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Investigations into the Synthetic Modifications of Terpenes for the Synthesis of Renewable Polyesters

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'I may not have gone where I intended to go, but I think I have ended up where I intended to be' – Douglas Adams

ABSTRACT

This thesis details the synthesis of four novel terpene-derived monomers *via* the derivatisation of α-pinene and limonene (two of the most abundant terpenes). The monomers have been used in the synthesis of sustainable polyesters, which all contain a unique cyclohexane ring in their backbone.

The functionalisation of limonene has enabled the synthesis of two renewably-sourced monomers for the formation of terpene derived polyesters. Three methods for the synthesis of a novel hydroxy-acid are reported and their green-credentials scrutinised through comparison of their sustainability-metrics. Step-growth homo-polymerisation of the hydroxy-acid is demonstrated to yield a low molecular weight novel polyester with 100% of its carbon content originating from the terpene starting material. The corresponding limonene diol is shown to act as a co-monomer with a renewable diacid. The resultant polyesters display impressive M_ns of up to 30 kDa with T_gs between -6 and 24 ^oC. The degradation of these materials were shown to allow recyclability of the diol monomer.

α-Pinene was used for the synthesis of two polyols, which served as comonomers with a renewable diacid, enabling the synthesis of two novel polyesters with high T_gs. The corresponding enantiomers of the α-pinene derived polymers were blended to form stereocomplexes, leading to improved thermal properties of the polyester.

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Finally, I would like to acknowledge my friends and family outside of chemistry, for their love and encouragement throughout my PhD.

ABBREVIATIONS

ATR – Attenuated Total Reflectance

BAIB- Bis-acetoxyiodobenzene

COSY – Correlation Spectroscopy

Đ – Dispersity Index

Da – Daltons

DA – Diels Alder

DCM- Dichloromethane

DFT- Density Functional Theory

DSC – Differential Scanning Calorimetry

DMA – Dynamic Mechanical Analysis

ESI – Electrospray Ionisation

FA – Furfuryl Alcohol

FRP – Free Radical Polymerisation

FTIR – Fourier Transform Infrared Spectroscopy

GPC- Gel Permeation Chromatography

HSQC-Heteronuclear single quantum correlation

HMF – Hydroxymethyl Fufural

HMQC – Heteronuclear Multiple Quantum Correlation

HSQC-Heteronuclear single quantum correlation

KTA – Kilotonnes per annum

MALDI - TOF – Matrix Assisted Laser Desorption Ionisation Time of Flight

MAO-methylaluminoxane

*m*CPBA – *meta*-chloroperoxybenzoic acid

M_n – Number average molecular weight

M_w – Weight average molecular weight

NCS- *N*-chlorosuccinimide

NMI- *N*-methylimidazole

NMO- *N*-Methylmorpholine *N*-oxide

PDI – Polydispersity Index

PET – Polyethylene Terephthalate

PLA – Poly(Lactic Acid)

ROP – Ring Opening Polymerisation

$scCO_2$ – Supercritical Carbon Dioxide

SEC – Size Exclusion Chromatography

TBD – Triazabicyclodecene

TCNE - Tetracyanoethylene

TEMPO- 2,2,6,6-Tetramethyl-1-piperidinyloxy

T_g – Glass Transition Temperature

TPAP- Tetra-*n*-propylammonium perruthenate

XRD – X-Ray diffraction

TABLE OF CONTENTS

ABSTRACT ..... **ii**

ACKNOLEDGEMENTS ..... **iii**

ABBREVIATIONS ..... **iv**

1. Introduction to Sustainable Polymers **1**
1.1. Monomers from Biomass **3**

2. Direct Polymerisation of Terpenes **7**
2.1. β-Pinene (11) **7**
2.1.1. Homopolymers of β-pinene (10) 8
2.1.2. Copolymers of β-pinene (10) with synthetic monomers 13
2.2. Homopolymers of α-pinene (11) **13**
2.3. Polymers from other terpenes **15**
2.3.1. Limonene (6) 15
2.3.2. Myrcene (8) 17

3. Polymers from functionalised terpenes **18**
3.1. Limonene (6) **18**
3.2. Myrcene (8) **20**
3.3. Carvone (42) and Menthol (49) **21**
3.4. Pinenes **25**
3.5. Rosin Acids **31**

4. Conclusions and Outlook **34**

5. Introduction to Polymerisations **36**
5.1. Step-Growth Polymerisation **37**
5.2. Chain-Growth Polymerisation **38**

Chapter 1- Investigations into the Synthesis of Limonene Derived Monomers for Studies into Step-Growth Polymerisation **40**

1. Introduction **40**
1.1. Limonene (6) as a Waste Stream **40**
1.2. Step Growth Terpene Polymers **40**

2. Aims and Objectives **44**

3. Results and discussion **46**
3.1. Synthesis of Limonene Derived Hydroxy-Acid (105) **46**
3.1.1. Synthesis of limonene diol intermediate 104 47
3.1.2. Investigations into the Optimal Synthesis of Hydroxy-Acid 105 53
3.2. Polymerisation Studies of Hydroxy-Acid 105 ..... **64**
3.3. Polymerisation of the Limonene Derived Lactone 111 ..... **69**
3.3.1. DFT Studies of the Lactone 111 70
3.3.2. Investigations into the ROP of 111 71
3.1.1. Initiation and Propagation studies of 111 73
3.2. Conclusions from the Synthesis and Polymerisation of 111 ..... **76**
3.3. Towards the Synthesis of a Limonene Derived Hydroxy-Ester **76**

3.4. Synthesis of Polymers from Limonene Diol (104) 81
3.4.1. Investigations into the synthesis of polymers 127 and 128 using solution polycondensation 82
3.4.2. Investigations into the synthesis of polymer 127 using melt polycondensation 88
3.5. Investigations into the Degradation of Polymer 127 92

4. Conclusions 98

5. Experimental 100
5.1. General Experimental 100
5.2. Experimental Procedures for Monomer Synthesis 102
5.3. Experimenal Procedures for Polymer Synthesis 112

Chapter 2 – Investigations into the Synthesis and Polymerisation of Monomers Derived from α-Pinene 115

1. Introduction 115
1.1. The chemistry of α-pinene oxide (129) 116

2. Aims and Objectives 121

3. Results and Discussion 122
3.1. Towards the Functionalisation of α-Pinene Oxide (129) 122
3.1.1. Towards the Synthesis of Monomers for Homopolymerisation 122
3.1.2. Optimisation of the Synthesis of *trans*-Sobrerol (136) for Copolymerisation 132
3.1.3. Attempted Polymerisation of trans-Sobrerol (136) with a Comonomer 138
3.2. Synthesis of *trans*-Sobrerol derived diols for copolymerisation 141
3.2.1. Synthesis of Monomers 141
3.2.2. Polymerisations of triol 161 and tetraol 162 148
3.3. Investigations into the Stereocomplexation of Polymer 165 152

4. Conclusions 158

CONCLUSIONS 160

5. Experimental 162
5.1. General Experimental 162
5.2. Synthesis of Compounds 163
5.3. Synthesis of Polymers 169

REFERENCES 171

1. Introduction to Sustainable Polymers

If the consumption of fossil fuels by our society continues at the current rate, our oil feedstocks will be expended within the next century. This, combined with the associated environmental issues around global warming and environmental pollution has resulted in a drive for scientific research to alleviate the dependence of our society on polymers and plastics derived from fossil fuels.[1] The utilisation of fossil fuels in the manufacture of plastics currently accounts for approximately 7% of worldwide oil and gas usage and is likely to strongly increase.[2] Moreover, a recent report clearly demonstrates that polymer wastes are increasing and by 2050 we may have more polymer waste than fish in our oceans.[3] Some of these issues can be addressed through the synthesis of polymers from renewable resources, and also by targeting materials that are naturally degradable into environmentally benign molecules. However, of the 300 million tonnes of plastics produced annually worldwide, renewable polymers contribute less than 1%.[1,4] The key reasons absenting renewable polymers from the commercial market are their high cost, and the relatively poor properties of the materials compared to their petrochemical equivalents.[5–7]

