Abstract

The Brown Spruce Longhorn Beetle (BSLB) made its first appearance in Canada in the late 1980s at Point Pleasant Park, NS, and has since then killed several thousand spruce trees in the area. If gone unchecked, the BSLB could decimate spruce populations across North America and cause tremendous economic losses. The wasp *W. occidentalis*, a native parasitoid of BSLB, could potentially be of use in curbing the invasive pest’s spread, provided that the chemical ecology of this wasp can be elucidated.

GC/MS and GC/EAD analysis of *W. occidentalis* extracts suggested that contact pheromones produced by females of the species are allenes — long chain hydrocarbons with two consecutive sites of unsaturation — which are extremely rare in insects. Furthermore, the pheromones appeared to consist of a homologous series of odd-numbered carbon units, ranging from 23 to 31 carbon atoms, with the sites of unsaturation suspected of being located at the 10, 11- and 11, 12-carbons. Racemic mixtures of the 27 and 29 carbon allenes were synthesized, each of which contained the 10, 11- and 11, 12-isomers, and subsequent GC/MS analysis showed similarity to what was observed in the *W. occidentalis* samples. Consequently, a synthetic route toward an optically enriched 29 carbon allene was devised and executed, but it was later discovered that these allenes (as well as the racemic versions) had no contact behavioral activity on live insects. Upon reexamination of the original GC/MS data alternative structures were postulated and 17-octacosynal and various long-chain alkynes were synthesized since alkynes are known to have an intermediate allenic state in the mass spectrometer ion source. Further spectral analyses of these
compounds point to 11-nonacosyne potentially being the *W. occidentalis* contact pheromone.
Dedication

This work is dedicated to all the spruce trees that lost relatives during the Brown Spruce Longhorn Beetle invasion of Eastern Canada. Hang in there, and we shall develop methods to prevent this from happening in the future!
Acknowledgements

Several people have been instrumental in helping me get to the end of this Master’s degree. Massive thanks to Dr. David MaGee for taking me on as a graduate student, and assigning me a very interesting project. Even more thanks are required for being patient with me when it came to my somewhat less-than-optimal progress rate when life threw me a bucket-load of lemons…and for putting up with the sometimes silly reaction mechanism questions I asked without first thinking things through! The other half of the supervisor duo, Dr. Peter Silk, also deserves a big “thank you” for all the help he has provided me over the last few years, especially where GC/MS analysis is concerned.

I also want to thank my parents, Raynald and Jolène, for the continued support, and for allowing me to live at home during my adventures in academia. David Green also provided tremendous support to me on campus, both emotionally and every time he fixed the NMRs, as well as in the woods and on the rivers: Dave is a great fishing coach!

And what would I have done without the help of some key people at the Canadian Forest Service labs? Dr. Peter Mayo has saved me many times when it came to running GC/MS samples, and Dr. Gaetan LeClair was helpful several times as well.

Lastly, I want to thank all my lab mates and friends as well, for showing support and for the interesting chats in the group office. Deepa, I miss your cooking!
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Å</td>
<td>Angstrom</td>
</tr>
<tr>
<td>Ac&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>acetic anhydride</td>
</tr>
<tr>
<td>BH&lt;sub&gt;3&lt;/sub&gt;-DMS</td>
<td>borane dimethylsulfide complex</td>
</tr>
<tr>
<td>br</td>
<td>broad</td>
</tr>
<tr>
<td>bs</td>
<td>broad singlet</td>
</tr>
<tr>
<td>BSLB</td>
<td>Brown Spruce Longhorn Beetle</td>
</tr>
<tr>
<td>c</td>
<td>concentration</td>
</tr>
<tr>
<td>13C</td>
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<td>CBS</td>
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<tr>
<td>CFIA</td>
<td>Canadian Forest Inspection Agency</td>
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<tr>
<td>CFS</td>
<td>Canadian Forest Service</td>
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<tr>
<td>cm&lt;sup&gt;−1&lt;/sup&gt;</td>
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<tr>
<td>Δ</td>
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</tr>
<tr>
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<td>DMAP</td>
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<td>DMPU</td>
<td>1, 3-dimethyl-3, 4, 5, 6-tetrahydro-2-pyrimidinone</td>
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<td>Acronym</td>
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<tr>
<td>EAB</td>
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<td>electroantennograph</td>
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<tr>
<td>GC/MS</td>
<td>gas chromatography – mass spectrometry</td>
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<td>H⁺</td>
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<td>hexamethylphosphoramide</td>
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<td>Hertz</td>
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<tr>
<td>IR</td>
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<tr>
<td>J</td>
<td>coupling constant in Hertz</td>
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<tr>
<td>KHMDS</td>
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<td>LAH</td>
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</tr>
<tr>
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<td>iodomethane</td>
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MHz  megahertz
min  minutes
mL  millilitre
mm/Hg  millimetres of mercury
mmol  millimole
MPt  melting point
m/z  mass to charge ratio
NBS  N- bromosuccinimide
nBuLi  n-butyllithium
nm  nanometre
NMO  N-methylmorpholine N-oxide
NMR  nuclear magnetic resonance
NPV  nucleopolyhedrovirus
p  pentet
PDC  pyridinium dichromate
PCC  pyridinium chlorochromate
PPh₃  triphenylphosphine
ppm  parts per million
PPTS  pyridinium para-toluenesulfonic acid
pTSA  para-toluenesulfonic acid
q  quartet
R  rectus (right handed, denotes configuration of a chiral centre)
RBF  round bottom flask
rt  room temperature
S  sinister (left handed, denotes configuration of a chiral centre)
s  singlet
SiO₂  silica gel
Sₙ₂’  bimolecular nucleophilic substitution with allylic rearrangement
t  triplet
TBAF  tetrabutylammonium fluoride
td  triplet of doublet
THF  tetrahydrofuran
THP  tetrahydropyran
TIPS  triisopropylsilyl
TLC  thin layer chromatography
TMEDA  tetramethylethylenediamine
TPAP  tetrapropylammonium perruthenate
UHR  ultrahigh release
μm  micrometre
UV  ultraviole
CHAPTER 1

Introduction

1.1: Brief Overview

The goal of this project involved the structural elucidation and synthesis of a putative cuticular contact pheromone of the braconid wasp *Wroughtonia occidentalis*, a recently identified parasitoid of the exotic brown spruce longhorned beetle (*Tetropium fuscum*). *W. occidentalis*, along with another braconid wasp, *Rhimphoctona macrocephala*, are currently the only known native biological threats to the invasive *T. fuscum*. Complete knowledge of both wasps’ chemical ecology and host-seeking behaviors coupled with methods to synthesize important wasp pheromones in the lab may allow the development of methods to increase parasitism of *T. fuscum* in affected areas.

1.2: The Brown Spruce Longhorned Beetle (*T. fuscum*)

The exotic brown spruce longhorned beetle (*Tetropium fuscum*) is an invasive pest species native to Europe. Upon its introduction to North America at Point Pleasant Park, Nova Scotia in the late 1980’s, *T. fuscum* has been responsible for the devastation of thousands of spruce trees in the area. Measures were, and are still being taken to curb its spread. The initial strategy consisted of selective tree harvesting to contain the growing infestation, but this was a temporary solution. A large part of the problem is that, unlike in Europe, *T. fuscum* has very few natural
predators in Eastern Canada — the only currently known predators being the aforementioned parasitoid wasps \textit{W. occidentalis} and \textit{R. macrocephala}.

\textit{T. fuscum} is known to affect pine, spruce, fir and larch trees in Europe, but has only been found in spruce trees in Nova Scotia so far. The beetle also has a preference for red spruce in North America, and typically attacks stressed trees.\textsuperscript{5} This is a cause for concern if the spruce budworm infestation coming from Quebec eventually spreads far enough Eastward to overlap areas where \textit{T. fuscum} is present.

Due to the impossibility of complete eradication of this pest, some more long-term – and preferably more “green” solutions — are required in order to minimize the beetle’s future impact on our forests. Such solutions coupled with current early identification methods will allow for a quicker and more efficient response when \textit{T. fuscum} inevitably spreads to nearby areas. The beetle is infesting and killing mature spruce trees, and spreading at 2 – 4 km/yr.\textsuperscript{6} The Canadian Food Inspection Agency (CFIA) has also confirmed the presence of BSLB near a campground within the Kouchibouguac National Park in New Brunswick, which was the first find of BSLB in New Brunswick and the first outside of Nova Scotia. Phytosanitary restrictions on the transporting of firewood have already been put into place in many campgrounds, as bringing potentially BSLB-infested wood to different areas will hasten the spread of \textit{T. fuscum}.

1.3: Pheromones

A pheromone is an excreted, or secreted, chemical factor that triggers a social response in members of the same species.\textsuperscript{7} These compounds are numerous and
highly common among insects, and are used extensively in communication between members of the same species. Different pheromones may function alone or synergize with other pheromones in order to elicit different types of behaviors from an insect. For example, an aggregation pheromone such as the Brown Spruce Longhorn Beetle’s “fuscumol” results in an aggregation response toward a host spruce tree when certain host volatiles are also present. Insects’ responses are not limited to aggregation toward a host or a mate, however. Other behaviors such as dispersion, courtship, oviposition, alarm, and colonial responses may also result from the presence of a specific pheromone.  

Pheromones are typically biosynthesized *de novo* using an organism’s own biological building blocks as precursors. These compounds can be of a low molecular weight, allowing for increased volatility and long-range communication, or they can be heavier contact pheromones that function at short range. The latter are typically hydrocarbons with a higher molecular weight, which decreases their volatility. However, at very low concentrations both can still be detected by insects, as receptors on antennae are incredibly sensitive.

### 1.4: Pheromones as bio-control agents

Synthetic pheromones have been used extensively and throughout the globe in the past to reduce and or control populations of various invasive insects. Typical strategies include baiting traps with pheromones, mating disruption, and increasing parasitism of the undesired insect. The importance of aggregation and sex pheromones for the purpose of trapping cannot be understated, whereas pheromones
involved in courtship and mating behavior are a must for any attempts to disrupt the mating practices of a species. Parasitism tactics usually require a greater variety of pheromones to be known, since the chemical ecology of the parasitic organism and how it interacts with its host must also be understood. For this reason, traps and mating disruption efforts usually precede tactics involving the increased parasitism of any insect pest.

1.4.1: Pheromone-baited traps

Pheromones of an insect pest can be used advantageously if their structures can be determined, and subsequently synthesized in a laboratory with relative ease. A common use of such pheromones – especially of the aggregation and courtship varieties – is to lure the insects into traps baited with said compounds. The primary purpose of doing so is early identification, because damage caused by destructive insects often only becomes apparent a year or more after the initial colonization of the host tree.

For example, the use of pheromone-baited traps was recently met with success in detecting low densities of Emerald Ash Borer (Agrilus planipennis) populations in Ontario. A. planipennis is an invasive pest native to Asia and Eastern Russia, and has been responsible for the death of thousands of ash trees in the central part of both the United States and Canada. It was earlier discovered that a female-produced macrocyclic lactone, (3Z)-dodecen-12-olide, increased attraction to host ash trees when combined with one of the tree’s own volatile compounds, (3Z)-hexenol. It was subsequently determined that green traps, high in the tree canopy and baited with
slow-release (3Z)-dodecen-12-olide and (3Z)-hexenol gave the best results, making them a useful tool for early detection and identification of *A. planipennis*. Although the capture rate was not sufficient to significantly reduce EAB populations, their use for early detection is of great importance.

It should be noted that many factors affect a pheromone trap’s efficacy, such as trap color, trap height, and the amount and release rate of volatiles. These factors typically differ from one species to the next, requiring trap optimization studies to be performed before they become an efficient tool in the management of an invasive pest.

### 1.4.2: Mating disruption

Mating disruption involves the use of synthetic pheromones of an insect pest species to disrupt its mating cycle. This is typically done by first gaining in-depth knowledge of the calling insect’s pheromone blend, which typically involves more than one compound, and then determining the proportions in which these compounds are present. The next task involves the synthesis of these attractant compounds, and their subsequent release into the environment where the pest is causing damage.

In many cases in nature, a male insect detects a volatile plume of courtship pheromones emitted by a female of the same species, or vice versa, and follows this trail back to the female in order to mate. When synthetic blends of the same pheromones are sprayed throughout the environment, the natural pheromone trails get masked, making it more difficult for the males to locate females of the same species, drastically reducing their chances of mating success.
The main advantage of mating disruption is that the pests do not develop resistance to pheromones of their own species — doing so would simply remove those “resistant” individuals from the gene pool. Additionally, the use of pheromones for controlling insect populations via mating disruption only targets one species, as opposed to the use of pesticides that may also cause the deaths of beneficial insects. Pesticides can also fail to have the desired effect if the insect is inaccessible. For example, *T. fuscum* larvae are protected from pesticides by the spruce tree’s bark while they cause damage.

Although mating disruption is a much “greener” tactic to combat invasive insects, it is not without drawbacks. First, many resources must be spent in order to accomplish the chemical ecology research required to isolate and understand the insect’s sex pheromones. The synthesis of these pheromones can also be costly depending on the difficulty of synthesizing large amounts of these compounds. The size of an infested area is another factor to keep in mind when applying synthetic pheromones, and affects their delivery method: traps would be sufficient in a small area, such as a crop, but a larger area or a forest would require the use of spraying technologies in order to disperse the pheromones in a useful manner. Large areas may also result in greater challenges due to the fact that some heavier compounds may not spray easily, requiring the development of new methods such as microencapsulation, followed by extensive testing in wind tunnels. Alternately, applying the pheromone to several locations in a certain area manually can also be expensive, again depending on the size of the area.
1.4.3: Biological control

Using an invasive pest species’ natural enemies is also a viable method for the control of said pests. Natural enemies can be predators, parasitoids, or pathogens such as fungi, bacteria, or viruses.

When dealing with exotic pests that have recently established themselves in an area where native predators are often not present, it is sometimes possible to import predators from the pest’s location of origin. For example, one strategy to battle the Emerald Ash Borer (EAB) infestation in the United States was to import and release one of the EAB’s natural enemies, the braconid wasp *Spathius agrili*. Both the pest and parasitoid were originally from China, but it was found that the release of *S. agrili* in several states had resulted in the successful establishment of the parasitoid in Michigan, Ohio, and Indiana.

The majority of parasitoids useful for pest-control purposes are wasps or flies, and typically in one of the Ichneumonidae, Braconidae, Chalcididae, or Tachinidae families. Parasitoids lay their eggs either inside or onto their crop-damaging hosts, which will later be fed upon and killed by the parasitoid larvae once they hatch from their eggs. Parasitoids have a narrow host range, but in some cases a small number of parasitoid species native to an area may be able to use an exotic pest species as their host. This is the case with *W. occidentalis* (Braconidae) and *R. macrocephala* (Ichneumonidae) being able to lay their eggs in *T. fuscum* larvae. These parasitoids can potentially be reared or attracted more successfully once their chemical ecology is understood.
The preservation or rearing of predators is also a viable tactic to aid in the control of insect pests, if the pest species already has natural enemies in the affected location. One needs to look no further than the typical back yard garden for an example, assuming said garden contains potato plants. The Colorado Potato Beetle (*Leptinotarsa decemlineata*) is a common pest whose larval stage causes damage to potato plants. Aside from isolating and crushing (or burning, or drowning) the adult beetles, it is also possible to purchase live Ladybugs that will prey upon the crop-damaging *L. decemlineata* larvae, saving the garden owner valuable time.

Bacteria, fungi, and viruses can also be of use in the battle against damaging insects.²² These pathogenic micro-organisms are generally species-specific and may be naturally present in the environment, with their numbers increasing as the insect pest population becomes denser. Insects are vulnerable to a number of different families of viruses,²³ and from these, the baculoviridae family is a great candidate for the control of forest pests due to its restriction to arthropods, and primarily to insects. The host-specificity and sudden, severe outbreaks among host populations makes baculoviridae an interesting tool for the eradication of forest pests. Sylvar Technologies Inc., a company headquartered in Fredericton, NB, is invested in partnered research for the advancement of baculovirus technologies, and developed Abietiv.²⁴ Abietiv is the trade name for a nucleopolyhedrovirus (NPV) specific to the Balsam Fir Sawfly, a common pest in Eastern Canada. The NPV subfamily of viruses is a genera of the baculoviridae family.

