 °C and stirred overnight at rt.

Yield: 55 %.

Reaction repeated with addition of base at RT, aldehyde at –30 °C and stirred overnight at rt.

Yield: 63 %.

The reaction was repeated with butyllithium as base added at –78 °C, aldehyde at –78°C and stirred overnight at rt.

Yield: 69 %.

^{1}H NMR: δ 1.32 (10 H, m,), 1.57 (2 H, m), 1.73 (3 H, d, J 6.6 Hz), 2.03 (2 H, m), 3.75 (2 H, dt, J 12.2, 2.4 Hz), 4.10 (2 H, ddd, J 10.7, 3.8, 1.2 Hz).

^{13}C NMR: δ 18.27, 23.89, 25.81, 29.06, 29.27, 32.47, 35.14, 66.79, 102.35, 126.48, 130.25, 131.73, 131.95.

m/e: M^+: 238.

Then repeated with butyllithium added at –78 °C and the aldehyde at –78 °C. The reaction vessel was then kept at 0 °C for 4 hrs and then at rt overnight.

Yield: 1.8 g, 56 %.

^{1}H NMR: δ 1.35 (10 H, m), 1.57 (2 H, m), 1.74 (2 H, d, J 6.9 Hz), 1.77 (2 H, d, J 6.6 Hz), 3.76 (2 H, dt, J 2.4, 12.3 Hz), 4.09 (2 H, ddd, J 10.6, 3.8, 1.2 Hz), 4.51 (1 H, t, J 5.1 Hz), 5.32 (1 H, dt, J^1 10.6, J^2 6.6 Hz), 5.74 (1 H, dq, J 14.8, 6.9 Hz), 5.99 (1 H, dd, J 10.6, 11.0 Hz), 6.39 (1 H, dd, J 11.0, 14.8 Hz).

^{13}C NMR: δ (E,Z) 18.27, 23.89, 25.85, 27.61, 29.02, 29.10, 29.32, 29.59, 35.2, 66.88, 102.4, 127.04, 128.46, 128.94, 129.76.

δ (E,E) 32.49, 126.63, 130.22, 131.71, 132.09.

$\nu_{(max)}$: 3014m, 2926s, 2851s, 1675m, 1458m, 1377m, 1144s, 991s cm^{-1}.

m/e: $[M-H]^+$: 237.

Then repeated with butyllithium added at –78 °C and the aldehyde at –78 °C. The reaction vessel was then kept at –25 °C overnight.

Yield: 1.32 g, 66 %.

Experiment 102

(Z,E)-8,10-Dodecadienal dimethyl acetal (180)

2-((Z,E)-7,9-Undecadienyl)-1,3-dioxane (0.87 g), was added to methanol (20 ml) and *p*-toluene sulphonic acid (0.02 g, 1.23 x 10^{-4} mole) and refluxed gently for 4 hrs. The reaction was then cooled with ice and the acid neutralised with sodium carbonate. Some methanol was evaporated and the product was then extracted with dichloromethane (20 ml) with was washed with water (2 x 10 ml). The solvent was dried with $MgSO_4$ and evaporated to give the acyclic acetal.

Yield: 0.76 g, 97 %.

^{1}H NMR: δ 1.33 (8 H, m), 1.61 (2 H, m), 1.78 (2 H, d, J 6.6 Hz), 2.14 (2 H, m), 3.32 (6 H, s), 4.36 (1 H, t, J 5.6 Hz), 5.30 (1 H, m), 5.67 (1 H, m), 5.94 (1 H, m), 6.32 (1 H, m).

^{13}C NMR: δ 18.2, 24.5, 27.6, 29.1, 29.3, 29.6, 32.4, 52.5, 104.5, 127.0, 128.4, 128.9, 129.75.

$\nu_{(max)}$: 3015m, 2928s, 2854s, 1452s, 1379s, 1190s, 1127s, cm^{-1}.

m/e: M^+-OCH_3: 195, M^+-$(OCH_3)_2$: 164.

Experiment 103

(Z,E)-8,10-Dodecadienal (127)

The (Z,E)-8,10-dodecadienal dimethyl acetal (0.7 g, 3.1 x 10^{-3} mol.) was dissolved in THF (2 ml) and added to 5 % HCl (10 ml). The mixture was refluxed for 6 hrs, when the product was extracted with dichloromethane, dried and the solvent evaporated. The product was chromatographed with silica using 5:1 petrol /ether.