Renewable raw materials have the potential to provide a wide range of monomers arguably as comprehensive as those provided by the petrochemical industry.[8] The increase in academic research, and recently, industrial attention are likely to ensure that society starts to utilise renewable chemicals for the production of plastics.[9,10] As mentioned above the renewable polymers currently on the market cannot compete with petroleum based plastics, and this will not change until the technology is developed further. These advances will require development of novel and truly sustainable polymers, and to achieve all of this, full integration of other essential disciplines is necessary.[11,12]

However, it is important to remember that sustainable polymers are relatively new when compared to petroleum based plastics. The high performance of plastics derived from fossil fuels is the outcome of many years of intensive research and commercial

scale optimisation. This will come for the next generation of renewably derived polymers, but will require significant and concerted academic and industrial research in the coming decades.[12]

The synthesis of macromolecules from natural sources is not a new idea. In fact, this area of research was the focus of pioneering explorations in polymer science.[13] However, these studies fell out of favour as the development of oil based synthetic chemicals grew. Only recently, in the light of environmental concerns, the recognition of our finite oil resource, and the need to utilise society's waste streams has there been a renaissance of research towards synthesis of sustainably produced polymers. This is emphasised and highlighted in the increased number of reviews published recently in this area. [1,8, 14,15]

In recent years considerable research has been devoted to finding renewable monomers for the synthesis of sustainable polymers. These include both new materials entirely derived from renewable feedstocks, and those that combine petroleum based and renewable monomers.[16] In order to successfully shift to sustainable alternatives, the chemical industry must develop both existing and new low cost polymers which, as a minimum are able to compete with current petroleum based plastics on price and more importantly on performance.

A high proportion of the plastics used today accumulate in landfill where they are bulky and pervasive. Polymers from renewable recourses are not inherently biodegradable, however it is now imperative that society considers carefully the end of life issue of our plastics. Since we cannot exist without them, we have to learn to live with the consequences of plastics in our society. New materials are currently being developed to be more easily recycled, degraded to useable by-products or safely incinerated to recover their embedded energy.[17,18]

1.1. Monomers from Biomass

Plant biomass is a major potential sustainable source of organic carbon.[19] Biomass-based processes that could replace crude oil could harness enzymatic methods, microbiology, and metabolic engineering to direct the transformation of sugars, lipids, and other biomass-derived molecules to the desired monomers. Monomers derived from biomass can be divided into three categories based on hydrogen, carbon, and oxygen compositions (**Figure 1**).[7]

1. Oxygen-rich molecular biomass with a molar ratio of C/O less than an arbitrary number 5.0,(carboxylic acids, polyols, dianhydroalditols, and furans).
2. Hydrocarbon-rich molecular biomass with the ratio of C/O larger than 5.0, (vegetable oils, fatty acids, terpenes, terpenoids, and resin acid).
3. Hydrocarbon molecular biomass with no oxygen (bioethene, biopropene, and bioisoprene).

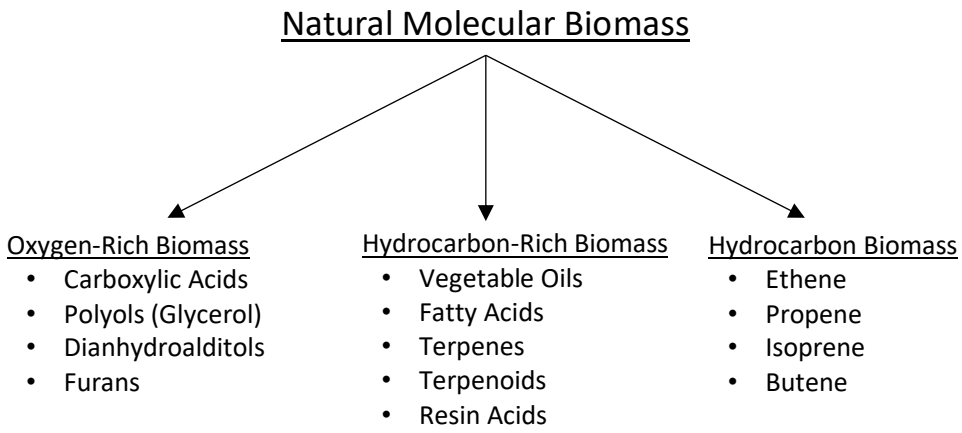


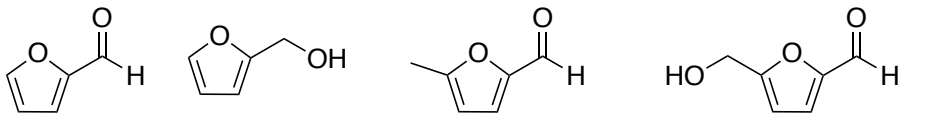
***Figure 1**: Categories of natural molecular biomass.*[7]

It is also important to mention opportunities around non-hydrocarbon molecular biomass. A very obvious example is carbon dioxide, which has the potential to be used as both a monomer,[20] and as a solvent for the sustainable synthesis of polymers.[21]

Using the renewable monomers mentioned above, there is now a plethora of polymers which can be synthesised from biomass. These polymers make use of many methods of polymerisation, such as free radical, ring opening, condensation and many other innovative approaches to produce polymers with a range of properties and sustainable characteristics.

Probably the most familiar renewable monomer is lactic acid for the synthesis of poly(lactic acid) (PLA).[22] PLA has received significant commercial attention as it displays suitable properties to replace polyolefins as well as potentially offering sustainability benefits over petrochemical based polymers.[23–26] A major drawback of PLA is the need for high quality land to grow the corn needed to extract the starch. In the future there will be a need to move away from such feedstocks, for example the use of waste CO_2 as an alternate carbon source .[27]

Furans are another group of monomers predominantly obtained from polysaccharides or sugars and encompass molecules such as furfural (**1**), furfuryl alcohol (**2**), 5-methyfurfural (**3**) and 5-hydroxymethylfurfural (HMF) (**4**) (**Figure 2**).[28] These are well developed monomers which can be used directly in step growth polymerisation or can participate in Diels-Alder reactions to introduce new functional groups into the polymer. [29–32] Furfural (**1**) and its derivatives are a particularly rich source of potential renewable monomers. Moreover, the fact that these can be produced directly from waste biomass is extremely attractive since this overcomes important ethical issues surrounding food *vs* fuel. Because of high production costs, **3** is not yet a high-volume chemical and the potential uses of HMF-derived compounds have currently not been fully exploited.[33] Vegetable oils and fatty acids also represent a large area of opportunity in new sustainable polymers.[34,35]



Furfural | Furfural Alcohol | 5-Methyl Furfural | 5-Hydroxymethyl Furfural

1 | **2** | **3** | **4**

Figure 2: *Furfural and some common derivatives.*

Within the category of hydrocarbon rich biomass are terpenes and terpenoids, and these represent a vast range of molecules which are of great interest to polymer science. The many desirable properties of terpenes have recently made them very attractive for polymer research and this is highlighted by reviews which have been published within the past five years.[14,36]

This review will focus on the use of monoterpenes and resin acids as monomers for the synthesis of renewable, thermoplastic polymers. Initial attempts at polymerising the most abundant terpenes (**6**, **10** and **11)** concentrated on using their olefinic moieties for free radical or cationic polymerisation. Although this method showed some success,[37] the data was not compelling and recently attention has shifted to perform synthetic modifications to the terpenes in order to synthesise a terpene based molecule which can more easily undergo polymerisation. This process has been substantially aided by the corresponding advances in sustainable synthetic methodologies that have enabled prefunctionalisation of terpenes in polymer chemistry. This aspect will be covered at length in this chapter.