1.5: The battle against *T. fuscum*
The chemical ecology of *T. fuscum* has been elucidated, in large part through the work of Dr. Peter Silk and co-workers at the Canadian Forest Service – Atlantic Division.\(^{25}\) The structures of the beetle’s aggregation and sex pheromones have been determined and confirmed via synthesis, and large-scale syntheses of said compounds can be readily accomplished.\(^{26,27}\) Having this knowledge has allowed for both studies using pheromone-baited traps, as well as studies in mating disruption of *T. fuscum*.

### 1.5.1: Disruption of *T. fuscum* mating

The first method consisted of pheromone-mediated mating disruption with “fuscumol”, Figure 1, a male-produced attraction pheromone that synergizes with host volatiles to attract both *T. fuscum* sexes to the host tree.\(^ {28}\) Biodegradable Hercon Bio-flakes® containing 10% fuscumol were applied to various 4 ha plots containing either spruce bait logs or girdled spruce trees. An equal amount of lots containing bait spruces and no fuscumol were also used as controls. Several intercept traps baited with fuscumol and spruce volatiles were placed in the plots in order to capture females and record their mating status via dissection. It was found that the fuscumol-impregnated Bio-flakes® were successful in reducing *T. fuscum* mating success,

![Figure 1: “Fuscumol”, a pheromone emitted by *T. fuscum* males that synergizes attraction of both sexes to host volatiles.](image-url)
implying that pheromone-mediated mating disruption shows promise as a tool to slow the beetle’s spread.28

1.5.2: Mass-trapping studies

Pheromone traps have already been used against T. fuscum to both impede the beetle’s spread and to reduce its numbers. The study in question consisted of the mass-trapping of T. fuscum to reduce infestation. It was previously known that mass trapping could reduce damage caused by bark beetles29-31 and had the potential for suppression of populations of invasive pest species.32 To test this method’s efficiency on T. fuscum population suppression, traps were baited with Fuscumol, Ultra-High Release (UHR) spruce blend lure, and UHR ethanol lure. Spruce logs were placed near traps for the beetles to infest, and these logs were later peeled in order to determine the density of the T. fuscum larval population within. It was found that mass-trapping did reduce the mean percentage of infested spruce logs relative to control logs by approximately 30%, and similar studies aiming to optimize the cost-effectiveness and viability of the mass-trapping method are currently underway.

The traps also serve a second purpose: early identification of T. fuscum, which is critical. Due to the beetle’s life cycle, damage to spruce trees only becomes apparent approximately one year after the beetle’s arrival in the area, meaning that it has likely already spread to adjacent areas. Early detection therefore allows measures to be taken against T. fuscum immediately after it is found in a new area, as opposed to a year later when damage becomes visible.
T. fuscum adults emerge in late spring/early summer and mate shortly after. Females then deposit their eggs either under a spruce tree’s bark scales or in bark crevices, and larvae hatch 10 to 14 days later. The larvae overwinter under the bark and feed when the temperature permits, tunneling into the wood and damaging the spruce tree in the process. T. fuscum larvae pupate in spring, and adult beetles emerge approximately two weeks later, continuing the cycle.

The T. fuscum life cycle thus gives rise to two problems. First, the fact that larvae are hidden beneath bark makes the use of pesticides inefficient, requiring a different approach for the management of this pest. Second, the sighting of an adult longhorn beetle often means that a complete life cycle has already occurred, and that the beetle is already well-established in the area. Therefore even if pesticides were a viable option against T. fuscum adults, spraying would not prevent damage to trees. Early detection methods are therefore a necessity.

Typical damage caused by T. fuscum larvae includes 4 mm oval or round holes in a spruce tree’s bark, as well as sap “weeping”. Sawdust may also be present at the base of the tree. Larvae feed in the phloem (inner bark) of the spruce tree, and infestations are usually more prominent in the lower portion of the tree although it is possible for the entire stem to be affected. If the infestation is severe and lasts for a number of years, the spruce tree may perish.

1.5.3: Increasing the parasitism of T. fuscum by W. occidentalis and R. macrocephala
Another potential method to minimize *T. fuscum*’s impact consists of biological control via the increase of parasitism rates. The recent discovery by Dr. Jon Sweeney *et al.* that *T. fuscum* is host to two native parasitic wasps, *W. occidentalis* and *R. macrocephala*, prompted efforts to elucidate the chemical ecology and host-seeking behaviors of both wasp species. This thesis describes the structural elucidation process and attempted syntheses targeting what is believed to be a contact pheromone that affects mating behavior. This task is only one part of the overall, multidisciplinary project involving the fields of spectroscopy, organic synthesis, ecology, and molecular biology.

*W. occidentalis* is a solitary koinobiont parasitoid of *T. fuscum*, with the *Tetropium* genus currently being the wasp’s only known hosts. Parasitoids are organisms that spend a portion of their life history attached to, or inside their host in a parasitic relationship. A parasitoid will eventually sterilize or kill, and possibly even consume its host, unlike a true parasite.

Research to fully understand the *W. occidentalis* life cycle is ongoing, but so far it is known that adult wasps emerge 12 to 15 days after *T. fuscum* adults, which is approximately the time when the *T. fuscum* eggs hatch. *W. occidentalis* likely oviposits in early instar *T. fuscum* larvae, but the parasitoid does not grow to consume and kill its host until the larva has reached the prepupal stage.

### 1.6: PREVIOUS WORK
1.6.1: Structural elucidation

Insects carry cuticular compounds, typically long-chain hydrocarbons, for the primary purposes of preventing dessication and waterproofing of the insect’s cuticle. These cuticular compounds may also play an integral part in chemical communication, functioning as short-range and non-volatile pheromones. The use of NMR spectroscopy was not initially possible due to the small, nanogram scale quantities of cuticular compounds involved. For this reason, one of the initial steps in the quest to fully understand the chemical ecology of W. occidentalis and R. macrocephala was to subject extracts of their cuticular compounds to GC/MS analysis, which was performed at the Canadian Forest Service – Atlantic division by Dr. Peter Silk et al. The results, seen in Figure 2, would be helpful in order to

Figure 2: Gas chromatography portion of GC/MS data obtained from cuticular extracts of W. occidentalis (upper) and R. macrocephala (lower). Only the former displays a homologous series of unsaturated, long-chain hydrocarbons.
determine what similarities and differences existed between the two species. Extracts of both male and female specimens of the two species were analyzed due to the possibility of sexual dimorphism.

Differences between the two wasp species were readily observable. The *W. occidentalis* cuticular extracts appeared to contain a homologous series of odd-numbered, long-chain hydrocarbons ranging from 23- to 31-carbons in length. Although various homologues were present, the C29 compound was the most prominent.

The mass spectrum at the site of the 29-carbon peak revealed a molecular ion peak at 404, which was representative of a hydrocarbon with two sites of unsaturation. This meant that the compound could potentially be a conjugated acyclic diene, a non-conjugated acyclic diene, an acyclic alkyne, a cyclic alkene, or an allene. The fragmentation pattern arising from the unknown compound was not at all consistent with that of cyclic alkenes, conjugated dienes, or non-conjugated dienes, resulting in the quick elimination of these possibilities. Alkynes were also initially ruled out due to the fact that the corresponding alkynes for each peak typically had longer retention times on the gas chromatography column. This left an allenic hydrocarbon as the primary option.

The possibility of a McLafferty rearrangement also supported the hypothesis that the homologous series of compounds were allenes. Strictly speaking, the term “McLafferty rearrangement” refers to the loss of an alkene from molecular ions of saturated aliphatic compounds bearing a carbonyl group via a mechanism analogous to that of the Norrish type-II photo-fragmentation that occurs in condensed-phase
chemistry. More broadly speaking, McLafferty rearrangements include all “alkene losses” essentially following this mechanism. Any fragmentation that can be described as a transfer of a γ-hydrogen to a double-bonded atom through a 6-membered transition state with β-bond cleavage is regarded as a McLafferty rearrangement. The McLafferty rearrangement is usually observed in the vacuums involved in mass spectrometry, typically with compounds bearing a keto-group. In such a case, the ketone carbonyl undergoes β-cleavage and gains the γ-hydrogen, as shown in figure 3.

![Figure 3: Molecular ion containing a keto-group undergoing a McLafferty rearrangement.](image)

McLafferty rearrangements can also happen with various double bond-containing compounds, allenes included, as shown in figure 4. Allenes, compounds with two consecutive sites of unsaturation, are extremely rare in the insect world and previously unseen in the order Hymenoptera. One example is the male Japanese dried bean beetle, *Acanthoscelides obtectus*, which bears a pheromone containing a conjugated allene moiety, as well as a methyl ester, compound 3 in figure 6. This compound has been synthesized by three different groups. A second example is the Australian “Canegrub” beetles, also known as Melolonthine scarabs (*Melolonthinae* being a subfamily in the *Scarabidae* family). The invasive and crop-
Figure 4: One of the hypothesized *W. occidentalis* compounds, Δ^{11,12}-heptacosadiene 2 undergoing a McLafferty rearrangement. Only molecular ions are shown for clarity.

In the case of a), the 27-carbon allene fragments in such a way that results in the longer end of the chain becoming the molecular ion, resulting in a peak at m/z 250 in the mass spectrum. Alternately, the shorter end of the carbon chain fragmenting would result in a molecular ion peak at m/z 194, as seen in b). These peaks are visible in figure 5.

Figure 5: Mass spectrum of the C-27 cluster of the unknown *W. occidentalis* female compound, which is believed to be a mixture of two 27-carbon allene isomers — one with unsaturation sites at the 10, 11-position, and one with unsaturations at the 11, 12-position.
damaging species of interest are *Antitrogus consanguineous*, *Dermolepida albohirtum*, *Lepidiota crinite*, *L. negatoria*, and *L. picticollis*. These pests carry a homologous series of long-chain, allenic cuticular hydrocarbons with unsaturations at the 9, 10-position,\textsuperscript{44,45} compounds 4-10 in figure 6, as discovered by the Kitching group.

**Figure 6**: a) *A. obtectus*, the Japanese dried bean beetle, and its pheromone, compound 3. b) *L. negatoria*, one of the Australian “canegrub” species. Cuticular compounds isolated from various Melolonthine scarabs consist of long chain allenic hydrocarbons. Various long chain allenic hydrocarbons have been isolated and identified from five species of Canegrub beetles in Australia. These allenes have unsaturations at the 9, 10-position and are a homologous series much like the *W. occidentalis* compounds, and range from 23 to 31 carbons in length.
Figure 7: Comparison of gas chromatography spectra of cuticular extracts from *W. occidentalis* males (upper) and females (lower) reveals that the homologous series of hydrocarbons are female-produced only. Data obtained at the Canadian Forest Service – Atlantic division (CFS) laboratories by Dr. Peter Silk *et al.*

Both *A. obtectus* and the Canegrub species belong to the order *Coleoptera*, not the wasp-containing order *Hymenoptera*. The possibility of discovering allenic pheromones in a different order was intriguing.

Since the allenic hydrocarbons present in the Canegrub beetle cuticules were very similar to the hypothesized *W. occidentalis* cuticular compounds, it made sense to use similar strategies in certain aspects of this project. For instance, similarities arose during the structural elucidation process when the *W. occidentalis* GC/MS spectra displayed peaks arising from a McLafferty rearrangement. These peaks were consistent with the allenic spectral data present in the Canegrubs article, where the shorter fragment generated by the McLafferty rearrangement of Canegrub 9, 10-
Table 1: Comparison of mass spectrometry data of allenic compounds isolated from various Canegrubs and *W. occidentalis*. The former bears unsaturation sites at the 9, 10-position and result in the consistent generation of a short molecular ion fragment of m/z = 166 for every homologous allene, whereas the latter is made up of a mixture of hydrocarbons with unsaturation sites at the 10, 11-position, and others with unsaturation sites at the 11, 12-position. The short fragments arising from a McLafferty rearrangement in the mass spectrometer are consistent across both species, adding further weight to the hypothesis that the *W. occidentalis* compounds are likely allenes.
The last step for the Kitching group was the synthesis of the homologous series of Canegrub allenic compounds for the purpose of comparing the spectroscopic data of the synthetic compounds with that of the compounds isolated from Canegrub beetles. The allenes were first synthesized in a racemic manner, as shown in Figure 8. Alkynyllithium reagents of various lengths were added to nonanal in order to generate long-chain propargylic alcohols that would then be subjected to a stannylation-deoxystannylation protocol to yield the corresponding allenes. Allenes could also be obtained from propargylic alcohols by use of o-nitrobenzenesulfonylhydrazine (NBSH), triphenylphosphine (PPh₃), and diethylazodicarboxylate (DEAD).

**Figure 8:** Two methods by which the Kitching group generated long-chain, racemic allenes of various lengths.

To synthesize these allenes in an optically enriched manner, the long-chain propargylic alcohols synthesized in the first step had to be oxidized, and then reduced using an asymmetric reducing agent. This implemented nonracemic chirality was then
transferred to the product via one of the methods in Figure 8 above, yielding an optically enriched allene.

Given the brevity and success of the route utilized by Kitching et al. for the work with the Canegrub compounds, it was felt that many of the same protocols could be implemented for the targeted synthesis in this project, after all the main goal of the project was to simply elucidate the structure of the pheromone as quickly as possible. However, as shown in Scheme 1, some modifications were envisaged. For instance, it was decided to avoid the stannylation-deoxystannylation reaction due to the toxicity of tributyltin hydride, a necessary reagent in the procedure, and that preliminary studies indicated that this reaction was inefficient. A second concern was the use of DEAD, which is a controlled substance with rather prohibitive costs.

Yield improvement was also a goal that could potentially be accomplished via the use of a slightly different synthetic scheme. The yield obtained with the stannylation-deoxystannylation procedure was only 8%, followed by TBAF deprotection in 77% yield. The synthetic route that made use of the DEAD reagent obtained the optically enriched allene in a yield of 38%.

Lastly, the use of a different synthetic route was also thought to be desirable due to the simple need to not entirely repeat others’ work, and the fact that, in organic synthesis, having more possible pathways toward a certain type of compound provides increased opportunities for success during future syntheses of said compounds.
Scheme 1: The proposed retrosynthetic plan for the synthesis of non-racemic allene 12.
CHAPTER 2
Results and Discussion

2.1. Achiral non-specific allene synthesis

The initial task was to confirm via synthesis and GC/MS spectral comparison that the cuticular compounds in question were indeed allenes. As previously mentioned, the GC/MS data generated by *W. occidentalis* cuticular extracts suggested that the naturally occurring allenic pheromone was a mixture of two compounds, 10, 11- and 11, 12-regioisomers, Figure 9. It was not known if one optical or regioisomer predominated over another, thus the first goal was to simply obtain a mixture of the regioisomers for each homologous compound. If the resulting GC/MS spectrum of this mixture matched that of the same homologous compounds present in the natural sample, efforts would then be expended to synthesize the compounds in an optically pure and regioselective manner.

Although it was known that the 29-carbon homologue was present in greater amounts in the natural sample, it was decided to target the 27-carbon allene first because bromopentadecane was available in larger quantities and for a more reasonable price compared to bromoheptadecane. A procedure could therefore be elucidated for the synthesis of the 27-carbon compound and, if successful, be repeated for the larger, more expensive 29-carbon homologue if the spectral data was consistent with the *W. occidentalis* data.

It is known that direct isomerizations of alkyne derivatives to allenes yields two different regioisomers,\(^ {47}\) making this type of reaction undesirable for the purpose
of organic syntheses due to lack of stereocontrol. However, for the purposes of the first goal of this thesis this reaction would be ideal as the generation of both 10, 11- and 11, 12-isomers (21, 22 respectively) would be obtained from the same starting compound, 11-heptacosyne 20, figure 9. This long-chain alkyne could be prepared in one step by coupling 1-dodecyne and bromopentadecane, as seen in the first part of Scheme 2.

![Scheme 2](image)

**Figure 9:** Alkynes subjected to a strong base to form two different allene isomers, depending on which side of the alkyne gets deprotonated.