Yield: 0.31 g, 53.6 %.

^{1}H NMR: δ 1.35 (8 H, m), 1.64 (2 H, m), 1.79 (3 H, d, J 6.7 Hz), 2.15 (2 H, m), 2.43 (2 H, dt, J 7.2, 1.8 Hz), 5.29 (1 H, dq, J 10.8, 7.6 Hz), 5.67 1 H, 5.93 (1 H, dd, J 10.8, 1.8 Hz), 6.32 (1 H, dd, J 14.8, 12.1 Hz) 9.7 (1 H, t, J 1.8 Hz).

^{13}C NMR: δ 18.1, 21.8, 27.3, 28.7, 28.8, 29.1, 43.6, 126.7, 128.4, 128.9, 129.6, 202.6.

$\nu_{(max)}$: 3017m, 2927s, 2854s, 1726s, 1450m cm^{-1}.

Experiment 104

2-(7-Bromooctanyl)-1,3-dioxane (167)

Bromononanal (18.0 g, 0.081 mole, 1 mol. eq.), 1,3-propanediol (12.3 g, 0.162 mole, 2 mol. eq.), *p*-toluene sulphonic acid (0.77 g, 4.07 x 10^{-3} mole, 0.05 mol. eq.) in toluene (100 ml) were refluxed in a Dean-Stark apparatus overnight. The mixture was cooled and a sat. aq. solution of sodium bicarbonate (30 ml) was added and the product extracted with dichloromethane (2 x 20 ml). The organic layer was dried with $MgSO_4$ and concentrated. The product was columned in petrol/ether (5:2).

Yield: 15.1 g, 66 %.

^{1}H NMR: δ 1.33 (13 H, m), 1.57 (2 H, m), 1.83 (2 H, m), 2.08 (1 H, m) 3.40 (2 H, t, J 6.8 Hz), 3.77 (2 H, dt, J^1 12.1, J^2 2.0 Hz), 4.10 (2 H, dd, J 10.8, 4.9 Hz), 4.51 (1 H, t, J 5.0 Hz).

^{13}C NMR: δ 23.8, 25.8, 28.1, 28.6, 29.2, 29.3, 32.7, 34.0, 35.1, 66.8, 102.3.

$\nu_{(max)}$: 2928s, 2853s, 1465m, 1376m, 1240m, 1145s, 1000m cm^{-1}.

Experiment 105

2-(Octanyl)-1,3-dioxane-8-triphenylphosphonium bromide (168)

Triphenylphosphine (14.1 g, 0.053 mole, 1 mol. eq.), was dissolved in dry toluene (70 ml). 2-(7-Bromoheptanyl)-1,3-dioxane (15.0 g, 0.053 mole, 1 mol. eq.) was added and the mixture was refluxed for 48 hrs. The toluene was evaporated and the product was washed with pentane and dried thoroughly to give *2-(octanyl)-1,3-dioxane-8-triphenylphosphonium bromide* as a thick sticky oil.

Yield: 18 g, 62.7 %.

^{1}H NMR: δ 1.15 (9 H, m), 1.45 (2 H, m), 1.54 (4 H, m), 1.97 (1 H, m), 3.68 (4 H, m), 4.00 (2 H, dd, J 5.0, 10.7 Hz), 4.42 (1 H, t, J 5.1 Hz) 7.62-7.88 (15 H, m).

^{13}C NMR: δ 22.3, 23.1, 25.7, 28.9, 29.2, 30.1, 30.4, 35.0, 66.8, 102.2, 130.4, 130.6, 133.5, 133.6, 135.0.

CHN: $C_{30}H_{38}O_2PBr$ (451.50): calcd.: C 66.67, H 6.90. Found: C 66.63, H 6.77.

Experiment 106

Pent-2-yn-1-ol (169)

Liquid ammonia (200 ml) was condensed into a 3 necked flask (500 ml) using a liquid nitrogen/methylated spirits condenser. Lithium amide (15 g, 0.802 mole, 3 mol. eq.) was added over 0.5 hrs, and stirred for 0.5 hrs. Propargyl alcohol (15 g, 0.267 mole, 1 mol. eq.) in dry ether (20 ml) was added dropwise over 0.5 hrs. Ethyl bromide (26.1 g, 0.238 mole, 0.9 mol. eq.) in dry ether (50 ml) added dropwise over 0.5 hrs. The reaction vessel was kept cool to stop ammonia evaporation for 5 hrs, after which the condenser was removed to allow the ammonia to evaporate overnight. A white sludge was left. This was acidified to pH 1 with 10 % H_2SO_4. The product was extracted with ether (4 x 250 ml), washed with sat. aq. sodium bicarbonate, dried with $MgSO_4$, and the solvents evaporated. The product was columned in 5:2 petrol/ether, giving *pent-2-yn-1-ol*.[120]

Yield: 12 g, 54 %.