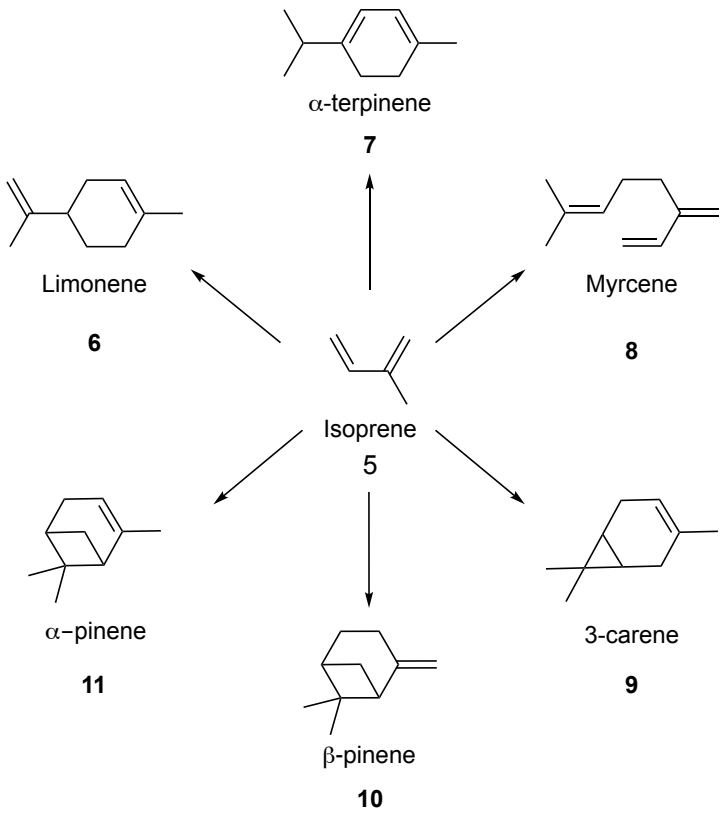


***Figure 3**: Some common monoterpenes.*

Terpenes, terpenoids and resin acids are a group of non-polar molecules and share a building block, isoprene (**5**), as a common elementary unit (**Figure 3**). The most common terpenes contain two isoprene units and are known as monoterpenes, these are typically produced biosynthetically by many classes of trees and plants.[38] This class of molecules is grouped under hydrocarbon rich biomass, and contains a vast family of naturally occurring compounds which show enormous structural diversity (**Figure 3**). Some common terpenes are limonene (**6**), α-terpinene (**7**), myrcene (**8**), 3-carene (**9**), α-pinene (**11**) and β-pinene (**10**) (**Figure 3**). Terpenes are abundant, inexpensive and do not directly compete with food sources, and are therefore ideal small molecule building blocks for many applications.[38] These hydrocarbon based molecules usually contain one or more carbon-carbon double bonds and have a general formula $C_{10}H_{16}$. Turpentine is the volatile fraction isolated from pine resin and is produced on a scale of 330 kilotonnes per annum (KTA).[39]

The composition of turpentine is dependent on the age and species of the tree, among other factors. However, the major components are **11** (45-97%), **10** (0.5-28%) and smaller amounts of other monoterpenes.[40] This class of molecules can easily interconvert to give a number of basic monoterpene skeletons starting from many precursors.[41] Monoterpenes are particularly diverse structurally due to the presence of numerous stereogenic centres, but also because of the many oxygenated compounds which can easily be generated from the basic skeletons.[38] Despite the vast range of terpenes available, α-pinene (**11**), β-pinene (**10**), myrcene (**8**) and limonene (**6**) are the most widely studied for polymerisation applications. This is because of their high abundance, low cost and ease of isolation and these terpenes will be the main focus of this review.

2. Direct Polymerisation of Terpenes

Owing to the exo- and endocyclic carbon-carbon double bonds possessed by many of the terpenes, initial research focused upon polymerisation of terpenes *via* their double bonds through radical or cationic polymerisation.[37,42] These processes include the homopolymerisation of terpenes and also their copolymerisation with other synthetic monomers such as styrene. This section will highlight the direct polymerisation of terpenes through their carbon-carbon double bonds.

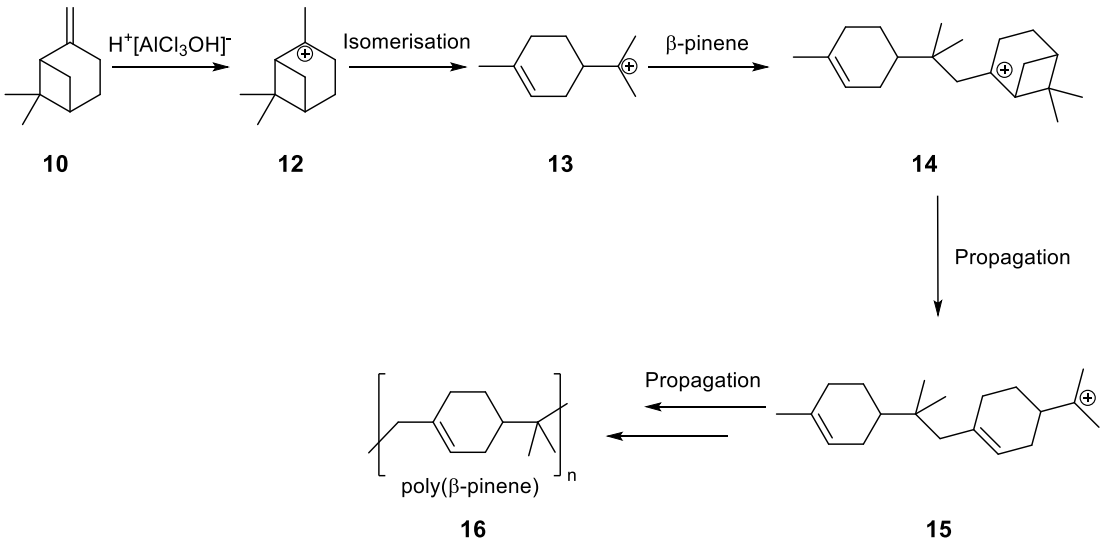
2.1. β-Pinene (11)

Pinenes are the most abundant of the terpenes and are isolated using steam distillation of resinous sap obtained from pine or conifer trees.[38] Perhaps the earliest evidence of the polymerisation of the pinenes was in 1937, however the paper did not report molecular weights and it was not specified which isomer of pinene was used.[43] Early research on terpene polymerisation was largely focused on β-pinene because it was abundantly available from pine trees. β-pinene (**10**) has two alkyl groups on its exocyclic double bond, these have an electron donating effect, thus stabilising carbenium ion **12.** This stabilisation effect combined with the sterically accessible

exocyclic double bond in **10** results in β-pinene (**10**) readily undergoing cationic polymerisation.[44]

2.1.1. Homopolymers of β-pinene (10)

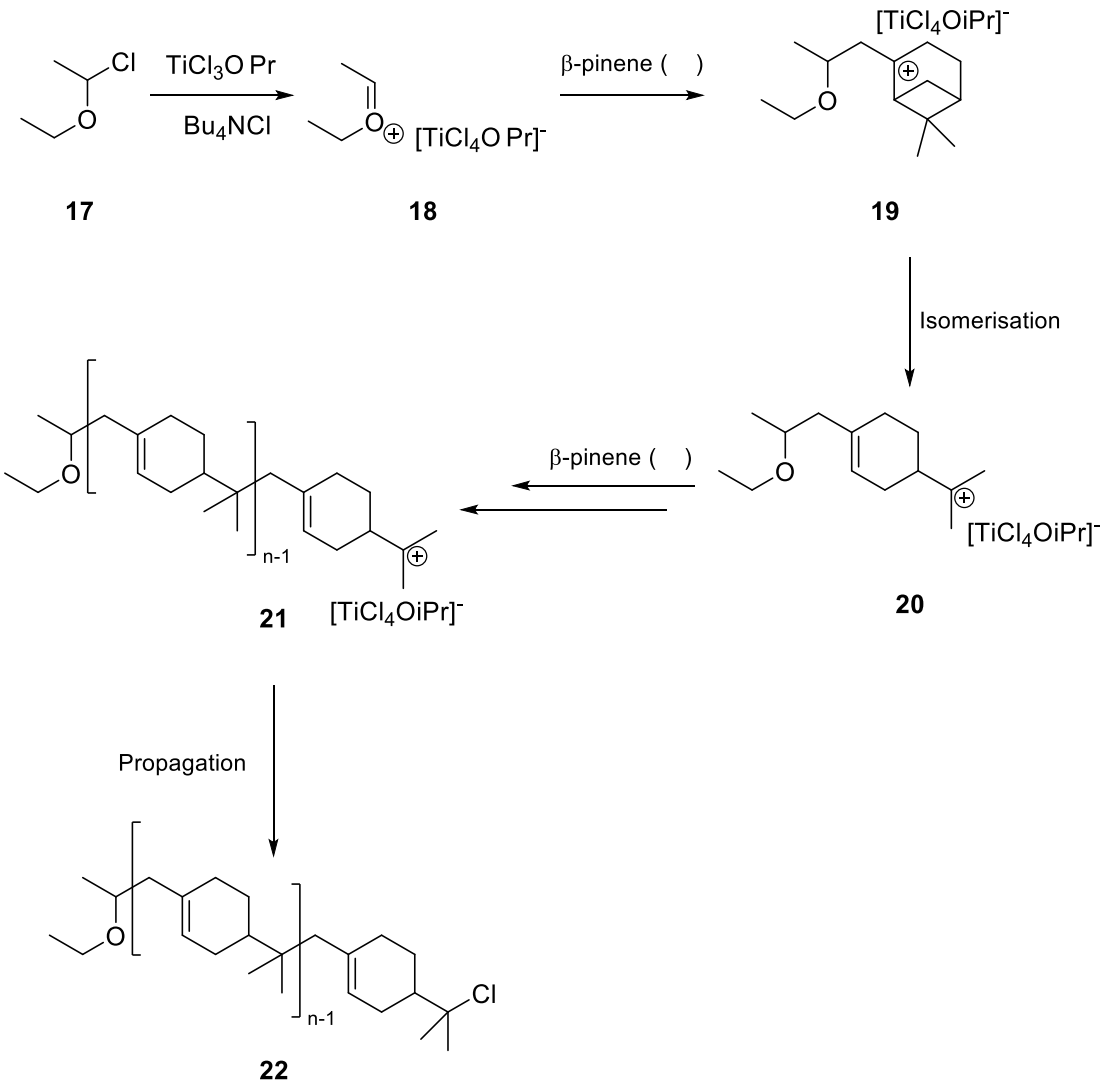
The first study of the cationic homopolymerisation of β-pinene (**10**) to give homopolymers was carried out in 1950 by Roberts *et al*. under Friedel-Crafts conditions (**Scheme 1**).[37]