The procedure for the synthesis of long chain allenes is depicted in Scheme 2.\textsuperscript{48} The synthesis of the 27-carbon alkyne was required as a precursor to the allene, and began by first attempting alkyne alkylation with the anion of 1-dodecyne, 18, and 1-bromopentadecane, 19, in the presence of N, N’-dimethylpropyleneurea (DMPU),\textsuperscript{49} a non-toxic HMPA alternative; however, production of 11-heptacosyne was
unsuccessful. Fortunately, use of HMPA provided the desired compound 20 in good yield.

Scheme 2: Synthetic route for the synthesis of both regioisomers of the 27-carbon allenes 21 and 22.

Purification of 20 was difficult since 1-dodecyne 18 and alkyne 20 co-eluted during chromatography in hexanes, with the left over pentadecyl bromide 19 eluting slightly faster than the alkyne. Fortunately, any remaining 1-dodecyne could be easily removed by heating the mixture of alkynes in a Kugelrhon apparatus at 110 °C at reduced pressure (1.5 mm/Hg) to give pure alkyne in an excellent 77% yield.

With sufficient quantities of alkyne 20 in hand, deprotonation using n-butyllithium and TMEDA resulted in a 16% yield of allenes, as a 50/50 mixture of the 10, 11-isomer 21 and 11, 12-isomer 22. The reaction was conducted at -20 °C, as any lower temperature caused the bulky alkynes to solidify in the syringe needle during transfer; the literature procedure called for a temperature of -78 °C, but the original procedure was performed with compounds of much lower molecular weight. The allenes were then separated from starting materials via flash chromatography in
hexanes, using double the amount of silica normally used and the smallest possible collection tubes.

Spectral data showed the diagnostic peaks for an allene at δ 5.07 in the $^1$H-NMR and δ 210 in the $^{13}$C-NMR, and was comparable with the allenic spectral data reported for the Australian “canegrub” beetle. GC/MS comparison of this synthetic allene mixture with the natural W. occidentalis 27-carbon compound also revealed a very similar peak pattern, with both spectra displaying the expected McLafferty ion peaks. These can be seen in figure 10, at m/z 180 and 194, and m/z 250 and 264. The difference of 1 m/z between the spectra was ascribed to self-protonation of the ion, which can be both concentration dependent or due to the background solvent. The exception to this was the molecular ion at 376 m/z, which was already fully saturated.

It was then time to synthesize the 29-carbon allene homologue, using the same procedure, Scheme 3. The bulkier 29-carbon allene was targeted for two reasons: for further confirmation that the proposed allenic structure was the correct one, and to have a supply of the compound for future bioassays since it was the most prominent homologue found in the wasp cuticule according to GC/MS data. As was seen for the C-27 homologue, coupling between heptadecyl bromide 23 and 1-dodecyne 18 proceeded efficiently to give alkyne 24 in 75% yield. Separation issues were again encountered, and it was found that if excess acetylide was used then almost all of the halide was consumed, thus allowing for easier separation of the unreacted halide from the co-eluting alkynes 18 and 24. Kugelrhor distillation was again used to separate the alkyne mixture.
Figure 10: GC/MS spectra of a) the synthesized mixture of 21 and 22, and b) the unknown 27-carbon compound from a W. occidentalis cuticular extract. Both spectra display prominent McLafferty peaks at m/z 180, 194, 250, and 264.
Scheme 3: Synthetic route for the synthesis of both regioisomers of the 29-carbon allenes 25 and 26.

With gram quantities of alkyne 24 synthesized, treatment with n-butyllithium and TMEDA resulted in a 23% yield of both the 10,11-allene isomer 25 and the 11,12 allene isomer 26 as a 50/50 mixture. The GC/MS spectrum again appeared to match that of the natural sample of the same molecular weight, figure 11.

2.2. Optically enriched synthesis.

The synthetic allene spectra were consistent with those of the compounds isolated from female *W. occidentalis* cuticules, further supporting the allene hypothesis. The next step of the project was to develop a method to synthesize the same allenes in an optically-enriched and regioisomerically pure manner. The homologous series of compounds ranged from 23 to 31 carbons in length and consisted of only the odd-numbered carbon chains, meaning that 5 allenes of different length would potentially need to be synthesized. Both the 10, 11- and 11, 12-regioisomers would have to be synthesized for each allene length, increasing the amount of compounds to be synthesized to 10. Furthermore, allenes have a chiral
**Figure 11**: GC/MS spectra of a) the synthesized mixture of 25 and 26, and b) the unknown 29-carbon compound from a *W. occidentalis* cuticular extract. McLafferty peaks are again present in both spectra, at m/z 180, 194, 292, and 278.
axis, therefore the synthesis of both the R and S versions of each of these compounds would have to be performed. In total, 20 different long-chain allenes would have to be made in order to test each allenic variant for biological activity.

Before embarking on this task, two things were required. First, a procedure to synthesize such long-chain allenes with reliable regioselectivity and enantioselectivity would have to be developed. Second, the synthetic compounds (e.g. 21, 22, 25, and 26) would have to be screened by electroantennogram (EAG) in order to determine if these compounds had an effect on W. occidentalis’s behavior prior to synthesizing the whole series, as it would not be sensible to synthesize all of the allene variants if the more prominent ones in the natural sample showed no effects.

Focus was initially on the synthesis of the C-29 allene due to its greater abundance in the natural sample compared to the other homologues, with the assumption that a method for the synthesis of this allene with high optical purity would also be applicable to the synthesis of all other homologues.

A survey of the literature\textsuperscript{51-57} revealed that well-established, widely applicable access to various enantiomerically enriched and pure allenes relies on the $S_N2'$ substitution of chiral propargylic derivatives with nucleophiles, in particular with organocuprates. Of particular note was the work of Alexakis and co-workers\textsuperscript{58} where they demonstrated that dialkylallenes could be efficiently generated from optically enriched propargylic ethers or acetates. With that in mind, a retrosynthetic pathway for the synthesis of the 11, 12-allene isomer 26 was devised, Scheme 4. It was thought that optically enriched propargylic ethers or acetates like 27, 28, 30 and 31 could be readily accessed by CBS-reduction of the propargylic ketones,\textsuperscript{59} which in
turn could be prepared by alkynyl anion addition to the requisite aldehyde. Finally, although two routes were designed they differed only from the standpoint of which aldehyde and alkyl Grignard reagent were used. For example, the 11, 12-allene could be obtained either by starting with undecanal and adding hexadecylmagnesium bromide in the final step, pathway on the right in Scheme 4, or by starting with heptadecanal and adding decylmagnesium bromide in the final step, pathway on the left in Scheme 4. The former route was taken initially due to the lower cost of the starting aldehyde, but this resulted in problems that will be discussed later. Description of the synthesis of optically enriched allene 26 will therefore focus on the route using heptadecanal synthesized from heptadecanol as a starting point.

Scheme 4: Retrosynthetic analysis for the synthesis of optically enriched 11, 12-allene 26. Two routes were possible.
Selecting between the 10, 11- and 11, 12-regioisomers was simply a matter of using a different starting compound, either heptadecanal or hexadecanal, respectively, left hand route above. At this time it was felt that both the 10, 11- and the 11, 12-regioisomers would have to be synthesized, thus the reaction sequence would have to be repeated, therefore it made little difference which isomer was targeted first.

With a plan now firmly in place, the synthesis began by oxidizing commercially available heptadecanol to heptadecanal using pyridinium chlorochromate (PCC), Scheme 5. This reaction proceeded as expected to give the aldehyde in 88% yield. Reacting the lithium anion of TIPS-acetylene with heptadecanal resulted in the formation of racemic propargylic alcohol in an excellent 80% yield. After exploring a variety of oxidative conditions (PCC, PDC, Swern) it was found that treating alkynyl-alcohol with tetrapropylammonium perruthenate (TPAP) and N-methylmorpholine N-oxide (NMO) resulted in alkynyl-ketone being realized in a yield of 91%.

With the desired ketone now in hand, subsequent asymmetric reduction with (S)-Me-CBS was performed to produce optically enriched alkynyl-alcohol in excellent yield. Although the absolute configuration was not determined, it was assumed that the S-alcohol was produced based on literature precedent. To continue, treatment of with tetrabutylammonium fluoride (TBAF) uneventfully removed the TIPS-protecting group, resulting in propargyl alcohol in 95% yield. At this point, the degree of enantioselectivity was determined by treating alcohol with (S)-(−)-2-acetoxypropionyl chloride and pyridine to yield ester. GC
Scheme 5: Synthetic route toward an optically enriched allene 26, using heptadecanol 34 as a starting material.

Analysis of this compound showed that reduction of ketone 36 had occurred with 78% ee, figure 12.
Figure 12: GC-MS trace of (S)-2-acetoxypropionyl derivatized propargyl alcohol

In preparation for the organocopper assisted Grignard addition to produce allene 26, propargyl alcohol 38 was then converted to its methyl ether 27 and acetate 28 in 71% and 95% yields, respectively. Subjecting ether 27 or acetate 28 to the
conditions described by Alexakis\textsuperscript{58}, which involved the use of decylmagnesium bromide as the Grignard reagent and copper bromide-bis(triethylphosphite) as the copper source, resulted in a 75\% and 65\% yield, respectively, of optically enriched allene 26. At this time, the absolute configuration and enantiomeric excess of the allene was not determined, as the goal was to first assess the allene’s effectiveness in live animal testing. That said, based on work by Alexakis\textsuperscript{58} (mechanism) and McGrath\textsuperscript{61} (synthesis of similar compounds) it was assumed that the enantioselectivity was similar to that of the starting ether and acetate; that is around 78\%. To support this supposition, in McGrath’s studies, he demonstrated that (R)-(\_)-\(\Delta^9,10\)-pentacosadiene of 80 – 85\% ee, based on NMR analysis, had an optical rotation of -15.6, while the \(\Delta^{11,12}\)-pentacosadiene just synthesized had an optical rotation of -15.8. Although it is realized that using comparison of optical rotation data is very speculative, given the close structural similarities of the two compounds and that the starting alkynyl ethers and acetates had ee’s of 78\%, it was all very supportive.

Finally, it should be noted that attempts to synthesize 26 using propargyl acetate 31 and Grignard 32 were proven to be ineffective. The reason for the lack of success was ascribed to solubility issues with Grignard 32 in THF at low temperature. Unfortunately, this led to the need to conduct the reaction at 0 °C or above or adding a co-solvent such as CH\textsubscript{2}Cl\textsubscript{2}. Both modifications to the procedure resulted in poor yields, that is, if any product was recovered at all.

2.3. Allene hypothesis incorrect
Live *W. occidentalis* specimens were beginning to emerge at this point, and some of the wasps were subjected to a contact sexual activity assay using the previously synthesized racemic allene mixtures. Unfortunately, it was observed that the synthetic allenes elicited no response from the wasps. Mating behaviour was unaffected, as was behaviour in general. Bio-assays using the optically enriched allene were not performed due to its synthesis not being complete at this time. It was briefly considered that perhaps no response was elicited from *W. occidentalis* due to the racemic characteristic of the allene mixture, but upon further examination and comparison of the GC-MS spectral data obtained from synthetic and natural samples generating a molecular ion with an m/z of 404, it was noticed that the retention times differed slightly between the two compounds, with times of 40.4 minutes and 38.6 minutes, respectively. Although small differences in retention times are not uncommon from one run to the next, the magnitude observed here was too large to ignore and meant that the hypothesized allenic structures were perhaps incorrect.

Based on the above results a second potential structure was proposed, octacos-17-ynal 42 (scheme 6). This compound also had a molecular weight of 404, which was consistent with the molecular ion peak seen in the GC/MS spectrum of the 29-carbon homologue, as seen in Figure 11 b). It was also known that alkynes may transiently rearrange to allenes after being ionized inside the GC/MS vacuum, and thus the internal alkyne of octacos-17-ynal could potentially account for the observed McLafferty peaks in the mass spectrum if it were converted to an allene in the MS vacuum.
Much like the first alkyne coupling, Scheme 2, the plan to synthesize octacos-17-ynal 42 included the coupling of a 16-carbon, THP-protected bromoalcohol 41 to 1-dodecyne 18, Scheme 6. The former compound was not commercially available, so it was proposed that this compound could be accessed from the coupling of two 8-C-units that could be generated from 1, 8-octane diol 40.

![Diagram of retrosynthetic analysis for the synthesis of 17-octacosynal 40.]

**Scheme 6**: Retrosynthetic analysis for the synthesis of 17-octacosynal 40.

It was felt that 1, 8-octanediol 40 could be used as the precursor for two different 8-C-compounds that could be joined together again to generate the 16-carbon chain required for the coupling to 1-dodecyne 18. This synthetic route was viewed as attractive as it would allow for the use of only one starting material, 1, 8-octanediol 40, for both synthons 44 and 49.

To initiate this route, 1, 8-octanediol 40 was converted to 8-bromo-1-octanol 43 following the Girland-Junges protocol using a 50/50 mixture of cyclohexane and aqueous 48% HBr solution, Scheme 7. The rationale behind the two-phase solvent system was that the starting octanediol would initially be present in the aqueous HBr phase until bromination occurred, which would make the resulting bromoalcohol more soluble in the cyclohexane layer, thus protecting it from further bromination.
Scheme 7: The Julia-Kocienski trans-olefination route to synthesize octacos-17-ynal.

Upon completion of the reaction, the organic layer was isolated and the solvent evaporated, yielding the desired 1-bromo-8-octanol. Unfortunately, in this particular instance it was discovered that the 6 h of refluxing suggested in the literature resulted in large amounts of undesired 1, 8-dibromooctane, and only 26% of 8-bromo-1-octanol 43. When the reflux time was lowered to approximately 40 minutes, then an acceptable yield of 63% was obtained. Fortunately, when the
conditions were changed to those reported by Chong\textsuperscript{66} a reproducible and excellent yield of 87\% was obtained.

With gram quantities of \textbf{43} in hand, the synthesis of the two halves required to make the 16-C unit was undertaken. First, PCC\textsuperscript{67} oxidation to 8-bromo-octanal \textbf{44} proceeded uneventfully in an acceptable 67\% yield. Simultaneously, a second batch of \textbf{43} was converted to its THP derivative \textbf{45} under standard conditions\textsuperscript{68} in excellent yield. It was then attempted to make Wittig salt \textbf{46} from this THP-protected compound. Unfortunately, the resulting product had the consistency of a syrup, and the pure salt could not be isolated from excess PPh\textsubscript{3}, unreacted halide and some other organic impurities. Live \textit{W. occidentalis} wasps were emerging at this time, and the target compounds were needed as quickly as possible, therefore it was decided that optimizing reaction conditions and exploring purification methods for this Wittig salt would be too time consuming, therefore an alternative coupling was pursued, Scheme 7.

To explore this route involving a modified version of the Julia-Kocienski coupling, THP-ether \textbf{45} was added to a mixture containing 1-phenyl-1H-tetrazole-5-thiol \textbf{47},\textsuperscript{69} sodium hydride and a catalytic amount of sodium iodide in THF to generate sulfide \textbf{48} in 90\% yield. Oxidation of \textbf{48} to its sulfone\textsuperscript{70} \textbf{49} was accomplished using an ammonium molybdate catalyst (NH\textsubscript{4})\textsubscript{6}Mo\textsubscript{7}O\textsubscript{24}•4H\textsubscript{2}O and hydrogen peroxide, H\textsubscript{2}O\textsubscript{2}. Unfortunately, attempted Julia-Kocienski coupling\textsuperscript{71} of sulfone \textbf{49} with aldehyde \textbf{44} to generate \textbf{50} under a variety conditions did not produce the desired compound.
Given the time pressures to synthesize this compound, close examination of the literature provided two straightforward strategies starting from the commercially available 16-hexadecanolid 51, Scheme 8. The first route explored involved hydrolyzing ester 51 using catalytic acid and methanol\textsuperscript{72} to give methyl 16-hydroxyhexanoate 52 in excellent yield. The resultant alcohol was then protected as its THP ether\textsuperscript{68} 53, and the ester moiety was then reduced with lithium aluminum hydride (LAH) to provide the mono-THP-protected 16-C diol 54 in 54\% yield over

**Scheme 8:** Successful route toward the synthesis of the left hand fragment of 17-octacosynal.
the two steps. Finally, conversion of the alcohol to a bromide was attempted using a variety of conditions with varying success and reproducibility. For instance, treatment of alcohol 54 with PPh₃ and NBS⁷³ or PPh₃ and CBr₄⁷⁴ provided bromide 41 in a disappointing 10-15% yield.