^{1}H NMR: δ 1.15 (3 H, t, J 7.5 Hz), 1.18 (1 H, OH, br), 2.22 (2 H, qt, J^1 7.5, J^2 2.15 Hz), 4.26 (2 H, t, J 2.15 Hz).

^{13}C NMR: δ 12.4, 13.7, 51.3, 73.7, 87.8.

$\nu_{(max)}$: 3343br, 2977s, 2937s, 2877s, 2230m, 1715m, 1455s, 1319s, 1012s, cm^{-1}.

Experiment 107

Pent-2-ynal (170)

Pent-2-yn-1-ol (3.0 g, 0.035 mole, 1 mol. eq.) was added to a stirred solution of pyridinium chlorochromate (18.3 g, 0.714 mole, 2 mol. eq.) in dichloromethane (50 ml). The mixture was refluxed for 2 hrs and the reaction was followed by G.C.. When the reaction was completed,

petrol/ether (5:2) was added and the products filtered through silica under vacuum. The solvents were evaporated to leave the product, *pent-2-ynal.*[121]

Yield: 1.66 g, 56 %.

^{1}H NMR: δ 1.22 (3 H, t, J 7.4 Hz), 2.42 (2 H, q, J 7.4 Hz), 9.16 (1 H, s).

^{13}C NMR: δ 12.53, 12.83, 80.98, 100.25, 177.22.

$\nu_{(max)}$: 29984w, 2942w, 2856w, 2209m, 1666s, 1459w, 1140m, 910s, 732s cm^{-1}.

Experiment 108

2-((Z)-8-Tridecen-10-ynyl)-1,3-dioxane (171)

2-(Octanyl)-1,3-dioxane-8-triphenylphosphonium bromide (2.2 g, 4.26 x 10^{-3} mole, 1 mol. eq.) was dissolved in dry THF (30 ml) under an argon atmosphere. At rt sodium bis(trimethylsilyl)amide (5.1 ml, 1 M in THF, 1.2 mol. eq.) was added carefully dropwise. The reaction was stirred for 1 hr before being cooled to –78 °C for the addition of pent-2-ynal (0.35 g, 4.26 10^{-3} mole, 1 mol. eq.). The reaction was then stirred overnight at rt, cooled to 0 °C, quenched with sat. aq. ammonium chloride solution (10 ml), and the products extracted with ether (2 x 10 ml). The ether layer was dried and the solvents evaporated. The crude products were diluted in petrol/ether (5:2) and flash columned through a pad of silica. Evaporation of the solvents gave the product *2-((Z)-8-tridecen-10-ynyl)-1,3-dioxane.*

Yield: 0.55 g, 48 %.

^{1}H NMR: δ 1.18 (3 H, t, J 7.4 Hz), 1.31 (12 H, m), 1.58 (2 H, m), 2.08 (2 H, m), 2.28 (2 H, m), 2.34 (2 H, dt, J 7.4, 2.1 Hz), 3.76 (2 H, dt, J 12.1, 2.3 Hz), 4.09 (2 H, ddd, J 11.7, 4.9, 1.2 Hz), 4.50 (1 H, t, J 5.1 Hz), 5.45 (1 H, dt, J 10.3, J 2.1 Hz), 5.81 (1 H, dt, J 10.3, 7.3 Hz).

^{13}C NMR: δ 13.2, 14.0, 23.9, 25.8, 29.0, 29.3, 29.4, 29.9, 35.9, 66.8, 77.5, 96.5, 102.4, 109.2, 142.6.

$\nu_{(max)}$: 3018m, 2922s, 2850s, 2214w, 1460s, 1377s, 1144s, 1002m cm^{-1}.

m/z: M^+-CH_3: 263, M^+-C_2H_5: 249.