Scheme 1: *The cationic polymerisation of β–pinene.*[37]

The polymerisation of **10** using $AlCl_3$ as a catalyst was found to be fast and very exothermic, yielding a solid polymer with relatively low molecular weight (M_n) *ca.* 2 kDa. This reaction is driven by the high reactivity of the *exo*-methylene double bond, the breaking of the highly strained fused cyclobutane ring and the formation of the relatively stable *para*-menthene carbenium ion **13**. The mechanism for the cationic polymerisation of **10** utilises aluminium trichloride as a Lewis acid (**Scheme 1**). Aluminium trichloride reacts with water to form a strong proton donor which subsequently protonates the double bond of **10**, the carbenium ion **12** then rearranges to form a *para*-menthene type carbenium ion **13** responsible for the propagation reaction.

Conventional cationic polymerisations have shown that it is possible to homopolymerise β-pinene (**10**). However, the molecular weights obtained are only low to moderate and have a very broad distribution of molecular weights.



***Scheme 2**: The living cationic polymerisation of β–pinene (**10**)*[45–47]

The first example of a living cationic polymerisation of **10** was carried out by Lu *et al.* in 1997 to give **22** with a narrow dispersity (Đ) (*ca.* 1.3).[46,45] The controlled living polymerisation of **10** was carried out using combinations of α-chlorodiethyl ether as an initiator and [$TiCl_3(O^iPr)$] as an activator in the presence of ($^nBu_4NCl$) (**Scheme 2**). The optimal results were achieved using the above conditions in dichloromethane at

temperatures in the range -40 °C to -78 °C, yielding **22,** with again relatively low molecular weight *ca.* 5 kDa, with narrow dispersity Đ *ca.* 1.1-1.2 and high conversion. The living nature of this system was confirmed by the linear increase of M_n with monomer conversion.[45–47]

Cationic polymerisation using Lewis acid catalysts such as $AlCl_3$ and $ZnCl_2$ produced homopolymers of **10** with relatively low molecular weights ($M_n \leq 1$ kDa).[37] The cationic method has limitations. To obtain polymers with high molecular weights the polymerisation must be carried out at low temperatures (-40 °C to -78 °C) in order to minimise the relative kinetic contribution of the transfer reaction with respect to chain propagation. Even at low temperatures, the molecular weights of **16** obtained were relatively low, and a high concentration of Lewis acid was needed for a satisfactory conversion.

To try and combat the issues commonly associated with cationic polymerisation Lu *et al.* synthesised a Schiff-base nickel catalyst **23** (**Figure 4**).[48]

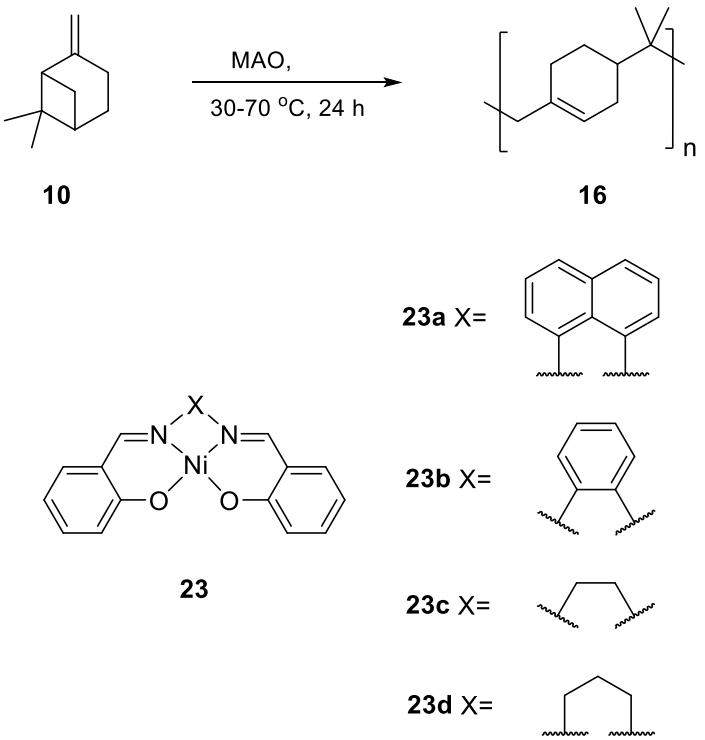
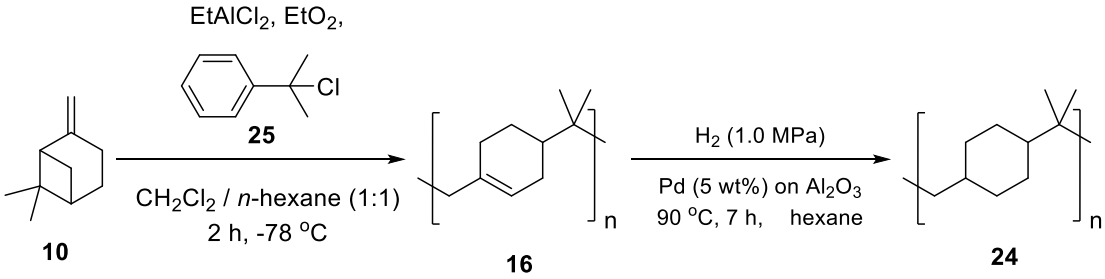


***Figure 4**: Schiff base nickel catalyst **23**[48]*

Single site late transition metal-based catalysts are more tolerant than Lewis acids, of functional monomers and are less oxophilic. Their single site nature enables ligand tailoring resulting in a system which can be modified in numerous ways to tune the polymerisation process. Nickel and palladium based catalysts are often chosen for the polymerisation of α-olefins but, nickel is more desirable because of the high cost and low abundance of palladium.[49]

The nickel catalyst alone could not polymerise β-pinene (**10**). However upon addition of an activator, methylaluminoxane (MAO), the catalyst **23** showed very high activity. Using this catalytic system at 40 °C, polymers with a molecular weight M_n = 11 kDa and a Đ of 1.70 were obtained. The ratio of MAO to nickel complex **23** determined the rate of polymerisation, and the molecular weight of polymers. Four ligands were synthesised to produce complexes **23a-d** and investigated for catalytic activity (**Figure 4**). It was observed that the less rigid aliphatic ligands (complexes **23c** and **23d)** were preferred, suggesting that a more open active site facilitates coordination of the bulky β-pinene (**10**) molecule. This catalyst is a key example of production of high molecular weight poly(β-pinene) (**16**) at temperatures above 0 °C with extremely high productivity, up to 1.25 x10^7 g of **16** / mol of **23c** or **23d**, and these conditions could be utilised on an industrial scale.