Fortunately, at the same time an alternative route to 41 was being pursued, Scheme 8. First, 16-hexadecanolide 51 was reduced with LAH⁷⁵ in refluxing THF to generate diol 55 in excellent yield. Using the Chong procedure,⁶⁶ once again diol 55 was conveniently converted to 16-bromo-1-hexadecanol 56 in 88% yield.

Scheme 9: Completion of the synthesis of 17-octacosynal.
Straightforward protection of the free alcohol as its THP-ether proceeded uneventfully to give 41 in 95% yield. The brevity and high yields of this route were welcomed, especially as large quantities of this compound were potentially going to be needed for future field-work.

The THP-protected long chain alkyl bromide 41 was then coupled with the anion of 1-dodecyne 18, and the resulting 28-C alkyne 57 was generated in 82% yield, Scheme 9. Subsequent removal of the THP group yielded octacos-17-yn-1-ol 58, which was uneventfully oxidized using PCC and SiO$_2$ to produce octacos-17-ynal 42 in 73% yield over the two steps.

Both octacos-17-ynal 42 and octacos-17-yn-1-ol 58 were subjected to GC/MS analysis. The spectrum of the aldehyde resembled that of the 29-carbon *W. occidentalis* homologue of the same molecular weight, but the synthetic compound took approximately 15 minutes longer to elute from the gas chromatography column, thus ruling out octacos-17-ynal 42 as the potential structure of the pheromone. The same phenomenon was true for alcohol 58.

### 2.4. New targets: long-chain alkynes

The amount of structures with a molecular weight of 404 that potentially matched the unknown compound was diminishing, and attention was refocused on simple alkynes. As mentioned previously, alkynes may transiently rearrange to allenes in the mass spectrometer. Could it be possible that the *W. occidentalis* compounds under study were simply long-chain alkynes? In order to determine if this were the case, it was felt that a homologous series of 29-C alkyne isomers should be
investigated where the position of the alkyne unit would be altered. Consequently, 11-nonacosyne 24, 12-nonacosyne 61, 13-nonacosyne 64 and 14-nonacosyne 67 were targeted for synthesis, Scheme 10.

![Scheme 10](image)

**Scheme 10**: Synthesis of a homologous series of C-29 alkynes.

As a route to alkyne 24 had already been delineated, it was decided to simply follow the same procedure to make the other three alkynes. Consequently the corresponding alkynes 59, 62 and 65 were deprotonated with n-BuLi and then treated with bromohexadecane 60, bromopentadecane 63 and bromotetradecane 66 to give the requisite nonacosynes 61, 64 and 67 in 88%, 74% and 76%, respectively. It should be noted that for each of these syntheses excess alkyne was used such that all of the haloalkane would be consumed as the unreacted alkyne could be conveniently removed via Kugelrhor distillation.

With the four alkynes in hand, each was subjected to GC/MS analyses, figures 13 – 16. The retention times obtained from the pure nonacosyne samples were 36.51,
Figure 13: Mass spectrum of 11-nonacosyne at 36.51 minutes. McLafferty peaks at $m/z = 292, 180, 194,$ and 278.

36.06, 35.92 and 35.94 minutes, respectively. It should be noted that the retention time of the natural sample, 38.87 min, was acquired a year prior using a different GC column. Additionally, there were some previously acquired MS from less pure nonacosyne samples on the same GC column as the natural sample and their retention times were 38.5, 38.7, 38.6 and 37.6 minutes, respectively. Spectra of the less pure nonacosynes are not shown herein, and a new spectrum of the natural sample using the newer column will need to be acquired as soon as possible, for the sake of completeness and to confirm that the retention times do match.
Figure 14: Mass spectrum of 12-nonacosyne at 36.06 minutes. McLafferty peaks at $m/z = 194$, 278, 208, and 264.

The position of the triple bond in long chain alkynes can be determined by the fragments arising from chemical ionization in the MS vacuum. Fragmentation of these alkynes can occur in more than one manner, but the presence of the McLafferty ion peaks are the most telling features in these spectra. Recall that the peaks of interest in the natural $W. occidentalis$ sample were at 180, 193, 278, and 291, which were initially thought to be the result of an allenic fragmentation pattern, as shown in figure 17. The mass spectrum of 11-nonacosyne seen in Figure 13 displays these peaks (with an additional +1 m/z due to re-protonation) although they do not appear to be as prominent as they were in the natural sample. This difference in peak intensity may be concentration dependent and needs to be further explored.
Figure 15: Mass spectrum of 13-nonacosyne at 35.92 minutes. McLafferty peaks at m/z = 208, 264, 222, and 250.

At first glance, the spectra of 11-nonacosyne does not look like it corresponds to that of the natural sample, which displayed much more prominent McLafferty peaks. When 11-nonacosyne was presented to live *W. occidentalis* specimens, however, behavioral change was observed. This prompted re-examination of the mass spectra. One factor that can account for the differences in McLafferty peak intensities is the sample concentration that was injected into the GC/MS — the natural sample had a much lower concentration compared to the synthetic alkynes.

Supporting evidence that long chain alkynes can undergo conversion into allenes, and subsequent McLafferty rearrangement, in a GC-MS can be found in the spectral data of long-chain alkynes located in the NIST11 library. 11-Nonacosyne
Figure 16: Mass spectrum of 14-nonacosyne at 35.94 minutes. McLafferty peaks at m/z = 222, 250, and 236.

was not present in this library, but a very similar long-chain alkyne, 11-hexacosyne, was available for comparison. 11-Hexacosyne also displays prominent McLafferty peaks, as seen in figure 18 below. Another factor affecting peak intensity was the mass spectrometer itself. The mass spectrum of 11-nonacosyne obtained from the GC/MS instrument at the Canadian Forest Service labs was a quadrupole mass spectrometer, whereas the NIST11 library data all came from a magnetic sector mass spectrometer. This difference in instrument type can also account for the lack of intensity in the 11-nonacosyne spectra’s McLafferty peaks in figure 13.
Figure 17: 11-Nonacosyne can transiently re-arrange into an allene bearing unsaturations at the 10, 11-position or the 11, 12-position following exposure to the MS ion source. Each one of these allenes can undergo a McLafferty rearrangement in two possible ways, resulting in peaks that can appear at m/z 180, 194, 278, and 292.

The retention time of the alkyne was a much closer match to that of the unknown than were the previously synthesized allenes, leading to the belief that 11-nonacosyne is the unknown contact pheromone in question. The behavioral response
displayed by living *W. occidentalis* specimens further supported this theory: the presence of 11-nonacosyne did elicit an antennation response, tapping of the

![Graph showing McLafferty rearrangement peaks](image)

**Figure 18:** A similar example from the NIST11 library, 11-hexacosyne, also displays McLafferty rearrangement peaks at m/z = 180, 194, 250, and 236. (The 180 and 194 peaks even correspond with those of 11-nonacosyne due to the unsaturation being at the 11\(^{th}\) position in both compounds).

compound location with the antenna, when placed in the vicinity of live wasps. Efforts continue to determine if this response is concentration dependent, or if the presence of other long chain alkyne homologues can have a synergistic or antagonistic effect.
CHAPTER 3
Conclusions and Future Work

Conclusions

The project began with some unusual GC/MS spectra isolated from *W. occidentalis* cuticular extracts provided by the Canadian Forest Service. The fragmentation pattern closely matched that of a homologous series of long-chain allenic hydrocarbons, and thus the synthesis of allenes seemed a logical starting point. The molecular weights of the target allenes also corresponded with those of the unknowns, and supported this hypothesis.

Racemic mixtures of 27 and 29 carbon-bearing allenes were synthesized as mixtures of the 10, 11- and 11, 12-isomers, but these allenes could not be tested for a response from *W. occidentalis* immediately due to the unavailability of adult wasps at the time. However, the GC-MS data from the synthetic allenes was very similar to that produced from the wasp. Consequently a synthetic route to obtain optically enriched and regiospecific long-chain allenes was devised and a seven step synthesis of optically enriched (R)-Δ^{11, 12}-pentacosadiene 26 was executed. Although the optical purity of the final product was not determined, its immediate precursor was determined to have 78% ee, and given that the reaction to produce the allene was known to retain its stereochemical integrity, it was assumed that allene 26 had similar ee. This was further supported by comparing its optical rotation with the known (R)-(−)-Δ^{11, 12}-pentacosadiene which had 80-85% ee, based on NMR analysis.⁴⁵
With the availability of the racemic and optically enriched allenes in place, their biological activity against adult *W. occidentalis* wasps was investigated. A contact sexual activity assay was performed with both allenes and it was determined than neither elicited a response.

The original spectral data was re-examined and it was determined that octacos-17-ynal 42 also corresponded with the molecular weight of the unknown *W. occidentalis* compound, as well as the fragmentation pattern since it was known that alkynes can transiently be converted into allenes inside the mass spectrometer vacuum. Octacos-17-ynal 42 was synthesized in 6 steps from commercially available 16-hexadecanolide and its GC/MS data acquired; however, the retention time was much too different from that of the *W. occidentalis* compound to be the correct structure.

With few options remaining, it was felt that perhaps simple long-chain alkynes may be logical candidates, therefore they became the next targets. Various nonacosynes (11-, 12-, 13-, and 14-nonacosyne) were synthesized via alkylation of 1-haloalkanes with the requisite alkynyl anion. These compounds were then subjected to GC/MS analysis, and displayed to live *W. occidentalis* specimens. The alkynes’ presence did elicit a behavioral response from the wasps, indicating that the unknown cuticular compounds were alkynes. Based on GC/MS analyses and preliminary assays on live *W. occidentalis* specimens, it is currently believed that the contact pheromone compound is 11-nonacosyne.

**Future Work**
The nonacosynes eliciting a response from *W. occidentalis* leads to the exploration of further aspects of the wasp’s chemical ecology. The next important step will be to determine the function of the pheromone. Since various odd-numbered homologues of these compounds are present in the wasp’s cuticle, each homologue must also be synthesized and subsequently tested in order to know what one(s), if any, elicit a response. Perhaps different homologues, when present together in certain concentrations, could have a synergistic or antagonistic effect. Or could the longer chain alkyne homologues have a more pronounced response than shorter ones, or vice versa? Do the relative concentrations of each alkyne homologue in the *W. occidentalis*’s cuticle remain identical throughout the wasp’s entire adult life?

If these alkyne pheromones prove to be useful as an aggregation pheromone, then methods would have to be developed to lure *W. occidentalis* to areas infested by *T. fuscum* where the wasps could function as biological control agents. In lieu of developing a lure for the wasps, an alternative could perhaps be to simply infest an area under BSLB attack with these wasps and with the aggregation pheromone applied in locations where BSLB have been observed. In order for this to be possible, a method to synthesize the alkynes in bulk would have to be developed, as well as encapsulation and spraying technologies. Additionally, complete knowledge of *W. occidentalis*’s chemical ecology could likely lead to the development of more efficient strategies to breed the wasps.

In short: there is much more work to be done.
CHAPTER 4

Experimental Methods

4.1 General

All glassware used was oven dried at 110 °C overnight, assembled while hot and then put under an atmosphere of argon and allowed to cool to room temperature unless otherwise stated. Anhydrous solvents used in reactions were dried using a Grubbs solvent dispensing system designed by J. C. Meyer or were purchased from commercial suppliers and used as received. All reagents were used as received from commercial suppliers without further purification.

Silica gel 60, F254 on 250 μm thickness glass plates were used to perform analytical thin layer chromatography (TLC). Visualization of TLC and preparatory plates was accomplished by short wave UV light or by KMnO4 or phosphomolybdic acid dip followed by development on a hot plate. Purification by flash column chromatography was performed on silica gel 230-400 mesh with the specified eluent.

NMR spectra were recorded on Varian INOVA 300 MHz or Varian UNITY Agilent 400 MR 400 MHz spectrometers. 1H-NMR chemical shifts are reported in parts per million (δ ppm) using the residual solvent as reference (e.g. δ 7.26 ppm for CHCl3). Coupling constants are reported in Hz. 13C-NMR data are given in δ ppm relative to residual solvent (e.g. δ 77.16 ppm for CDCl3). Infrared spectra were recorded on a NEXUS 470 or a Nicolet iS10 FTIR spectrometer, using KBr discs. Neat solid samples were prepared by first dissolving the compound in CH2Cl2 and then putting a drop or two on a KBr disc and allow the solvent to evaporate. The peak positions are reported in wavenumbers (cm⁻¹). GC-MS analysis was performed on an
Agilent 7890A GC coupled with an Agilent 5975 MS with a triple-axes detector using a Phenomenex ZB-FFAP column [30 m (l), 0.25 mm (ID), 0.25 mm (film thickness)]. The initial temperature was set at 70 °C, held for 3 min and then ramped to 245 °C at 15 °C/min. Optical rotation values were recorded on Perkin Elmer Precisely Polarimeter model No. 341, using a Na light (589 nm wavelength). Melting points were measured on a digital Gallenkamp melting point apparatus and are uncorrected.

4.2 Synthesis of pheromones

4.2.1 Synthesis of 11-heptacosyne (20):

\[
\text{Br} + \text{n-BuLi, HMPA, THF, 0 °C - rt}
\]

In a 100 mL RBF was made a solution of THF (25 mL) and 1-dodecyne 18 (0.95 g, 5.7 mmol), which was then cooled to 0 °C. n-BuLi (2.5 M, 2.2 mL, 5.7 mmol) was added and the solution was stirred at this temperature for 15 min, then 1-bromopentadecane 19 (1.1 g, 3.8 mmol) dissolved in THF/HMPA (1:5, 6 mL) was added drop wise. After complete addition the cooling bath was removed and the reaction was stirred at room temperature overnight. The solution was poured into saturated NH₄Cl (50 mL), diluted with hexane (50 mL) and the layers were separated. The aqueous phase was extracted once more with hexane (25 mL) and the combined organic phase was washed with H₂O (2 × 50 mL), brine (25 mL), dried (MgSO₄),
filtered and the solvent evaporated. The residue was purified via SiO₂ flash chromatography (eluent: hexane) to give a white solid of product alkyne contaminated with a small amount of 1-dodecyn. This mixture was then heated to 110 °C in a Kugelrohr apparatus (1.5 mm/Hg) for 1 h to give pure 11-heptacosyne 20 as a colourless waxy solid.

Yield: 1.1 g, 2.9 mmol, 77%

IR (Neat): 2953, 2915, 2849, 2248, 1748, 1471, 1433, 1376, 1241, 1031, 908, 735, 717, 648, 531 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 6H), 1.20 – 1.42 (m, 38H), 1.47 (p, J = 7.2 Hz, 4H), 2.12 – 2.17 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): δ 14.3, 18.9, 22.9, 29.0, 29.3, 29.5, 29.5, 29.7, 29.8, 29.8, 29.8, 29.9, 29.9, 32.1, 32.1, 80.4.

Eleven carbons are not showing due to overlap.

4.2.2 Synthesis of 27-carbon allene as a mixture of 10,11 and 11,12 isomers (21, 22):

![Synthesis Reaction Diagram]
In a 10 mL RBF under argon was placed 11-heptacosyne 20 (91 mg, 0.24 mmol) and THF (4 mL), which was cooled to -20 °C. Then a solution of n-BuLi (2.5 M, 0.1 mL, 0.25 mmol) was added followed 5 minutes later by TMEDA (1 mL). The cooling bath was removed and the reaction was allowed to stir overnight. The dark solution was quenched by addition of 0.1 M HCl (5 mL) followed by dilution with H₂O (25 mL) and extraction with Et₂O (3 × 25 mL). The combined organic phase was washed with H₂O (25 mL), brine (25 mL), dried (MgSO₄), filtered and the solvent evaporated. Careful SiO₂ flash chromatography was performed (eluent: hexane) to give an inseparable mixture of allenes 21 and 22 as a waxy solid.

Yield: 0.036 g, 0.096 mmol, 57%

IR (Neat): 2922, 2852, 1962, 1466, 1378, 872, 721 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, J = 7.2 Hz, 6H), 1.22 – 1.60 (m, 40H), 1.90 – 2.05 (m, 4H), 5.02 – 5.15 (m, 2H).