Experiment 109

2-((Z,Z)-8,10-Tridecadienyl)-1,3-dioxane (172)

The procedure was as for Experiment 33, but using (0.5 g, 1.89 x 10^{-3} mole, 1 mol. eq.), nickel tetra-acetate (0.047 g, 1.89 x 10^{-4} mole, 0.1 mol. eq.), sodium borohydride (0.007 g, 1.89 x 10^{-4} mole, 0.1 mol. eq.) and ethylenediamine (0.03 ml, 0.028 g, 4.73 x 10^{-4} mole, 0.25 mol. eq.). The product, *2-((Z,Z)-8,10-tridecadienyl)-1,3-dioxane*, showed one peak by g.l.c..

Yield: 0.42 g, 83 %

^{1}H NMR: δ 0.95 (3 H, t, J 7.5 Hz), 1.25 (12 H, m), 1.53 (2 H, m), 2.01 (2 H, m), 2.13 (2 H, m), 3.72 (2 H, dt, J 12.3, 2.5 Hz), 4.07 (2 H, ddd, J 11.7, 4.9, 1.2 Hz), 4.46 (1 H, t, J 5.1 Hz), 5.39 (2 H, dt, J 10.5, 6.8 Hz), 6.18 (2 H, dd, J 10.5, 5.2 Hz).

^{13}C NMR: δ 14.1, 20.7, 23.9, 25.8, 27.4, 29.1, 29.3, 29.5, 35.2, 66.8, 102.4, 122.9, 123.4, 132.0, 133.5.

$\nu_{(max)}$: 3035m, 3002m, 2925s, 2351s, 1463s, 1434m, 1376m, 1145s cm^{-1}.

Experiment 110

(E,E)-2,4-Hexadien-1-ol (173)

Lithium aluminium hydride (2.1 g) in ether (40 ml) was stirred at room temp under argon. Sorbic acid (5.0 g) in ether (100 ml) was added dropwise to the flask to allow for a gentle reflux. The mixture was stirred for 1 hr. Ethyl acetate (20 ml) was added dropwise, followed by water (20 ml) and H_2SO_4 was then added to pH 1. (E,E)- 2,4-Hexadien-1-ol showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[121]

Yield: 4.1 g, 91 %.

^{1}H NMR: δ 1.66 (1H, OH), 1.76 (3 H, d, 6.57 Hz), 4.16 (2 H, d, J 6.0 Hz), 5.65-5.79 (2 H, m), 6.01 (2 H, m).

^{13}C NMR: δ 18.08, 63.49, 129.12, 130.14, 130.69, 131.94.

$\nu_{(max)}$: 3330br, 3019s, 2914s, 2854s, 1447m, 1376m, 1244m, 1096s, 986s cm^{-1}.

Experiment 111

1-Bromo-(E,E)-2,4-Hexadiene (174)

(E)-2-(E)-3-Hexadien-1-ol (0.5 g, 5.1 x 10-3 mole, 1mol. eq.) in dry ether (5 ml) was stirred at 0 °C under an argon atmosphere. Phosphorus tribromide (0.24 ml, 0.69 g, 2.55 x 10^{-3} mole, 0.5 mol. eq.), added dropwise over 5 mins. The mixture was stirred for a further 5 mins at room temp. Water (10 ml) and then ether (10 ml) were added. The ether layer was washed with sat. aq. sodium bicarbonate solution and dried with $MgSO_4$ and evaporated to give the bromide. The product showed one peak by g.l.c. and gave an identical ^{1}H NMR spectrum to that in the literature.[103]

Yield: 0.74 g, 91 %.

^{1}H NMR: δ 1.79 (3 H, d, J 6.6 Hz), 4.05 (2 H, d, J 7.9 Hz), 5.70-6.36 (4 H, m).

^{13}C NMR: δ 18.21, 33.85, 125.94, 130.15, 132.18, 135.39.

$\nu_{(max)}$: 3019s, 2964s, 2915s, 1656s, 1436s, 1200s, 986s cm^{-1}.

Experiment 112

(E,E)-2,4-Hexadien-1-yl acetate (177)

To (E)-2-(E)-4-hexadien-1-ol (1.3 g, 0.013 mole) in dry dichloromethane (30 ml), was added triethylamine (1.4 ml, 2.01 g, 0.019 mole, 1.5 mol. eq.) at 0 °C. After 15 mins acetyl chloride (1.4 ml, 1.56 g, 0.019 mole, 1.5 mol. eq.) was added dropwise. The mixture was allowed to reach room temperature and stirred overnight. Ether (20 ml) was added and the mixture was filtered through silica. The solvents were evaporated and the product was columned in petrol/ether (5:1) to give *(E,E)-2,4-hexadien-1-yl acetate*.[122]

Yield: 1.65 g, 90 %.