More recently Kamigaito and co-workers reported the synthesis of a high molecular weight hydrogenated poly(β-pinene) (**16**) which showed some interesting and useful properties.[50,51] Polymers with high molecular weights M_n > 40 kDa and M_w *ca.* 100 kDa were achieved using $EtAlCl_2/Et_2O$ in a solvent mixture of CH_2Cl_2 and *n*-hexane and a halide **25** as the initiator. The olefinic groups of **16** were then hydrogenated using various catalysts. The optimal conditions for the hydrogenation were found to be using *n*-hexane under molecular hydrogen at 1 MPa pressure with a Pd/Al_2O_3 species as a catalyst, inducing >99 % conversion of the double bonds (**Scheme 3**).



Scheme 3: *Hydrogenation of poly(β-pinene) (**16**).*[51]

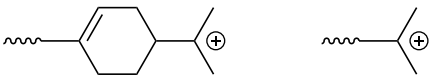
The hydrogenation of high molecular weight **16** was carried out in an attempt to improve the thermal resistance, durability and optical properties. The increase of the molecular weight resulted in **16** possessing mechanical strength comparable to other commercial polymers and displayed a flexural strength high enough to be classed as a plastic material. This is most likely a consequence of the chair conformation of the less-strained cyclohexane ring in the main chain. This is an example of post modification of polymers derived directly from terpenes in order to improve their properties.

In order to overcome the problems encountered during low temperature polymerisation of β-pinene (**10**), Kukhta *et al.* investigated the use of $AlCl_3$ etherates for the room temperature polymerisation.[52] Using an initiating system of $H_2O/AlCl_3OPh_2$ **16** was synthesised at room temperature with molecular weight in the range of 9-14 kDa and a T_g of 82-87 °C. This research demonstrates that it is possible to produce homopolymers of β-pinene (**10**) using ambient temperatures and catalyst systems which are inexpensive and commercially available.

The discussed work has established the potential to synthesise polymers based on **10** and other renewable feedstocks with properties at least equalling current commercially available plastics. For these polymers to become economically viable, more work is certainly needed to create, cheaper, green and sustainable routes to the synthesis of both the polymers and their monomers.

2.1.2. Copolymers of β-pinene (10) with synthetic monomers

A number of copolymers of β–pinene (**10**) and synthetic monomers such as styrene have been synthesised and studied. The incorporation of well-studied synthetic monomers into poly(β–pinene) (**16**) allows tuning of the properties of the resultant polymer, [42,53,54] such as preparation of a random copolymer of **10** and isobutylene [55] which used a common initiating system. Additionally a 1-phenylethyl chloride with a $TiCl_4/Ti(OiPr)_4/nBuN_4Cl$ system was used in dichloromethane at −40 °C.[46] β-pinene (**10**) and isobutylene have similar propagating cationic structures (**Figure 5**) and therefore their reactivity was predicted to yield a random copolymer.



13 **26**

Figure 5: *Propagting species of β–pinene (**10**) and isobutene*

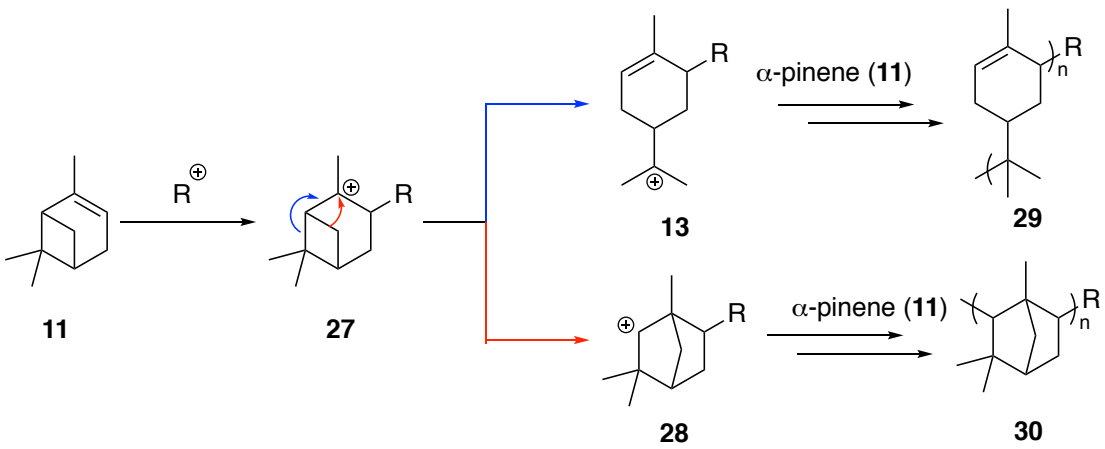
Both monomers were consumed at comparable rates, suggesting similar cationic polymerisation reactivity of the two monomers and therefore the formation of random co-polymers under the above conditions. The polymerisation progressed in a controlled manner, yielding high molecular weight polymers (M_n *ca.* 25 kDa) with $Đ < 1.2$. The increase of the β-pinene (**10**) fraction, which offers rigidity to resultant polymers, from 10% to 30%, increased the T_g of final polymers by 60 °C. This clearly demonstrates that the properties of polymers containing **10** can be tuned by introducing specific amounts of synthetic monomer to the feed.

2.2. Homopolymers of α-pinene (11)

α-Pinene (**11**) is the most abundant turpentine component and this has led to numerous attempts of the cationic polymerisation of this compound. The polymerisation of **11** has not been as successful as β–pinene (**10**) largely because of the lack of a reactive *exo*cyclic double bond. The sterically shielded endocyclic double

bond in **11** is obstructed and consequently chain propagation is slowed.[56] However, **11** is readily protonated and can form a tertiary carbenium ion **27** (**Scheme 4**) , but the attack of the endocyclic double bond to the isopropenyl cationic site is limited by steric hindrance.

The first polymerisation of **11** was reported in 1950 by Roberts *et al.* and used a Lewis acid to promote the cationic polymerisation.[37] The process was found to be very low yielding (*ca.* 35%), this low conversion was improved by using elevated temperatures, (up to 40 °C), but only resulted in oligomers of **11**. There are two proposed methods for the mechanism of polymerisation of α-pinene, one involves the same *para*-menthene intermediate, **13**, as obtained in the β–pinene (**10**) polymerisation. The second involves the rearrangement of the tertiary pinene carbenium ion **27** to a saturated secondary bornane isomer **28** (**Scheme 4**).[44] The main chain of poly(α-pinene) consists of two different repeating units, one of which is similar to that of poly(β–pinene) (**29**), the other is a norbornane-like structure **30** (**Scheme 4**).



Scheme 4: *The two proposed mechanisms of polymerisation of α-pinene (**11**)*

Despite the lack of reactivity exhibited by **11**, a considerable amount of research has been devoted to the cationic polymerisation because α-pinene (**11**) is the most naturally abundant terpene, as previously mentioned. Initial attempts at the

polymerisation using traditional Lewis acid catalysts proved to be ineffective. However, many groups have successfully produced homopolymers of **11** by combining Lewis acids with $SbCl_3$ as an activator.[57–59] The cocatalytic effect of the $SbCl_3$ is a result of the stabilisation of the growing carbenium ion, which favours the formation of polyterpenes. The polymerisation of **11** was carried out in toluene at -15 °C using an $AlCl_3/SnCl_3$ system to produce poly(α-pinene) (**29**) with M_n = 1.1-1.6 kDa. These conditions produced a negligible proportion of dimers compared to when $AlCl_3$ was used without the presence of $SbCl_3$.

The polymerisation of **10** was also investigated using these conditions, and interestingly it was found that $SbCl_3$ actually inhibited the polymerisation rate and resulted in a poorer molecular weight distribution.[44,56] Other attempts at the polymerisation of α-pinene (**11**) include the hydrothermal deposit of $AlCl_3$ onto a zirconium mesoporous material and the use of the resultant solid Lewis acid as a catalyst.[60]

Despite the many attempts at polymerisation of α-pinene, most studies have been less than successful, yielding only oligomers. This suggests that even though α-pinene is an abundant, cheap and renewable resource it does not have the required reactivity to be utilised as a renewable monomer, for homopolymerisation.