¹³C NMR (75 MHz, CDCl₃): δ 14.2, 22.8, 22.9, 29.2, 29.3, 29.32, 29.4, 29.5, 29.7, 29.9, 29.9, 31.8, 32.1, 91.1, 204.1. Twelve carbons are not showing due to overlap.

4.2.3 Synthesis of 11-nonacosyne (24):
In a 100 mL RBF was made a solution of THF (25 mL) and 1-dodecyne (0.95 g, 5.7 mmol), which was then cooled to 0 °C. n-BuLi (2.5 M, 2.2 mL, 5.7 mmol) was added and the solution was stirred at this temperature for 15 min, then 1-bromoheptadecane (1.2 g, 3.8 mmol) dissolved in THF/HMPA (1:5, 6 mL) was added drop wise. After complete addition the cooling bath was removed and the reaction was stirred at room temperature overnight. The solution was poured into saturated NH₄Cl (50 mL), diluted with hexane (50 mL) and the layers were separated. The aqueous phase was extracted once more with hexane (25 mL) and the combined organic phase was washed with H₂O (2 × 50 mL), brine (25 mL), dried (MgSO₄), filtered and the solvent evaporated. The residue was purified via SiO₂ flash chromatography (eluent: hexane) to give a white solid of product alkyne contaminated with a small amount of 1-dodecyne. This mixture was then heated to 110 °C in a Kugelrohr apparatus (1.5 mm/Hg) for 30 min to give pure 11-nonacosyne as a colourless waxy solid.

Yield: 1.15 g, 2.8 mmol, 75%

MP 41 – 42 °C

IR (Neat): 2953, 2915, 2849, 1471, 1455, 1434, 1384, 889, 717, 658, 531, 514 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 6H), 1.22 – 1.42 (m, 42 H), 1.47 (p, J = 7.2 Hz, 4H), 2.10 – 2.18 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): δ 14.4, 19.0, 23.0, 29.1, 29.5, 29.6, 29.64, 29.8, 29.9, 29.9, 29.9, 30.0, 30.0, 32.2, 32.21, 80.5.

Thirteen carbons are not showing due to overlap.
4.2.4 Synthesis of 29-carbon allene as a mixture of 10,11 and 11,12 isomers (25, 26):

In a 10 mL RBF under argon was placed 11-nonacosyne (100 mg, 0.25 mmol) and THF (4 mL), which was cooled to -20 °C. Then a solution of n-BuLi (2.5 M, 0.10 mL, 0.25 mmol) was added followed 5 minutes later by TMEDA (1 mL). The cooling bath was removed and the reaction was allowed to stir overnight. The dark solution was quenched by addition of 0.1 M HCl (5 mL) followed by dilution with H₂O (25 mL) and extraction with Et₂O (3 × 25 mL). The combined organic phase was washed with H₂O (25 mL), brine (25 mL), dried (MgSO₄), filtered and solvent evaporated. Careful SiO₂ flash chromatography was performed (eluent: hexane) to give an inseparable mixture of allenes 25 and 26 as a waxy solid.

Yield: 0.057 g, 0.14 mmol, 57%

IR (Neat): 2922, 2852, 1962, 1712, 1378, 872, 721 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, J = 7.2 Hz, 6H), 1.22 – 1.60 (m, 44H), 1.90 – 2.05 (m, 4H), 5.02 – 5.15 (m, 2H).
$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 14.3, 22.9, 29.2, 29.3, 29.4, 29.5, 29.7, 29.9, 32.1, 91.1, 204.0. Eighteen carbons are not showing due to overlap.

4.2.5 Synthesis of heptadecanal (33)$^{77}$:

\[
\begin{align*}
\text{In a 100 mL RBF was put heptadecanol 34 (1.0 g, 3.9 mmol), celite (0.5 g), 4Å molecular sieves (0.25 g) and CH}_2\text{Cl}_2 (20 mL). To this heterogenous solution was added PCC (1.0 g, 4.6 mmol) and stirring was continued overnight. After dilution with Et}_2\text{O (25 mL) the black slurry was filtered through a pad of SiO}_2 \text{ that was rinsed thoroughly with a hexane/ethyl acetate mixture (10:1, 250 mL). The solvent was evaporated and the residue was purified by SiO}_2 \text{ flash column chromatography, (eluent: 20:1 hexane/EtOAc) to give heptadecanal 33 as a colourless liquid.}
\end{align*}
\]

Yield: 0.90 g, 3.4 mmol, 88%

IR (Neat): 2926, 2855, 2709, 1728, 1467, 1408, 1384, 1152, 719, 661 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.88 (t, $J = 7.2$ Hz, 3H), 1.22 – 1.38 (m, 26H), 1.58 – 1.68 (m, 2H), 2.41 (dt, $J = 2.0, 7.2$ Hz, 2H), 9.76 (t, $J = 2.0$ Hz, 1H).
\[^{13}\text{C} \text{NMR} \ (100 \ \text{MHz}, \ \text{CDCl}_3): \quad \delta \ 14.3, \ 22.2, \ 22.8, \ 22.9, \ 29.3, \ 29.5, \ 29.6, \ 29.7, \ 29.8, \ 29.81, \ 29.83, \ 29.84, \ 29.85, \ 31.7, \ 32.1, \ 44.1, \ 203.1.\]

4.2.6 Synthesis of 1-(triisopropylsilyl)-nonadec-1-yne-3-ol (35):

\[
\begin{align*}
\text{IP} & + 35 \quad \text{n-BuLi, THF, 0 °C} \\
\text{16} & \quad \text{33} \\
\rightarrow & \quad \text{35}
\end{align*}
\]

In a 25 mL RBF was put triisopropylsilylacetylene 16 (0.88 mL, 3.8 mmol) and THF (10 mL). The solution was cooled to 0 °C and n-BuLi (2.6 M, 1.52 mL, 3.8 mmol) was added drop wise over 1 min. After complete addition and stirring for 10 min, heptadecanal 33 (0.9 g, 3.4 mmol) in THF (5 mL) was added. The solution was stirred at 0 °C for 0.5 h and then quenched with saturated aq. NH\textsubscript{4}Cl (5 mL) and diluted with Et\textsubscript{2}O (20 mL). The layers were separated and the aqueous phase was extracted with Et\textsubscript{2}O (2 × 20 mL). The combined organic phase was washed with brine (20 mL), dried (MgSO\textsubscript{4}), filtered and the solvent evaporated. The residue was purified by SiO\textsubscript{2} flash column chromatography, (eluent: 20:1 hexane/EtOAc) to give alcohol 35 as a colourless liquid.

Yield: 1.2 g, 2.8 mmol, 80%

IR (Neat): 3332 (br), 3294, 2921, 2854, 2169, 1464, 1383, 1018, 997, 883, 678 cm\textsuperscript{-1}. 
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 0.88\) (t, \(J = 7.2\) Hz, 3H), 0.99 – 1.13 (m, 22H), 1.20 – 1.36 (m, 25H), 1.42 – 1.52 (m, 2H), 1.62 – 1.79 (m, 3H), 4.38 (dd, \(J = 6.0\) Hz, 10.8 Hz, 1H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 11.2, 11.3, 14.3, 18.6, 18.7, 22.9, 25.3, 29.4, 29.5, 29.7, 29.7, 29.81, 29.8, 29.9, 29.9, 32.1, 38.1, 63.2, 85.5, 94.9, 109.1\). One carbon is not showing due to overlap.

### 4.2.7 Synthesis of 1-(triisopropylsilyl)-nonadec-1-yne-3-one (36):

![Synthesis Reaction Scheme](image)

In a 100 mL RBF cooled to 0 °C was put N-methylmorpholine-N-oxide (0.5 g, 4.2 mmol), 4 Å molecular sieves (0.8 g), CH\(_2\)Cl\(_2\) (40 mL) and tetrapropylammonium perruthenate (0.04 g, 0.1 mmol) and CH\(_2\)Cl\(_2\) (10 mL). The reaction mixture was stirred for 0.25 h and then alcohol 35 (1.2 g, 2.8 mmol) in THF (5 mL) was added. The solution was allowed to warm to rt and stir until TLC showed complete consumption of starting material (ca. 4 h). The solution was filtered through a plug of SiO\(_2\) that was thoroughly washed with a hexane/ethyl acetate (10:1) mixture. The solvent was evaporated to give a pale yellow oil that was purified by SiO\(_2\) flash column chromatography, (eluent: 20:1 hexane/EtOAc) to give ketone 36 as a colourless liquid.
Yield: 1.1 g, 2.5 mmol, 91%


¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 3H), 1.02 – 1.18 (m, 21H), 1.22 – 1.38 (m, 26H), 1.70 (p, J = 7.6 Hz, 2H), 2.55 (t, J = 7.2 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 11.2, 14.3, 18.6, 18.6, 22.8, 24.5, 29.1, 29.50, 29.52, 29.6, 29.7, 29.8, 29.81, 29.82, 29.85, 32.1, 45.8, 95.5, 104.4, 188.3. Two carbons are not showing due to overlap.

4.2.8 Synthesis of (S)-1-(triisopropylsilyl)-nonadec-1-yn-3-ol (37):

In a 25 mL RBF was put ketone 36 (1.1 g, 2.5 mmol) and THF (10 mL). The solution was cooled to -50 °C and (S)-Me-CBS (1 M, 5 mL, 5.0 mmol) was added followed by borane dimethylsulfide (2 M, 2.5 mL, 5.0 mmol). The reaction mixture was stirred at -50 °C for 2 h and was then quenched by the drop wise addition of methanol (2 mL). The solution was then diluted with Et₂O (25 mL) and washed with saturated aq NH₄Cl (25 mL), H₂O (25 mL) and brine (25 mL). The combined aqueous layer was extracted with Et₂O (20 mL) and the combined organic phase was dried.
(MgSO₄), filtered and the solvent evaporated. The residue was purified by SiO₂ flash column chromatography, (eluent: 20:1 hexane/EtOAc) to give alcohol 37 as a colourless liquid.

Yield: 0.9 g, 2.1 mmol, 85%
Optical rotation: +1.9 (c = 1.08, CH₂Cl₂)
IR (Neat): 3332 (br), 3294, 2921, 2854, 2169, 1464, 1383, 1018, 997, 883, 678 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 7.2 Hz, 3H), 1.22 – 1.38 (m, 28H), 1.40 – 1.51 (m, 2H), 1.65 – 1.78 (m, 2H), 1.83 (d, J = 4.4 Hz, 1H), 2.45 (d, J = 2.4 Hz, 1H), 4.36 (bs, 1 H).

¹³C NMR (100 MHz, CDCl₃): δ 14.3, 22.9, 25.2, 29.4, 29.5, 29.67, 29.7, 29.79, 29.8, 29.84, 32.1, 32.8, 62.5, 73.0, 85.2, 126.7, 128.6. Five peaks not observed due to overlap.

4.2.9 Synthesis of (S)-nonadec-1-yne-3-ol (38):

In a 25 mL round bottom flask was put alcohol 37 (0.9 g, 2.1 mmol) and THF (15 mL). The solution was cooled in an ice bath and tetrabutylammonium fluoride (1 M, 2.5 mL, 2.5 mmol) was added drop wise over 2 min. After complete addition the
ice bath was removed and the reaction was allowed to stir at rt until TLC showed complete consumption of starting material (ca. 2 h). The solution was poured into aq. NH₄Cl (25 mL) and diluted with Et₂O (20 mL). The layers were separated and the aqueous phase was extracted with Et₂O (2 × 20 mL). The combined organic phase was washed with brine (20 mL), dried (MgSO₄), filtered and solvent evaporated. The residue was purified by SiO₂ flash column chromatography, (eluent: 15:1 hexane/EtOAc) to give alcohol 38 as a colourless solid.

Yield: 0.56 g, 2.0 mmol, 95%
mp: 55 – 56 °C
Optical rotation: -1.9 (c = 2.9, CH₂Cl₂)
IR (Neat): 3321 (br), 3278, 953, 2916, 2848, 2113, 1470, 1384, 1063, 718, 668 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 7.2 Hz, 3H), 0.99 – 1.13 (m, 26H), 1.42 – 1.52 (m, 2H), 1.62 – 1.79 (m, 2H), 1.81 – 1.87 (m, 1H), 2.46 (dd, J = 2.0, 2.3 Hz, 1H), 4.38 (dd, J = 6.0 Hz, 10.8 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 11.2, 11.3, 14.3, 18.6, 18.7, 22.9, 25.3, 29.4, 29.5, 29.68, 29.7, 29.81, 29.8, 29.85, 29.9, 32.1, 38.1, 63.2, 85.5.

4.2.10 Synthesis of (S)-3-methoxynonadec-1-yne (27):
In a 25 mL RBF was put sodium hydride (60% in oil, 0.1 g, 2.6 mmol) and THF (10 mL). The solution was cooled in an ice bath and then iodomethane (0.1 mL, 1.5 mmol) was added followed by alcohol 38 (0.26 g, 0.9 mmol) in THF (2 mL). The ice bath was removed and the solution was stirred at rt until TLC showed complete consumption of starting material (ca. 2 h). The mixture was then poured into saturated NH₄Cl (25 mL) and diluted with Et₂O (25 mL). The layers were separated and the aqueous phase was extracted with Et₂O (2 × 25 mL). The combined organic phase was washed with brine (20 mL), dried (MgSO₄), filtered and solvent evaporated. The residue was purified by SiO₂ flash column chromatography, (eluent: 50:1 hexane/EtOAc) to give methyl ether 27 as a colourless oil.

Yield: 0.2 g, 0.66 mmol, 71%

Optical rotation: -28.7 (c = 1.8, CH₂Cl₂)

IR (Neat): 3311, 2924, 2853, 2822, 2125, 1466, 1335, 1130, 1107, 657, 627 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 3H), 1.18 – 1.34 (m, 26H), 1.38 – 1.48 (m, 2H), 1.60 – 1.78 (m, 2H), 2.42 (dd, J = 2.0, 2.3 Hz, 1H), 3.41 (s, 3H), 3.93 (dt, J = 2.0, 6.4 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 12.0, 14.3, 18.1, 22.9, 25.3, 29.5, 29.53, 29.67, 29.7, 29.75, 29.80, 29.83, 29.9, 32.1, 35.7, 56.6,
721.3, 73.8, 82.9. One carbon is missing due to overlap.

4.2.11 Synthesis of (S)-3-acetoxynonadec-1-yn (28):

\[
\text{CH}_3 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CHOH} \xrightarrow{\text{Ac}_2\text{O, DMAP, pyridine, CH}_2\text{Cl}_2} \text{CH}_3 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{COAc}
\]

In a 25 mL RBF was put alcohol 38 (0.27 g, 1.0 mmol), CH₂Cl₂ (5 mL), pyridine (0.4 mL, 5.0 mmol), acetic anhydride (0.24 mL, 2.5 mmol) and DMAP (0.03 g). The solution was stirred at rt until TLC showed complete consumption of starting material (ca. 2 h). The solution was poured into H₂O (25 mL) and diluted with Et₂O (25 mL). The layers were separated and the aqueous phase was extracted with Et₂O (2 × 25 mL). The combined organic phase was washed with 1 M HCl (25 mL), saturated NaHCO₃ (25 mL), brine (20 mL), dried (MgSO₄), filtered and solvent evaporated. The residue was purified by SiO₂ flash column chromatography, (eluent: 25:1 hexane/EtOAc) to give acetate 28 as a colourless solid.