^{1}H NMR: δ 1.76 (3 H, d, J 6.6 Hz), 2.07 (3 H, s), 4.57 (2 H, d, J 6.6 Hz), 5.57-5.83 (2 H, m), 6.00-6.31 (2 H, m).

^{13}C NMR: δ 18.0, 20.9, 123.6, 130.3, 131.2, 134.9, 170.8.

$\nu_{(max)}$: 3024m, 2937m, 1739s, 1662m, 1444m, 1378m, 1238s, 990s cm^{-1}.

Experiment 113

(E,E)-2-4-Tridecadiene (181)

Bromoheptane (1.0 g, 5.58 x 10^{-3} mole, 3 mol. eq.) was added carefully to magnesium (0.32 g, 0.014 mole, 7 mol. eq.) in dry THF (2 ml) under an argon atmosphere. The reaction was heated gently for 2 hrs and then cooled to rt. Sorbyl acetate (0.26 g, 1.86 x 10^{-3} mole, 1 mol. eq.) and lithium chlorocuprate (0.07 ml) in dry THF (3 ml) under an argon atmosphere were cooled to –78 °C and the Grignard solution was added dropwise. The mixture was kept at 0 °C for 1 hr then left at rt overnight. The flask was cooled to 0 °C and sat. aq. ammonium chloride solution (10 ml) was added, then the product was extracted with ether and dried with $MgSO_4$,. The solvents were evaporated to give *(E,E)-2-4-tridecadiene.*

Yield: 0.3 g, 89 %.

^{1}H NMR: δ 0.89 (3 H, t, 6.2 Hz), 1.27 (12 H, m), 1.74 (3 H, d, J 6.4 Hz), 2.07 (2 H, m), 5.56 (2 H, m), 6.01 (2 H, m).

^{13}C NMR: δ 14.07, 22.67, 29.21, 29.27, 29.36, 29.45, 29.69, 31.89, 32.56, 126.57, 130.17, 131.73, 132.21.

m/e: M^+: 180

Experiment 114

2-(5-Bromopentyl)-1,3-dioxane (178)

6-Bromohexanal (10 g), 1,3-propanediol (8.4 g, 0.11 mole, 2 mol. eq.) and *p*-toluene-sulphonic acid (0.52 g, 2.77 x 10^{-3} mole, 0.05 mol. eq.) in toluene (70 ml) were refluxed in a Dean-Stark apparatus overnight. The mixture was cooled and a sat. aq. solution of sodium bicarbonate (10 ml) was added and the product extracted with dichloromethane (2 x 20 ml). The organic layer was dried with $MgSO_4$ and concentrated. The product was purified by chromatography on silica eluting with petrol/ether (5:2) to *give 2-(5-bromopentyl)-1,3-dioxane.*

Yield: 10 g, 81 %.

^{1}H NMR: δ 1.44 (5 H, m), 1.59 (2 H, m), 1.86 (2 H, pent, J 6.8 Hz), 2.08 (1 H, m), 3.41 (2 H, t, J 6.8 Hz), 3.75 (2 H, dt, J 12.3, 2.2 Hz), 4.11 (2 H, ddd, J 11.7, 5.0, 1.1 Hz), 4.52 (1 H, t, J 4.9 Hz).

^{13}C NMR: δ 23.0, 25.8, 27.9, 32.6, 33.7, 34.9, 66.8, 102.1.

$\nu_{(max)}$: 2950s, 2350sm 2729m, 1460s, 1429s, 1377s, 1248s, 1144s, 1090s cm^{-1}.

Experiment 115

2-((E,E)-7,9-Undecadienyl)-1,3-dioxane (179)

2-(5-Bromopentyl)-1,3-dioxane (1.5 g, 6.33 x 10^{-3} mole, 1 mol. eq.) was added carefully to magnesium (0.43 g 0.089 mole, 3 mol. eq.) in dry THF (2 ml) under an argon atmosphere. The reaction was heated gently for 2 hrs and then cooled to rt. Sorbyl acetate (0.88 g, 6.33 x 10^{-3} mole) and lithium chlorocuprate (2.5 ml, 0.1 M in THF 0.4 mol. eq.) in dry THF (3 ml) were stirred under an argon atmosphere and cooled to –78 °C. The Grignard solution was then added dropwise. The mixture was kept at 0 °C for 1 hr then at rt overnight. The flask was cooled to 0 °C and sat. ammonium chloride solution (10 ml) was added, and the product was extracted with ether and dried with $MgSO_4$. The solvents were evaporated to give *2-((E,E)-7,9-undecadienyl)-1,3-dioxane.*

Yield: 0.5 g, 33 %.