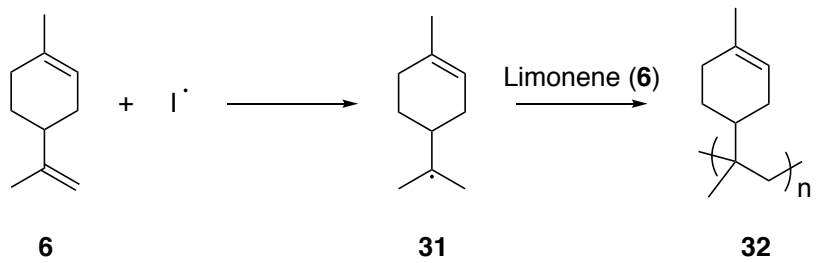
2.3. Polymers from other terpenes

2.3.1. Limonene (6)

Limonene (**6**) containins both chiral centres and carbon-carbon double bonds. The (*R*)-enantiomer is produced on a scale of over 70 KTA as a by-product of the citrus industry.[61] and the molecule is present in more than 300 plants.[62] The polymerisation of **6** was first carried out by Roberts and Day using Frieldel-Crafts conditions; early attempts were only capable of producing low molecular weight polymers.[37] The cationic polymerisation of limonene (**6**) using $AlCl_3$ as a catalyst was studied by Brum *et al.*[63] The poly(limonene) (**32**) produced had a very low molecular weight (*ca.* 0.5 kDa) and low conversions of only 7% were achieved, this is likely attributed to

chain termination *via* β-elimination. Satoh *et al.* were able to synthesise a copolymer of limonene and malemide *via* radical polymerisation.[64] When the polymerisatation was carried out in a fluroalcohol the polymer spontaneously formed an almost complete 1:2 sequence regulated polymer, thought to be due to the bulky structure of limonene.[65] The rigid cyclic structures of the monomer resulted in a polymer with a very high T_g *ca.* 220-250 °C, this highly ordered polymer could be used to mimic natural polymers. This material has good structural order and thermal properties however, within the repeating unit of the polymer only a third is composed of a terpene based monomer.

Recently, a study reported the radical homopolymerisation of **6** using benzoyl peroxide as an initiator at 85 °C in xylene (**Scheme 5**).[66] Only low conversions were achieved and the resultant polylimonene displayed a glass transition temperature (T_g) of 116 °C. This research indicates that it is perhaps possible to produce high molecular weight homopolymers of **6** through radical polymerisation, but more research is needed to improve the low conversions. Moreover, this research is contradictory to what has been reported previously regarding the radical polymerisation of limonene, and Indeed, **6** has been shown to act as a chain transfer agent for radical polymerisations hence producing very low M_w polymers.[67,68]

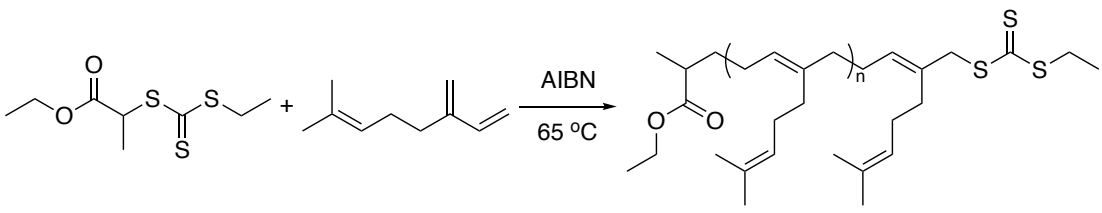


Scheme 5: *The radical polymerisation of* ***6*** *using benzoyl peroxide as an initiator*[66]

New methods to utilise limonene (**6**) in polymer chemistry are clearly required since it is such an abundant waste stream.[69,70]

2.3.2. Myrcene (8)

Myrcene (**8**) is a basic monoterpene that can be readily obtained from the essential oils of plants or from the pyrolysis of pinene.[71] Myrcene (**8**) has three double bonds meaning that there is the possibility for radical or cationic polymerisation at three sites. Myrcene can be functionalised through its double bonds leading to polymers with a range of applications. It was shown by Sarkar *et al.* that **8** can be polymerised through an environmentally benign emulsion polymerisation method.[72] The mild conditions (70 °C for 20 h) yielded polymers of 92 kDa with a T_g of -73 °C. The polymers displayed properties such as a low T_g, and thermal stability makes this polymer a good candidate for biobased elastomers. More recently Kali and co-workers have synthesised polymyrcene using a solvent free controlled radical polymerisation (**Scheme 6**).[73] This is the first time that myrcene (**8**) has been polymerised in a controlled way, in this case reversible addition-fragmentation chain transfer (RAFT) polymerisation was used, and this yielded polymers with low polydispersites, typically between 1.1-1.4. The polyterpene **34** had a T_g of -60 °C, and ^{1}H NMR analysis showed that at least 96% of the polymer consisted of 1,4 polymyrcene.



33 **8** **34**

***Scheme 6**: Syntheis of polymyrcene (**34**) using RAFT*[73]

The use of terpenes to produce 'green plastics' has been the subject of a large amount of research in the past decade, however many of the polymers produced using terpenes as monomers have not been able to compete with the current petroleum analogues. Various polymerisation processes lack control over molecular weight and structure, or require undesirable conditions such as high temperatures, toxic solvents or precious metal catalysts.[45,55] Development of controlled living mechanisms has led

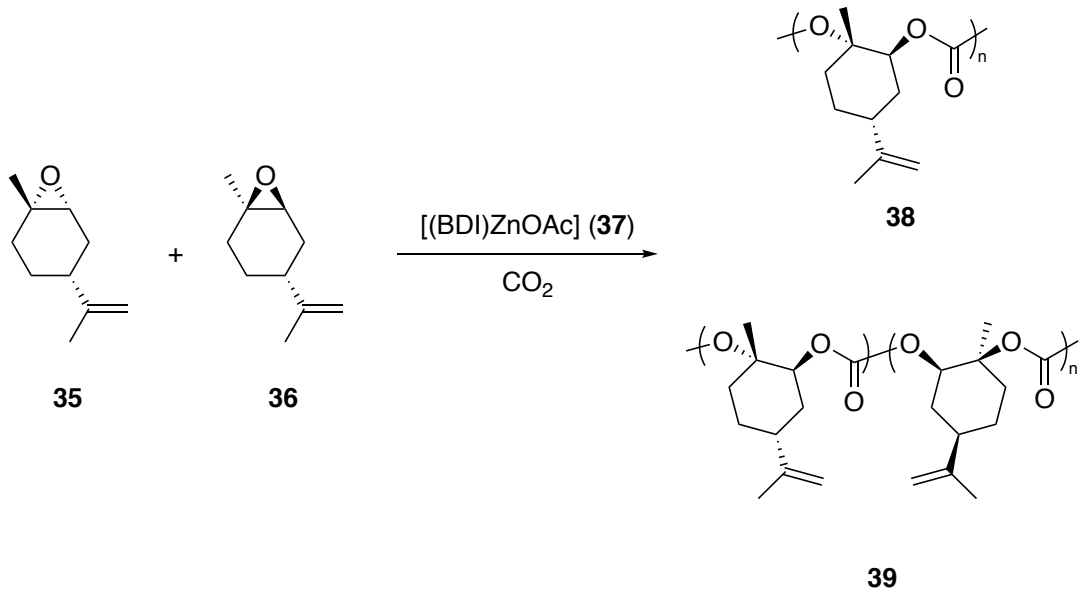
to the synthesis of terpene derived polymers with high molecular weights and useful properties. However, this was mainly achieved by the introduction of synthetic comonomers into the monomer feed, hence reducing the sustainability of the resulting polymer.[54]

Much of the research into the polymerisation of terpenes in their raw form has resulted in polymers which lack the desired properties to compete with the plastics currently used commercially. It is clear that although the use of renewable and sustainable materials is desirable, this path is futile if the synthesised polymers cannot compete with current plastics both in terms of cost and performance. New approaches are required to utilise terpenes as monomers for renewable polymers. One strategy is to perform controlled and sustainable functionalisation of the terpenes to transform them into monomers that can produce more competitive polymers. The following section will explore this strategy for the production of renewable polymers.