Yield: 0.3 g, 0.9 mmol, 96%

mp: 44.5 – 45.5 °C

Optical rotation: -38.3 (c = 2.1, CH₂Cl₂)

IR (Neat): 3250, 2951, 2915, 2847, 2123, 1725, 1469, 1377, 1245, 1025, 719, 700, 613, 557 cm⁻¹.
$^1$H NMR (400 MHz, CDCl$_3$): \[ \delta 0.88 \text{ (t, } J = 6.6 \text{ Hz, 3H)}, 1.20 - 1.36 \text{ (m, 26H),} \\
1.38 - 1.48 \text{ (m, 2H),} 1.77 \text{ (dd, } J = 6.8, 15.2 \text{ Hz,} \\
2H), 2.09 \text{ (s, 3H),} 2.44 \text{ (d, } J = 2.0 \text{ Hz, 1H),} 5.34 \text{ (t,} \\
J = 6.4 \text{ Hz, 1H).}
\]

$^{13}$C NMR (100 MHz, CDCl$_3$): \[ \delta 14.3, 21.2, 22.8, 25.0, 29.2, 29.5, 29.6, 29.7, \\
29.77, 29.8, 29.84, 32.1, 34.7, 64.0, 73.7, 81.5, \\
170.1. \text{ Four peaks not observed due to overlap.}
\]

4.2.12 Synthesis of optically enriched (S)-11, 12-nonacosadiene (26):

In a 25 mL RBF was put ether 27 (0.098 g, 0.33 mmol) and Et$_2$O (5 mL). To this was added CuBr$_2$P(OEt)$_3$ (0.1 M in Et$_2$O, 0.2 mL, 0.02 mmol) and the solution was cooled to -78 °C and decylmagnesium bromide (1 M in Et$_2$O, 0.7 mL, 0.7 mmol) was added rapidly. After 5 minutes of stirring the cooling bath was removed and the solution was allowed to warm to rt and stir until TLC showed complete disappearance of starting material (ca. 15 min). The solution was poured into an aqueous solution of NH$_3$/NH$_4$Cl (25 mL, 1:4 ratio) and diluted with Et$_2$O (25 mL). The layers were separated and the aqueous phase was extracted with Et$_2$O (2 × 25 mL). The combined organic phase was washed with brine (20 mL), dried (MgSO$_4$), filtered and solvent
evaporated. The residue was purified by SiO$_2$ flash column chromatography (eluent: hexane) to give allene 26 as a colourless waxy solid.

Yield: 0.079 g, 0.2 mmol, 59%

Optical rotation: $\Delta$ -15.8 (c = 1.73, CH$_2$Cl$_2$)

IR (Neat): 2950, 2918, 2849, 1964, 1460, 1378, 1282, 889, 875, 724 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.88 (t, $J = 6.8$ Hz, 6H), 1.20 – 1.44 (m, 44H), 1.92 – 2.02 (m, 4H), 5.06 (p, $J = 5.2$ Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.3, 22.9, 29.2, 29.3, 29.4, 29.5, 29.7, 29.8, 29.82, 29.83, 29.9, 32.1, 91.1, 204.0. Fifteen peaks not observed due to overlap.

**4.2.13 Synthesis of optically enriched (S)-11, 12-nonacosadiene (26):**

In a 25 mL RBF was put acetate 28 (0.3 g, 0.9 mmol) and Et$_2$O (15 mL). To this solution was added CuBr2P(OEt)$_3$ (0.1 M in Et$_2$O, 0.6 mL, 0.06 mmol) and the solution was cooled to -78 °C and decylmagnesium bromide (1 M in Et$_2$O, 1.8 mL, 1.8 mmol) was added rapidly. After 5 minutes of stirring the cooling bath was removed and the solution was allowed to warm gradually and when TLC showed complete disappearance of starting material (ca. 15 min) the solution was poured into
an aqueous solution of NH$_3$/NH$_4$Cl (25 mL, 1:4 ratio) and diluted with Et$_2$O (25 mL). The layers were separated and the aqueous phase was extracted with Et$_2$O (2 × 25 mL). The combined organic phase was washed with brine (20 mL), dried (MgSO$_4$), filtered and solvent evaporated. The residue was purified by SiO$_2$ flash column chromatography, (eluent: hexane), and then put under high vacuum (0.01 mm/Hg) for 24 h to remove any residual decane to give allene 26 as a colourless waxy solid.

Yield: 0.25 g, 0.62 mmol, 67%

Optical rotation: -15.1 (c = 2.8, CH$_2$Cl$_2$)

IR (Neat): 2950, 2918, 2849, 1964, 1460, 1378, 1282, 889, 875, 724 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, $J = 6.8$ Hz, 6H), 1.20 – 1.44 (m, 44H), 1.92 – 2.02 (m, 4H), 5.06 (p, $J = 5.2$ Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 14.3, 22.9, 29.2, 29.3, 29.4, 29.5, 29.7, 29.8, 29.82, 29.83, 29.9, 32.1, 91.1, 204.0. Fifteen carbons not observed due to overlap.

4.2.14 Synthesis of (S)-3-((S)-2-acetoxypropionyloxy)nonadec-1-yne (39):

In a 10 mL RBF was put alcohol 38 (0.025 g, 0.90 mmol), CH$_2$Cl$_2$ (2 mL) and pyridine (0.2 mL, 2.5 mmol). The solution was cooled to 0 °C and (S)-2-
acetoxypropionyl chloride (0.13 mL, 1.0 mmol) was added and stirring was continued at this temperature for 2 h. The solution was poured into H₂O (10 mL) and diluted with Et₂O (10 mL). The layers were separated and the aqueous phase was extracted with Et₂O (2 × 25 mL). The combined organic phase was washed with 1 M HCl (10 mL), saturated NaHCO₃ (10 mL), brine (10 mL), dried (MgSO₄), filtered and solvent evaporated to give proprionate 39 as a colourless solid.

Yield: 0.03 g, 0.8 mmol, 88%
Optical rotation: -51 (c = 1.53, CH₂Cl₂)
ee 77%
IR (Neat): 3250, 2951, 2915, 2847, 2123, 1725, 1469, 1377, 1245, 1025, 719, 700, 613, 557 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.87 (t, J = 6.8 Hz, 3H), 1.20 – 1.36 (m, 26H), 1.38 – 1.48 (m, 2H), 1.49 (d, J = 6.8 Hz, 3H), 1.74 – 1.83 (m, 2H), 2.12 (s, 3H), 2.44 (d, J = 2.4 Hz, 1H), 5.04 (q, J = 7.2 Hz, 1H), 5.37 (dd, J = 6.4, 2.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 14.3, 16.8, 17.0, 20.8, 22.8, 24.9, 29.1, 29.2, 29.5, 29.6, 29.7, 29.76, 29.8, 29.84, 32.1, 34.6, 34.62, 65.0, 68.6, 74.0, 80.8, 170.0, 170.4. One carbon is missing due to overlap.

LRMS (m/z): 394.9.

4.2.15 Synthesis of 8-bromo-1-octanol (43)⁷⁸:
In a 50 mL RBF was added toluene (25 mL), 1, 8-octanediol 40 (1.5 g, 10 mmol) and concentrated HBr (1.35 mL of a 48% (9 M) aqueous solution, 12.15 mmol). The heterogeneous solution was heated at reflux for 36 h and then an additional aliquot of concentrated HBr (0.5 mL, 4.5 mmol) was added and the solution heated at reflux for an additional 36 h. The reaction mixture was allowed to cool to rt and the phases were separated. The organic layer was diluted with Et2O (25 mL) and washed with 1 M NaOH (25 mL), brine (25 mL), dried (MgSO4), filtered and solvent evaporated. The resultant oil was purified by SiO2 chromatography (eluent: 2:1 hexane/EtOAc) to give 8-bromo-1-octanol 43 as a colourless oil.

Yield: 1.8 g, 8.7 mmol, 87%

IR (Neat): 3347, 2925, 2855, 1464, 1438, 1384, 1245, 1056, 724, 644, 562 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 1.22 – 1.48 (m, 8H), 1.56 (p, J = 6.9 Hz, 2H), 1.85 (p, J = 7.5 Hz, 2H), 3.41 (t, J = 6.9 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 25.7, 28.2, 28.8, 29.3, 32.8, 32.9, 34.1, 70.0.

4.2.16 Synthesis of 8-bromooctanal (44):
To a 100 mL RBF was added 8-bromo-1-octanol 43 (1.5 g, 7.2 mmol), CH$_2$Cl$_2$ (40 mL) and silica (2.9 g). To the solution was added PCC (2.9 g, 13.7 mmol) and the reaction was stirred for 3 h at rt. The solution was filtered through a pad of SiO$_2$, which was then thoroughly rinsed with a hexane/ethyl acetate mixture (10:1). The solvent was evaporated in vacuo and the residue was purified by SiO$_2$ chromatography (eluent: 10:1 hexane/EtOAc) to give 8-bromooctanal 44 as a colourless oil.

Yield: 1.0 g, 4.7 mmol, 67%

IR (Neat): 2932, 2856, 2719, 1725, 1463, 1439, 1410, 1247, 726, 644, 561 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.23 – 1.51 (m, 6H), 1.60 – 1.69 (m, 2H), 1.86 (p, $J = 8.0$ Hz, 2H), 2.44 (t, $J = 5.6$ Hz, 2H), 3.41 (t, $J = 6.8$ Hz, 2H), 9.77 (t, $J = 1.6$ Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 22.0, 28.1, 28.6, 29.1, 32.8, 34.0, 43.9, 202.8.

4.2.17 Synthesis of 8-bromo-1-tetrahydropyranoyloxyoctane (45)$_{80}$:
In a 50 mL RBF was made a solution of CH$_2$Cl$_2$ (25 mL), 8-bromo-1-octanol 43 (3.6 g, 17.1 mmol), and dihydropyran (1.7 mL, 18.8 mmol). The mixture was cooled to 0 °C, and PPTS (0.5 g, 10 mol %) was added, followed by removal of the cooling bath. The reaction was allowed to gradually warm to room temperature and stir overnight. Water was poured into the solution and the layers were separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 50 mL) and the combined organic layer was washed with saturated aqueous NaHCO$_3$ (50 mL), brine (50 mL), dried (Na$_2$SO$_4$), and the solvent evaporated. The resulting oil was subjected to SiO$_2$ flash chromatography (eluent: 15:1 hexane/EtOAc) to give 8-bromo-1-tetrahydropyranyloxyoctane 45 as a colourless oil.

Yield: 4.60 g, 15.7 mmol, 92%

IR (Neat): 2934, 2856, 1465, 1454, 1384, 1365, 1352, 1226, 1200, 1136, 1120, 1078, 1034, 987, 905, 869, 814, 724, 646, 563 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.23 – 1.46 (m, 8H), 1.46 – 1.62 (m, 6H), 1.65 – 1.73 (m, 1H), 1.78 – 1.88 (m, 3H), 3.32 – 3.41 (m, 3H), 3.44 – 3.52 (m, 1H), 3.67 – 3.74 (m, 1H), 3.81 – 3.89 (m, 1H), 4.52 – 4.58 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.8, 25.6, 26.2, 28.2, 28.8, 29.4, 29.8, 30.9, 32.9, 34.0, 62.4, 67.7, 98.9.

4.2.18 Synthesis of 8-(1-phenyl-1H-tetrazol-5-ylsulfanyl)-1-tetrahydropyranyloxyoctane (48)$^{81}$:
In a 100 mL RBF was made a solution of THF (35 mL) and 1-phenyl-1H-tetrazole-5-thiol 47 (1.0 g, 5.5 mmol), which was then cooled to 0 °C. NaH (0.22 g, 5.5 mmol, 60% suspension in mineral oil) was added and the solution was stirred for 30 min. Then bromide 45 (1.6 g, 5.5 mmol) in THF (5 mL) was added followed by NaI (0.07 g, 0.5 mmol). The reaction was warmed to rt and allowed to stir for 24 h. The contents of the flask were then poured into H₂O (50 mL) and extracted with CH₂Cl₂ (4 × 25 mL). The combined organic layer was washed with water (50 mL), brine (50 mL), dried (MgSO₄), filtered and the solvent evaporated. The crude product was purified by SiO₂ chromatography (eluent: 4:1 hexane/EtOAc) to give sulfide 48 as a colourless oil.

Yield: 1.9 g, 4.9 mmol, 90%

IR (Neat): 2933, 2855, 1597, 1500, 1464, 1440, 1412, 1386, 1135, 1120, 1076, 1032, 762, 695 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.22 – 1.62 (m, 20H), 1.63 – 1.72 (m, 1H), 1.76 – 1.86 (m, 3H), 3.32 – 3.40 (m, 3H), 3.44 – 3.51 (m, 1H), 3.70 (td, J = 6.8, 9.6 Hz, 1H), 3.81 – 3.88 (m, 1H), 4.54 (dd, J = 2.8, 4.4 Hz, 1H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.8, 25.6, 26.2, 28.7, 29.0, 29.1, 29.3, 29.8, 30.9, 33.4, 62.5, 67.7, 99.0, 123.9, 129.8, 130.1, 133.8, 154.6.

4.2.19 Synthesis of 8-(1-phenyl-1H-tetrazol-5-ylsulfonyl)-1-terahydropyranlyoxyoctane (49)$^{81}$:

![Chemical structure](image)

In a 100 mL RBF was made a solution of EtOH (50 mL) and sulfide 48 (1.6 g, 4.1 mmol), which was then cooled to 0 °C. To this was added Mo$_7$O$_{24}$(NH$_4$)$_6$4H$_2$O (0.7 g, 0.6 mmol) in 30 % H$_2$O$_2$ (6 mL, 53 mmol) drop wise. After complete addition the solution was allowed to slowly warm to rt and stir for 18 h. The contents of the flask were then poured into H$_2$O (350 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with saturated Na$_2$S$_2$O$_3$ (3 x 25 mL), brine (50 mL), dried (MgSO$_4$), filtered and the solvent evaporated. The crude product was purified by SiO$_2$ chromatography (eluent: 4:1 hexane/EtOAc) to give sulfone 49 as a colourless oil.

Yield: 1.5 g, 3.5 mmol, 85%

IR (Neat): 3479, 3072, 2930, 2857, 1596, 1498, 1464, 1384, 1354, 1077, 1027, 873, 763, 689, 629 cm$^{-1}$. 
\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)}: \delta 1.28 \text{–} 1.42 (m, 6 H), 1.45 \text{–} 1.63 (m, 9H), 1.62 \text{–} 1.75 (m, 1H), 1.77 \text{–} 1.86 (m, 1H), 1.89 \text{–} 1.99 (m, 2H), 3.37 (m, 1H) 3.46 \text{–} 3.53 (m, 1H), 3.68 \text{–} 3.76 (m, 2H), 3.82 \text{–} 3.89 (m, 1H), 4.54 \text{–} 4.58 (m, 1H), 7.56 \text{–} 7.74 (m, 5H). \]

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}: \delta 19.8, 22.1, 25.6, 26.2, 28.2, 29.0, 29.1, 29.8, 30.9, 56.1, 62.5, 67.6, 99.0, 125.2, 129.8, 131.6, 133.2, 153.6. \]

4.2.20 Synthesis of methyl 16-hydroxy-hexadecanoate (52)\[\text{82}]:

\[
\begin{align*}
\text{51} & \xrightarrow{\text{pTSA, MeOH,}} \text{52} \\
\end{align*}
\]

In a 250 mL RBF was put 16-hexadecanolide 51 (2.0 g, 7.9 mmol) dissolved in dry methanol (60 mL), followed by the addition of pTSA (60 mg, 0.3 mmol). The solution was heated at reflux for 24 h. The RBF contents were poured into water (70 mL) and extracted with CH\(_2\)Cl\(_2\) (3 × 50 mL). The combined organic phase was washed with saturated aqueous NaHCO\(_3\) (2 × 50 mL), brine (50 mL), dried (Na\(_2\)SO\(_4\)) and the solvent evaporated. The residue was purified by SiO\(_2\) chromatography (eluent: 3:1 hexane/EtOAc) to give ester 52 as a white solid.

Yield: 2.1 g, 7.2 mmol, 91%
mp: 53 – 54 °C

IR (Neat): 3312, 2919, 2894, 1744, 1473, 1463, 1384, 1214, 1193, 1164, 883, 732 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.22 – 1.38 (m, 22H), 1.53 – 1.66 (m, 5H), 2.30 (t, \(J = 7.6\) Hz, 2H), 3.64 (q, \(J = 6.4\) Hz, 2H), 3.67 (s, 3H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 25.1, 25.9, 29.3, 29.4, 29.58, 29.6, 29.7, 29.75, 29.8, 33.0, 34.3, 51.6, 63.3, 174.5. Three peaks not observed due to overlap.

4.2.21 Synthesis of methyl 16-(tetrahydropyranyloxy)hexadecanoate (53):
and solvent evaporated by rotary evaporation. The crude oil was purified by SiO₂ chromatography (eluent: 15:1 hexane/EtOAc) to give ester 53 as a white solid.