^{1}H NMR: δ 1.32 (5 H, m), 1.58 (2 H, m), 1.73 (3 H, d, J 6.49 Hz), 2.05 (3 H, m), 3.76 (2 H, dt, J 12.3, 2.4 Hz), 4.09 (2 H, ddd, J 10.7, 3.8, 1.2 Hz), 4.50 (1 H, t, J 5.0 Hz), 5.55 (2 H, m), 6.01 (2 H, m).

^{13}C NMR: δ 17.9, 23.8, 25.8, 29.0, 29.3 (x 2), 32.4, 35.2, 66.8 (x 2), 102.4, 126.6, 130.2, 131.7, 132.1.

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APPENDIX

This appendix contains a list of all known aldehyde insect sex phermones. A full list of all pheromones are found on the Pheronet web page:

http://www.nysaes.cornell.edu/pheronet/cpds.html

C-10

(Z)-5-Decenal

C-11

10-Undecenal

C-12

Dodecanal

(Z)-5-Dodecenal

(Z)-7-Dodecenal

(Z)-9-Dodecenal

(E)-9-Dodecenal

(Z,Z)-5,7-Dodecadienal

(Z,E)-5,7-Dodecadienal

(E,Z)-5,7-Dodecadienal

(E,Z)-7,9-Dodecadienal

(Z,E)-8,10-Dodecadienal

(E,Z)-8,10-Dodecadienal

(E,E)-8,10-Dodecadienal

(Z)-9,11-Dodecadienal

(E)-9,11-Dodecadienal

C-14

Tetradecanal

(Z)-5-Tetradecenal

(Z)-7-Tetradecenal

(Z)-9-Tetradecenal

(Z)-11-Tetradecenal

(E)-11-Tetradecenal

(E,E)-8,10-Tetradecadienal

(Z,Z)-9,11-Tetradecadienal

(Z,E)-9,11-Tetradecadienal

(Z,E)-9,12-Tetradecadienal

10,12-Tetradecadienal

(Z)-11,13-Tetradecadienal

(E)-11,13-Tetradecadienal

(Z,E)-9,11,13-Tetradecatrienal

C-15

(Z)-10-Pentadecenal

(E,Z)-9,11-Pentadecadienal

C-16

Hexadecanal

(Z)-7-Hexadecenal

(Z)-9-Hexadecenal

(Z)-10-Hexadecenal

(E)-10-Hexadecenal

(Z)-11-Hexadecenal

(E)-11-Hexadecenal

(Z)-12-Hexadecenal

(E,Z)-6,11-Hexadecadienal

(Z,Z)-7,11-Hexadecadienal

(Z,E)-7,11-Hexadecadienal

(Z,E)-9,11-Hexadecadienal

(E,Z)-9,11-Hexadecadienal

(Z,Z)-10,12-Hexadecadienal

(Z,E)-10,12-Hexadecadienal

(E,Z)-10,12-Hexadecadienal

(E,E)-10,12-Hexadecadienal

(Z,Z)-11,13-Hexadecadienal

(Z,E)-11,13-Hexadecadienal

(E,Z)-11,13-Hexadecadienal

(E,E)-11,13-Hexadecadienal

(Z)-13-Hexadecen-11-ynal

(E,E,Z)-4,6,11-Hexadecatrienal

(E,E,Z)-10,12,14-Hexadecatrienal

(E,E,E)-10,12,14-Hexadecatrienal

C-18

Octadecanal

(E)-2-Octadecenal

(Z)-9-Octadecenal

(Z)-11-Octadecenal

(E)-11-Octadecenal

(Z)-13-Octadecenal

(E)-13-Octadecenal

(E)-14-Octadecenal

(E,Z)-2,13-Octadecadienal

(Z,Z)-3,13-Octadecadienal

(Z,Z)-9,12-Octadecadienal

(E,E)-11,14-Octadecadienal

(Z,Z)-11,13-Octadecadienal

(Z,Z)-13,15-Octadecadienal

(Z,Z,Z)-9,12,15-Octadecatrienal