3. Polymers from functionalised terpenes

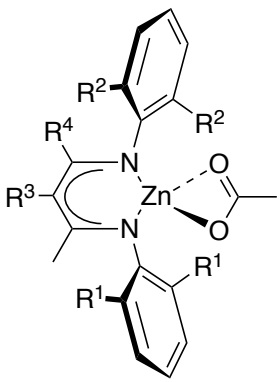
3.1. Limonene (6)

A common transformation of limonene is the epoxidation of the internal double bond to produce **35** and **36**. The Coates research group utilised carbon dioxide and **37** and **38** to produce linear polycarbonates based upon prior success of petroleum-based cyclohexane oxide/carbon dioxide copolymerisation (**Scheme 7**).[74]



Scheme 7: *Copolymerisation of **35** and **36** with carbon dioxide*[74]

β -Diiminate zinc acetate complexes **37** (**Figure 6**) were chosen as catalysts due to their high activity towards polymerisation of epoxides and carbon dioxide.



37

Figure 6*: β -Diiminate zinc complex **37** used as a catalyst for the copolymerisation of **35** and **36** with carbon dioxide.*[74]

The polymerisation was carried out at 25 °C, regioregular alternating polycarbonates, **38** and **39**, were produced with a high molecular weight $M_{n\,=}$ 25 kDa and a Đ of 1.16. When the temperature was increased to 50 °C the reaction yielded a more random copolymer of polycarbonate with a noticeable decrease of molecular weight and

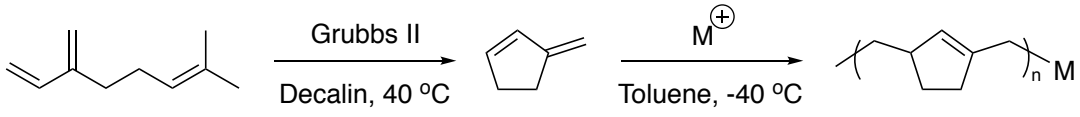
broadened dispersity (Đ = 1.34). Low temperature polymerisation facilitated the stereo- and regioregular ring-opening of **35** and **36**, but this was accompanied by longer reaction times required to yield high molecular weight. One drawback of this synthesis, is the polymerisation of only the *trans* isomer of limonene oxide resulting in a large amount of unreacted starting material.

In an attempt to combat this Greiner and co-workers developed a stereoselective synthesis of limonene oxide, producing little of the *cis* isomer of limonene oxide.[75] Not only was the synthesis more efficient, it also produced high molecular weight polymers (M_n >100 kDa) with attractive thermal properties (e.g. T_g = 130 °C) by reducing the amount of alcohol impurities, which can act as chain transfer agents, in the monomer feed. The monomer synthesis was scaled up to 1.3 kg of limonene oxide per batch, working in such a way that the organic solvents used could be recycled after use, imparting an additional sustainable aspect to this polymerisation.

Following their previous work, the Coates research group synthesised the single enantiomers of **38** and combined the two amorphous enantiomerically pure polymers together in a 1:1 ratio.[76] These polymers then formed a stereocomplexed, semi-crystalline polymer with enhanced mechanical properties compared to the single enantiomers of the polymer.

3.2. Myrcene (8)

Kobayashi *et al.* prepared high molecular weight poly(3-methylenecyclopentene) (**41**) using a combination of Grubbs metathesis and cationic polymerisation (**Scheme 8**).[71]



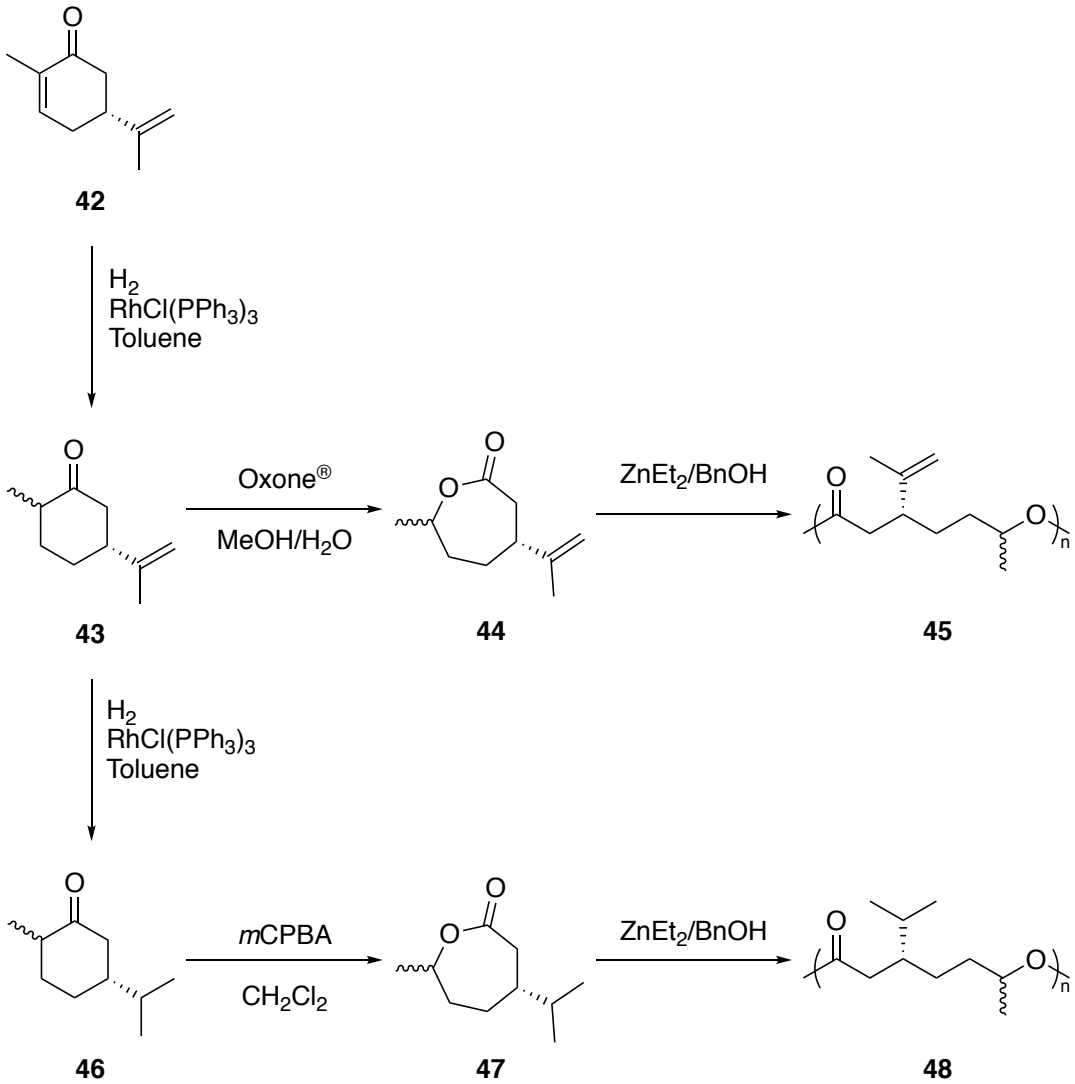
8 **40** **41**

Scheme 8: *Polymerisation of myrcene (**8**)*[71]

Grubbs second generation catalyst (Grubbs II) was used to convert **8** into 3-methylenecyclopentene (**40**), which was subsequently polymerised *via* cationic polymerisation. This process produced a high molecular weight and regiopure polymer **41**, M_n = 22 kDa with a Đ of 1.12. The cationic polymerisation was initiated using an ^{i}BuOCH(Cl)Me/$ZnCl_2$/Et_2O system at -40 °C in toluene, and demonstrated excellent control of the molecular weight. Low Đs indicated a living process was achieved and these polymers displayed a T_g of 11 °C. However the ring closing metathesis uses an expensive ruthenium metal catalyst, and is a low yielding step (45%).