Yield: 1.6 g, 4.2 mmol, 59%

mp: 47.5 – 48.5 °C

IR (Neat): 2920, 2850, 1734, 1654, 1472, 1384, 1169, 1121, 1029 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 1.22 - 1.40 (m, 16H), 1.44 - 1.91 (m, 16H), 2.30 (t, J = 7.8 Hz, 2H), 3.37 (td, J = 6.6, 9.6 Hz, 1H), 3.46 - 3.55 (m, 1H), 3.67 (s, 3H), 3.71 (td, J = 6.9, 9.6 Hz, 1H), 3.82 - 3.92 (m, 1H), 4.56 - 4.60 (m, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 19.9, 25.1, 25.7, 26.4, 29.3, 29.4, 29.6, 29.7, 29.75, 29.76, 29.77, 29.8, 29.81, 29.9, 31.0, 34.3, 51.6, 62.5, 67.9, 99.0, 174.5. One peak not observed due to overlap.

4.2.22 Synthesis of 16-(tetrahydropyranloxy)-hexadecan-1-ol (54)⁸⁴:

![Reaction Scheme]

```latex
\text{LAH, Et₂O \ 0 °C - rt}
```
To a 200 mL RBF was added Et₂O (50 mL) followed by LAH (0.2 g, 4.2 mmol) and the reaction vessel was cooled to 0 °C. Then THP-protected hydroxyester 53 (1.6 g, 4.2 mmol) in Et₂O (5 mL) was added drop wise over 2 minutes. After complete addition and stirring for 10 min, excess LAH was quenched via the successive addition of H₂O (0.2 mL), 1M NaOH (0.2 mL), and H₂O (0.6 mL). After a white solid had formed the solution was filtered through a pad of celite and rinsed thoroughly with diethyl ether. After drying (MgSO₄) and evaporation of solvent the crude product was purified by SiO₂ chromatography (eluent: 4:1 hexane/EtOAc) to give alcohol 54 as a colourless waxy solid.

Yield: 1.3 g, 3.9 mmol, 92%

IR (Neat): 3374, 2921, 2848, 1467, 1384, 1119, 1059, 1034, 965, 905 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 1.28 – 1.48 (m, 14H), 1.58 – 1.72 (m, 8H), 1.74 – 1.98 (m, 10H), 3.37 (td, J = 6.9, 9.3 Hz, 1H), 3.46 – 3.55 (m, 1H), 3.64 (q, J = 5.1 Hz, 1H), 3.68 – 3.78 (m, 1H), 3.83 – 3.92 (m, 1H), 4.56 – 4.60 (m, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 19.8, 25.7, 25.9, 26.4, 29.6, 29.63, 29.7, 29.75, 29.78, 29.8, 29.9, 30.9, 33.0, 62.5, 63.2, 67.8, 99.0. Four peaks not observed due to overlap.

4.2.23 Synthesis of 16-bromo-1-(tetrahydropyranloxy)hexadecane (41):
In a 200 mL RBF was successively put benzene (60 mL), PPh$_3$ (1.0 g, 3.7 mmol) and NBS (0.7 g, 3.7 mmol). Then THP-protected alcohol 54 (1.3 g, 3.9 mmol) in benzene (2 mL) was added drop wise over 2 min. After complete addition the reaction was stirred at rt for 48 h, then poured into H$_2$O (50 mL) and the layers were separated. The aqueous phase was washed with Et$_2$O (2 × 25 mL) and the combined organic phase was washed with brine (25 mL). The organic phase was dried (Na$_2$SO$_4$), filtered and the solvent evaporated. The resultant oil was purified by SiO$_2$ chromatography (eluent: 8:1 hexane/EtOAc) to give bromide 41 as a pale yellow oil.

Yield: 0.23 g, 0.56 mmol, 15%

IR (Neat): 2923, 2852, 1735, 1654, 1466, 1384, 1121, 1078, 1034, 669 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): δ 1.22 – 1.80 (m, 32H), 1.86 (p, $J = 7.5$ Hz, 2H), 3.37 (td, $J = 6.9$, 9.3 Hz, 1H), 3.41 (t, $J = 6.9$ Hz, 2H), 3.46 – 3.55 (m, 1H), 3.68 (td, $J = 6.9$, 9.3 Hz, 1H), 3.83 – 3.92 (m, 1H), 4.58 – 4.62 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 19.9, 25.7, 26.4, 28.3, 28.9, 29.6, 29.64, 29.7, 29.74, 29.76, 29.8, 29.9, 30.9, 33.0, 34.2, 62.5, 67.8, 99.0. Three carbons are missing due to overlap.
4.2.24 Synthesis of 1, 16-hexadecanediol (55)\textsuperscript{86}:

In a 200 mL RBF was put THF (75 mL) and LAH (0.5 g, 13.2 mmol). The solution was cooled in an ice bath and hexadecanolide 51 (1.3 g, 5.1 mmol) in THF (10 mL) was added drop wise over 5 min. After complete addition the reaction was heated at reflux for 2 h and then cooled to rt and allowed to stir for 14 h. The solution was carefully quenched by addition of Rochelle’s salt (1 M, 50 mL), stirred for 15 min and then the layers were separated and the aqueous phase was extracted with Et\textsubscript{2}O (2 × 30 mL). The combined organic phase was washed with brine (25 mL), dried (MgSO\textsubscript{4}), filtered and the solvent evaporated to give diol 55 as a colourless solid. No further purification was needed.

Yield: 1.28 g, 5.0 mmol, 97%

mp: 90.5 – 93.5 °C

IR (Neat): 3413, 3344, 2916, 2847, 2460, 1384, 1362, 1058, 1036, 994, 729, 610 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHZ, CDCl\textsubscript{3}): \( \delta \) 1.22 – 1.40 (m, 24H), 1.57 (p, \( J = 7.2 \) Hz, 4H), 3.64 (t, \( J = 6.4 \) Hz, 4H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 25.9, 29.6, 29.7, 29.75, 29.8, 33.0, 63.3. One peak not observed due to overlap.
4.2.25 Synthesis of 16-bromo-1-hexadecanol (56):$
\begin{align*}
\text{In a 50 mL RBF was put toluene (25 mL), diol } & 55 \text{ (1.2 g, 4.7 mmol) and } \\
\text{concentrated HBr (0.6 mL of a 48\% (9 M) aqueous solution, 5.3 mmol). The} \\
\text{heterogenous solution was heated at reflux for 36 h and if TLC showed remaining} \\
\text{starting material then an additional aliquat of concentrated HBr (0.2 mL, 2.0} \\
\text{mmol) was added and the solution heated at reflux for an additional 36 h. The} \\
\text{reaction mixture was allowed to cool to rt and the phases were separated. The} \\
\text{organic layer was diluted with Et}_2\text{O (25 mL) and washed with 1 M NaOH (25 mL),} \\
\text{brine (25 mL), dried (MgSO}_4\text{), filtered and solvent evaporated. The} \\
\text{resultant oil was purified by SiO}_2\text{ chromatography (eluent: 2:1 hexane/EtOAc) to give 16-bromo-1-hexadecanol 56} \\
\text{as a colourless solid.}
\end{align*}$

Yield: 1.3 g, 4.1 mmol, 88%

mp: 54 – 56 °C

IR (Neat): 3295, 3193, 2918, 2849, 1473, 1462, 1071, 1060, 1052, 1034, 1024, 1007, 906, 730, 720, 669, 651 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): δ 1.20 – 1.48 (m, 24H), 1.56 (p, $J = 7.2$ Hz, 2H), 1.84 (p, $J = 7.6$ Hz, 2H), 3.40 (t, $J = 6.8$ Hz, 2H), 3.63 (t, $J = 6.8$ Hz, 2H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 25.9, 28.3, 28.9, 29.6, 29.7, 29.72, 29.74, 29.8, 32.9, 33.0, 34.2, 63.2. Four peaks not observed due to overlap.

4.2.26 Synthesis of 16-bromo-1-(tetrahydropyranloxy)hexadecane (41):

![Chemical Structure]

In a 100 mL RBF was put 16-bromo-1-hexadecanol 56 (0.85 g, 2.6 mmol), CH$_2$Cl$_2$ (50 mL) and PPTS (25 mg). The solution was stirred at rt for 16 h and was then poured into saturated NaHCO$_3$ (50 mL) and the layers were separated. The aqueous phase was washed with CH$_2$Cl$_2$ (25 mL) and the combined organic phase was washed with brine (25 mL). The organic phase was dried (MgSO$_4$), filtered and the solvent evaporated. The resultant oil was purified by SiO$_2$ chromatography (eluent: 8:1 hexane/EtOAc) to give bromide 41 as a colourless oil.

Yield: 1.0 g, 2.5 mmol, 95%

See 4.2.21 for spectral data.

4.2.27 Synthesis of 1-(tetrahydropyranloxy)octacos-17-yne (57):
In a 100 mL RBF was made a solution of THF (20 mL) and 1-dodecyne 18 (0.95 g, 5.7 mmol), which was then cooled to 0 °C. n-BuLi (2.5 M, 2.2 mL, 5.7 mmol) was added and the solution was left to stir at this temperature for 15 min. Then 16-bromo-1-(tetrahydropyranloxy)hexadecane 41 (1.5 g, 3.8 mmol) in a mixture of THF (2 mL) and HMPA (5 mL) was then added drop wise over 2 min. The cooling bath was removed and the reaction was gradually warmed to room temperature and stirred overnight. The solution was diluted with saturated NH₄Cl (100 mL) and Et₂O (50 mL), the layers were separated and the aqueous phase was extracted with Et₂O (2 x 25 mL). The combined organic phase was washed with brine (25 mL), dried (MgSO₄), filtered and solvent evaporated. The residue was purified via SiO₂ flash chromatography (eluent: 25:1 hexane/EtOAc) to provide alkyne 57 as a pale brown oil.

Yield: 1.5 g, 3.1 mmol, 82%

IR (Neat): 2925, 2853, 2735, 2655, 2024, 1466, 1384, 1352, 1200, 1121, 1078, 1034, 906, 869, 816, 721 cm⁻¹.

¹H NMR (300 MHz, CDCl₃):  δ 0.88 (t, J = 6.9 Hz, 3H), 1.20 – 1.88 (m, 50H), 2.10 – 2.18 (m, 2H), 2.14 (t, J = 5.4 Hz, 2H), 3.38
(td, $J = 6.9, 9.3$ Hz, 1H), 3.46 – 3.55 (m, 1H), 3.74
(td, $J = 6.9, 9.3$ Hz, 1H), 3.83 – 3.92 (m, 1H), 4.56
– 4.60 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$):

δ 14.4, 19.0, 20.0, 22.9, 22.95, 25.8, 26.5, 29.1,
29.5, 29.6, 29.8, 29.83, 29.86, 29.87, 29.88, 29.9,
29.3, 29.95, 30.0, 31.1, 31.8, 32.2, 62.6, 68.0,
80.5, 99.1. Seven peaks not observed due to
overlap.

4.2.28 Synthesis of octacos-17-yn-1-ol (58):

A 25 mL RBF was charged with THP-protected octacos-17-ynol 57 (1.5 g, 3.1
mmol), methanol (25 mL), THF (10 mL) and a catalytic amount of pTSA (0.09 g).
The reaction was allowed to stir at rt for 4.5 h and then the solvent was removed via
rotary evaporation and the remaining solid was purified via SiO$_2$ flash
chromatography (eluent: 8:1 hexane/EtOAc) to provide alkyne 58 as a white solid.

Yield: 1.1 g, 2.6 mmol, 83%

mp: 63 – 64 °C
IR (Neat): 3147, 2917, 2848, 1471, 1459, 1384, 1059, 729, 661 cm$^{-1}$.

$^{1}$H NMR (300 MHz, CDCl$_3$): δ 0.88 (t, $J = 6.9$ Hz, 3H), 1.20 – 1.68 (m, 44H), 2.10 – 2.18 (m, 2H), 2.14 (t, $J = 5.4$ Hz, 2H), 3.64 (t, $J = 6.6$ Hz, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ 14.2, 18.8, 22.7, 25.8, 28.9, 29.2, 29.4, 29.5, 29.6, 29.65, 29.66, 29.67, 29.7, 29.71, 29.73, 32.0, 32.9, 63.2, 80.3. Nine peaks not observed due to overlap.

4.2.29 Synthesis of octacos-17-ynal (42):

In a 100 mL RBF was put CH$_2$Cl$_2$ (30 mL), octacos-17-yn-1-ol 58 (1.1 g, 2.6 mmol) and silica gel (0.9 g). To this was added PCC (0.8 g, 3.9 mmol) and the reaction mixture was allowed to stir for 3 h at rt. The solution was filtered through a pad of SiO$_2$, which was then thoroughly rinsed with a hexane/ethyl acetate mixture (10:1). The solvent was evaporated in vacuo and the residue was purified by SiO$_2$ chromatography (eluent: 15:1 hexane/EtOAc) to give aldehyde 42 as a white solid.
Yield: 0.93 g, 2.3 mmol, 88%

mp: 51 – 53 °C

IR (Neat): 2952, 2931, 2919, 2847, 2733, 1707, 1463, 1385, 724, 667 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.87 (t, J = 7.2 Hz, 3H), 1.20 – 1.68 (m, 42H), 2.10 – 2.18 (m, 2H), 2.13 (t, J = 6.8 Hz, 2H), 2.41 (dt, J = 2.0, 7.6 Hz, 2H), 9.75 (t, J = 2.0 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃): δ 14.1, 18.8, 22.1, 22.7, 28.9, 29.2, 29.3, 29.34, 29.4, 29.55, 29.57, 29.58, 29.6, 29.7, 31.9, 43.9, 80.2, 202.9. Ten peaks not observed due to overlap.

4.2.30 Synthesis of 12-nonacosyne (61):

In a 50 mL RBF was made a solution of THF (20 mL) and 1-tridecyne 59 (0.95 g, 5.3 mmol) which was then cooled to 0 °C. n-BuLi (2.5 M, 2.1 mL, 5.3 mmol) was added and the solution was stirred at this temperature for 15 min, then 1-bromohexadecane 60 (1.0 g, 3.3 mmol) dissolved in HMPA (5 mL) was added drop wise. After complete addition the cooling bath was removed and the reaction was
stirred at room temperature overnight. The solution was poured into saturated NH$_4$Cl (50 mL), diluted with hexane (50 mL) and the layers were separated. The aqueous phase was extracted once more with hexane (25 mL) and the combined organic phase was washed with H$_2$O (2 x 50 mL), brine (25 mL), dried (MgSO$_4$), filtered and solvent evaporated. The residue was purified via SiO$_2$ flash chromatography (eluent: hexane) to give a white solid of product alkyne contaminated with a small amount of 1-tridecyne. This mixture was then heated to 120 °C in a Kugelrohr apparatus (1.5 mm/Hg) for 1 h to give pure 12-nonacosyne 61 as a colourless waxy solid.

Yield: 1.2 g, 2.9 mmol, 88%
mp: 48 – 50 °C
IR (Neat): 2953, 2915, 2849, 2344, 1471, 1432, 1384, 716 cm$^{-1}$.
$^1$H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, $J = 6.8$ Hz, 6H), 1.20 – 1.34 (m, 38H), 1.34 – 1.41 (m, 4H), 1.47 (p, $J = 7.2$ Hz, 4H), 2.13 (t, $J = 7.2$, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 14.3, 18.9, 22.9, 29.0, 29.3, 29.5, 29.7, 29.8, 29.83, 29.85, 29.9, 32.1, 80.4. Sixteen peaks not observed due to overlap.

4.2.31 13-Nonacosyne (64):
In a 50 mL RBF was made a solution of THF (20 mL) and 1-tetradecyne 62 (1.0 g, 5.1 mmol) which was then cooled to 0 °C. n-BuLi (2.5 M, 2.0 mL, 5.1 mmol) was added and the solution was stirred at this temperature for 15 min, then 1-bromopentadecane 63 (0.95 g, 3.2 mmol) dissolved in HMPA (5 mL) was added drop wise. After complete addition the cooling bath was removed and the reaction was stirred at room temperature overnight. The solution was poured into saturated NH₄Cl (50 mL), diluted with hexane (50 mL) and the layers were separated. The aqueous phase was extracted once more with hexane (25 mL) and the combined organic phase was washed with H₂O (2 × 50 mL), brine (25 mL), dried (MgSO₄), filtered and solvent evaporated. The residue was purified via SiO₂ flash chromatography (eluent: hexane) to give a white solid of product alkyne contaminated with a small amount of 1-tetradecyne. This mixture was then heated to 120 °C in a Kugelrohr apparatus (1.5 mm/Hg) for 1 h to give pure 13-nonacosyne 64 as a colourless waxy solid.

Yield: 1.0 g, 2.5 mmol, 74%

mp: 43 – 45 °C

IR (Neat): 2954, 2916, 2867, 2849, 1472, 1430, 717 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 6H), 1.20 – 1.33 (m, 38H), 1.34 – 1.41 (m, 4H), 1.47 (p, J = 7.2 Hz, 4H), 2.13 (tt, J = 7.2, 1.6 Hz, 4H).
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 14.3, 18.9, 22.9, 29.0, 29.3, 29.5, 29.7, 29.8, 29.83, 29.85, 29.9, 32.1, 80.4\). Sixteen peaks not observed due to overlap.

4.2.32 14-Nonacosyne (67):

\[\text{In a 50 mL RBF was made a solution of THF (20 mL) and 1-pentadecyne 65 (1.1 g, 5.3 mmol) which was then cooled to 0 °C. n-BuLi (2.5 M, 2.1 mL, 5.3 mmol) was added and the solution was stirred at this temperature for 15 min, then 1-bromotetradecane 66 (0.9 g, 3.3 mmol) dissolved in HMPA (5 mL) was added drop wise. After complete addition the cooling bath was removed and the reaction was stirred at room temperature overnight. The solution was poured into saturated NH}_4\text{Cl (50 mL), diluted with hexane (50 mL) and the layers were separated. The aqueous phase was extracted once more with hexane (25 mL) and the combined organic phase was washed with H}_2\text{O (2 × 50 mL), brine (25 mL), dried (MgSO}_4\text{), filtered and the solvent evaporated. The residue was purified via SiO}_2\text{ flash chromatography (eluent: hexane) to give a white solid of product alkyne contaminated with a small amount of 1-pentadecyne. This mixture was then heated to 120 °C in a Kugelrohr apparatus (1.5 mm/Hg) for 1 h to give pure 14-nonacosyne 67 as a colourless waxy solid.}

Yield: 1.0 g, 2.5 mmol, 76\%}
mp: 42 – 43 °C

IR (Neat): 2954, 2914, 2859, 2344, 1471, 1432, 1384, 716 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 6H), 1.20 – 1.33 (m, 38H), 1.34 – 1.41 (m, 4H), 1.47 (p, J = 7.2 Hz, 4H), 2.13 (tt, J = 7.2, 2.0 Hz, 4H).

¹³C NMR (100 MHz, CDCl₃): δ 14.3, 18.9, 22.9, 29.0, 29.3, 29.5, 29.7, 29.8, 29.83, 29.85, 29.9, 32.1, 80.4. Sixteen peaks not observed due to overlap.
References


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    3067 – 3125.
57. Krause, N.; Hoffmann-Roder, A. in Modern Organocopper Chemistry, Ed:
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61. McGrath, M. J.; Fletcher, M. T.; König, W. A.; Moore, C. J.; Cribb, B. W.;
    58, 5417 – 5422.


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Appendix 1

IR spectra
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Scans: 32  
Resolution: 4.000
Appendix 2

$^1$H NMR’s
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Sample directory:
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Operator: users
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24 repetitions
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Total time 1862457 hr, 18 min

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5 2190.8 7.307 4.1
6 2057.7 2.020 5.2
7 2034.4 2.012 4.3
8 2163.3 1.560 10.6
9 2155.5 1.566 7.4
10 2120.3 1.442 5.0
11 2125.0 1.437 5.2
12 2118.6 1.379 7.5
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15 2029.8 0.533 24.7
16 2027.7 0.524 18.1
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STANDARD 1H OBSERVE

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Operator: users
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Total time 1042557 hr, 18 min

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Sample directory:
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Data collected on: Nov 4 2014
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4     | 553.2     | 1.259 | 139.5
5     | 252.8     | 0.497 | 9.5
6     | 352.1     | 0.800 | 26.3
7     | 345.1     | 0.883 | 11.1

9  8  7  6  5  4  3  2  1
ppm
$^{1}H$ NMR (400 MHz, ccdCl) 8 7.260, 3.939, 3.935, 3.923, 3.918, 3.907, 3.902, 3.541, 3.539, 3.409, 3.406, 3.379, 3.376, 2.429, 2.426, 2.424, 2.421, 1.851, 1.839, 1.806, 1.838, 1.739, 1.725, 1.722, 1.702, 1.685, 1.684, 1.657, 1.630, 1.605, 1.457, 1.441, 1.430, 1.427, 1.405, 1.276, 1.250, 1.128, 1.123, 1.119, 1.117, 1.104, 1.102, 1.090, 1.074, 1.061, 1.054, 1.050, 1.047, 0.892, 0.875, 0.858.
Thiol-heptadecan-1H

$^1$H NMR (400 MHz, c-dcl$_2$) δ 9.765, 9.760, 9.755, 7.259, 2.434, 2.429, 2.416, 2.411, 2.397,
2.393, 1.641, 1.623, 1.605, 1.586, 1.582, 1.568, 1.563, 1.332, 1.294, 1.231, 0.893, 0.879,
0.876, 0.868, 0.839, 0.853, 0.847.
TIPS-acetyleneheptadecanol-1H

^1H NMR (400 MHz, CDCl3) δ 7.260, 7.259, 4.386, 4.374, 2.351, 2.349, 1.772, 1.765, 1.740, 1.721, 1.701, 1.684, 1.666, 1.488, 1.471, 1.453, 1.431, 1.336, 1.317, 1.255, 1.219, 1.114, 1.108, 1.103, 1.091, 1.086, 1.074, 1.057, 1.052, 1.038, 1.028, 1.021, 1.014, 1.008, 0.996, 0.896, 0.889, 0.862, 0.097.
\text{H NMR (400 MHz, cdCl$_3$)} 8 7.260, 7.259, 5.296, 4.367, 4.353, 2.459, 2.457, 2.454, 2.452, 1.838, 1.827, 1.744, 1.737, 1.734, 1.727, 1.717, 1.713, 1.704, 1.696, 1.687, 1.679, 1.665, 1.470, 1.455, 1.444, 1.438, 1.417, 1.334, 1.298, 1.253, 1.221, 0.895, 0.879, 0.861.
16-bromo-1-OTHP-hexadecanol-1H

$^1$H NMR (400 MHz, cdc1) $^6$ 7.260, 7.247, 7.229, 7.176, 4.578, 4.571, 4.568, 4.560, 3.895, 3.837, 3.877, 3.868, 3.859, 3.849, 3.840, 3.752, 3.735, 3.728, 3.718, 3.711, 3.694, 3.620, 3.516, 3.513, 3.507, 3.504, 3.500, 3.494, 3.489, 3.482, 3.479, 3.476, 3.466, 3.417, 3.404, 3.390, 3.388, 3.382, 3.371, 3.364, 3.347, 2.349, 2.038, 1.883, 1.866, 1.859, 1.848, 1.829, 1.824, 1.811, 1.797, 1.786, 1.743, 1.736, 1.727, 1.711, 1.704, 1.695, 1.689, 1.682, 1.676, 1.623, 1.605, 1.587, 1.576, 1.568, 1.555, 1.531, 1.546, 1.537, 1.530, 1.523, 1.516, 1.513, 1.508, 1.502, 1.499, 1.495, 1.486, 1.470, 1.434, 1.416, 1.397, 1.380, 1.358, 1.345, 1.336, 1.271, 1.251, 1.220, 1.203, 1.185, 0.969, 0.953, 0.895, 0.878, 0.861, -0.005.
\[ \text{H NMR (400 MHz, c-dcl)} \delta 9.760, 9.765, 9.770, 7.267, 7.266, 7.266, 7.265, 7.264, 7.263, 7.262, 7.260, 7.259, 7.257, 7.256, 7.256, 7.255, 2.418, 2.413, 2.399, 2.395, 2.132, 2.147, 2.135, 2.122, 2.117, 1.627, 1.543, 1.542, 1.490, 1.471, 1.452, 1.378, 1.357, 1.343, 1.297, 1.263, 0.896, 0.879, 0.862, 0.812, 0.011, 0.008, 0.007, 0.006, 0.005, 0.004, 0.003, 0.002, 0.002, -0.002, -0.003, -0.004, -0.005, -0.005, -0.006, -0.007, -0.007, -0.009, -0.009, -0.010. \]
$^{1}H$ NMR (400 MHz, c,dcl) δ 7.260, 4.550, 4.540, 3.871, 3.865, 3.853, 3.845, 3.837, 3.827, 3.818, 3.735, 3.718, 3.711, 3.711, 3.701, 3.696, 3.694, 3.678, 3.677, 3.501, 3.489, 3.475, 3.461, 3.449, 3.397, 3.396, 3.380, 3.378, 3.369, 3.363, 3.361, 3.354, 3.353, 3.347, 3.345, 3.330, 3.229, 2.023, 2.020, 2.018, 1.847, 1.829, 1.812, 1.794, 1.779, 1.767, 1.750, 1.744, 1.736, 1.723, 1.716, 1.708, 1.691, 1.684, 1.694, 1.662, 1.588, 1.571, 1.556, 1.536, 1.520, 1.118, 1.512, 1.498, 1.485, 1.478, 1.442, 1.424, 1.406, 1.389, 1.373, 1.359, 1.316, 1.252, 1.243, 1.236, 1.234, 1.223, 1.221, 1.218, 1.216, 0.952, 0.951, 0.936, 0.934, 0.877, 0.862, 0.860, 0.843, 0.835, 0.833, -0.022, -0.023.
16-bromo-1-hexadecanol-1H

$^1$H NMR (400 MHz, c, d$_2$) δ 7.260, 3.644, 3.628, 3.611, 3.414, 3.397, 3.380, 1.880, 1.862, 1.844, 1.825, 1.808, 1.591, 1.574, 1.556, 1.538, 1.521, 1.430, 1.412, 1.394, 1.377, 1.355, 1.330, 1.307, 1.270, 1.251, 1.217, 1.199, 0.008.
$^1$H NMR (400 MHz, c-dcl$_2$) δ 7.265, 7.264, 7.264, 7.263, 7.262, 7.260, 7.259, 7.258, 7.257, 7.257, 7.256, 7.255, 7.255, 4.584, 4.578, 4.573, 4.566, 3.874, 3.757, 3.740, 3.733, 3.723, 3.716, 3.699, 3.513, 3.409, 3.394, 3.386, 3.377, 3.370, 3.353, 3.213, 2.153, 1.248, 2.136, 2.123, 2.118, 2.111, 1.717, 1.710, 1.686, 1.612, 1.591, 1.582, 1.573, 1.561, 1.557, 1.552, 1.537, 1.522, 1.515, 1.506, 1.491, 1.472, 1.454, 1.437, 1.358, 1.349, 1.341, 1.331, 1.265, 1.255, 1.073, 1.069, 1.063, 0.898, 0.881, 0.853, 0.069, 0.011, 0.010, 0.009, 0.008, 0.007, 0.007, 0.006, 0.005, 0.004, 0.004, 0.003, 0.002, 0.000, -0.001, -0.002, -0.003, -0.003, -0.004, -0.005, -0.005, -0.006, -0.007, -0.007, -0.008.
Appendix 3

$^{13}$C NMR’s
11-nonacosyne-13C

$^1$H NMR (101 MHz, c, d$_2$) 8 80.384, 77.475, 77.157, 76.840, 32.097, 32.089, 31.757,
29.875, 29.831, 29.831, 29.770, 29.747, 29.638, 29.555, 29.512, 29.511, 29.041,
27.065, 22.839, 18.928, 14.271.
Sample Name:

Data Collected on:
underwood990-vmcar
Archive directory:

Sample directory:

FidFile: CARSON

Pulse Sequence: CARSON (s2pul)

Sinewave: cdc13

Data collected on: Nov 4 2014

Temp. 25.0 C / 298.1 K
Operator: users

Relax. delay 0.001 sec
Pulse 45.0 degrees
Acq. time 1.000 sec
Width 25600.0 Hz
2500 repetitions

SOLVENT C13, 100.0000540 MHz
DECoupling H1, 299.393940 MHz
Power 43 dB

continuity on

WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz

FT size 324200

Total time 416362 hr, 24 min

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![Chemical Structure Image]
TIPS-acetyleneheptadecanol-13C

\[ ^{13} \text{C NMR (101 MHz, cdcl)} \] \( \delta \) 188.262, 104.376, 95.519, 77.472, 77.154, 76.836, 45.809, 32.081, 29.845, 29.823, 29.810, 29.803, 29.745, 29.577, 29.513, 29.497, 29.133, 24.471, 22.847, 18.834, 18.802, 14.268, 11.170, 11.150.
Sample Name:

Data Collected on:

Archive directory:

Sample directory:

File: CARSON

Pulse Sequence: CARSON (e2pul)

Data collected on: May 31, 2014

Temp. 25.0 C / 298.1K

Operator: users

Relax. delay 0.001 sec

Pulse 45.0 degrees

Acq. time 5.508 sec

Width 25000.0 Hz

2018 repetitions

DECOUPLING O1, 50.5529 MHz

DECOUPLING H1, 399.99408 MHz

Power 40 dB

CONTINUOUSLY ON

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

F1 size 524288

Total time 410962 hr, 34 min

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8-thiotetrazolyl-1-tetrahydropyranyloxycane-13C

48
$^{13}$C NMR (101 MHz, cdeo) δ 174.332, 77.304, 77.136, 77.148, 76.986, 76.669, 76.544, 63.100, 51.418, 34.110, 32.807, 29.612, 29.598, 29.582, 29.559, 29.420, 29.410, 29.234, 29.136, 25.720, 24.948, -0.024.
$\text{TB-2-3-1_13C} \hspace{1cm} $ \\
1,16-hexadecanediol-13C
$^{13}$C NMR (101 MHz, cddab) δ 77.474, 77.361, 77.156, 76.839, 63.264, 32.972, 29.780,
29.748, 29.724, 29.577, 25.388, 0.146.
16-bromo-1-hexadecanol 13C

$^{13}$C NMR (101 MHz, cde) δ 77.474, 77.156, 76.838, 73.198, 34.176, 32.978, 32.939, 29.774, 29.741, 29.724, 29.568, 29.568, 28.900, 28.312, 25.876.
17-octacosyn-1-ol-13C

$^{13}$C NMR (101 MHz, cdc$_5$) δ 80.394, 77.473, 77.156, 76.838, 63.255, 32.971, 32.070, 29.830, 29.813, 29.794, 29.770, 29.726, 29.747, 29.725, 29.590, 29.492, 29.332, 29.025, 25.394, 22.840, 18.916, 14.265.
12-nonacosyne-13C

13-noracetyl-13C

$^1$H NMR (101 MHz, CDCl$_3$) δ 80.382, 77.473, 77.155, 76.838, 76.092, 29.858, 29.851, 29.823, 29.809, 29.742, 29.530, 29.344, 29.033, 22.833, 18.924, 14.267.

$^1$H NMR (101 MHz, CDCl$_3$) δ 80.382, 77.473, 77.155, 76.838, 76.092, 29.858, 29.851, 29.823, 29.809, 29.742, 29.530, 29.344, 29.033, 22.833, 18.924, 14.267.
Vitae

Candidate’s Full Name: Thalie Renée Boucher

Universities Attended: University of New Brunswick, Chemistry

Master of Science candidate (2011 - 2014)


Conference Presentations:

Unusual Homologous Allenes from the parasitic wasp Wroughtonia occidentalis (Hymenoptera: Brachonidae), a native parasitoid of the exotic longhorned beetle, Tetropium fuscum (Coleoptera Cerambycidae);
Structure, Synthesis and Stereochemistry. SERG-I meeting, Quebec, QC. 2012.

Unusual Homologous Allenes from the parasitic wasp Wroughtonia occidentalis (Hymenoptera: Brachonidae), a native parasitoid of the exotic longhorned beetle, Tetropium fuscum (Coleoptera Cerambycidae);