3.3. Carvone (42) and Menthol (49)

Another common terpene is carvone (**42**), this can be found in both spearmint and caraway oils and is produced on the scale of 10 KTA.[77] Hillmyer and co-workers hydrogenated **42** using Wilkinson's catalyst to give dihydrocarvone (**43**) and carvomenthone (**46**), these monomers could be further modified by the Baeyer-Villiger reaction to produce lactones **44** and **47** respectively which can be polymerised through ROP (**Scheme 9**).[78]

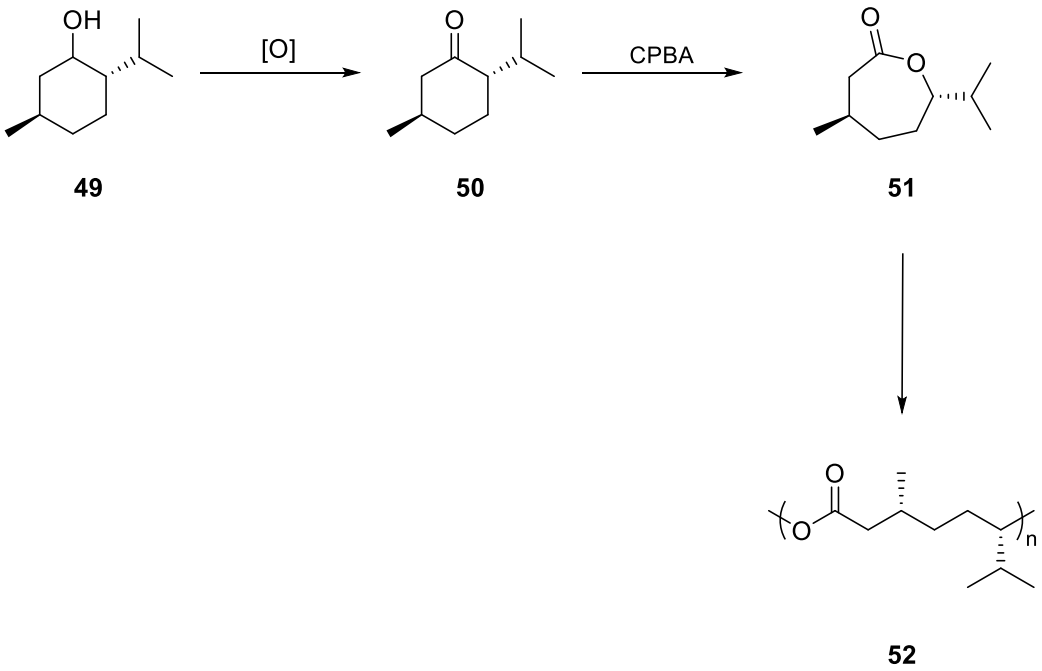


Scheme 9: *Ring opening polymerisation of carvone derived monomers **44** and **47***[78]

To avoid epoxidation of the terminal alkene of **43** Oxone® was chosen as the oxidant for the Baeyer-Villiger reaction. The polymerisation was carried out in bulk at 100 °C using diethylzinc as a catalyst and benzoyl alcohol as the initiator. The ROP yielded carvomenthone-based polymers **45** with high molecular weights M_n = 62 kDa, a Đ of 1.16 and a T_g of −27 °C and dihydrocarvone-based polymers **48** with a molecular weight M_n = 10.5 kDa, a Đ of 1.24 and a T_g of −20 °C.

Menthol (**49**) is another terpene and is commercially available in its oxidised form, a compound known as menthone (**50**). Hillmyer and co-workers were able to synthesise

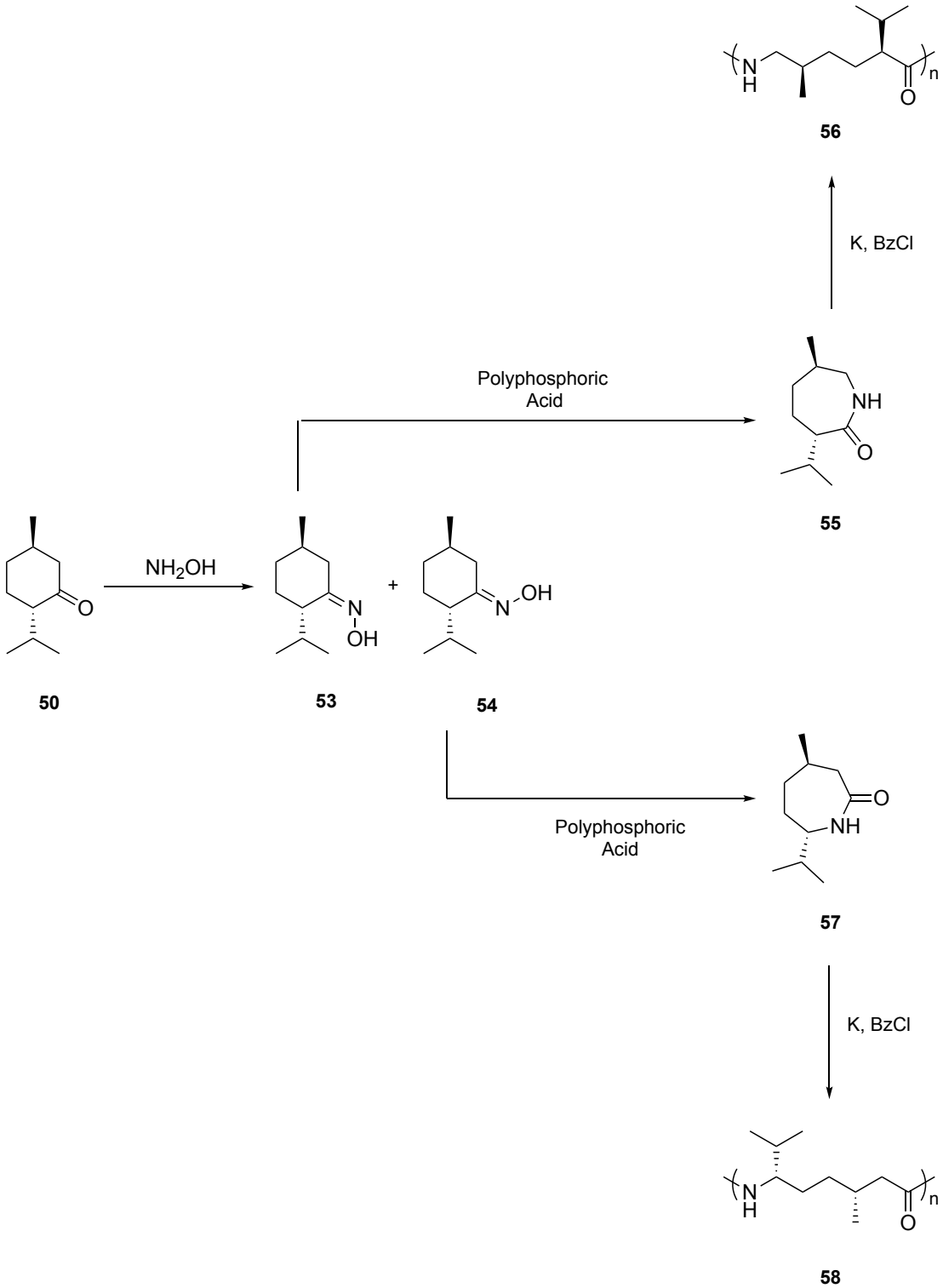
polymers (**52**) based on menthol using a similar method to the previously mentioned ROP of carvone derivatives (**Scheme 10**).[79] **50** is readily converted to a lactone monomer, menthide (**51**), by the Baeyer-Villiger oxidation using *m*CPBA as an oxidising agent. The ROP of **51** utilised a highly active zinc alkoxide catalyst which was previously discovered within the Hillmyer group, allowing the polymerisation to run at room temperature in toluene for 8.5 hours. By adjusting the monomer to catalyst ratio, polymers with molecular weights ranging from $\dot{M}_n$ = 3 kDa to 91 kDa with the Đs below 1.6 were formed.



***Scheme 10**: Synthesis of polymers from menthol 49**4**)*[79]

Using similar principles to Hillmyer, the Winnacker research group utilised the Beckman rearrangement to synthesise lactams **55** and **57** from menthone (**50**) (**Scheme 11**).[80,81] Anionic ring opening polymerisation (ROP) using potassium and benzoyl chloride subsequently produced oligomers (M_w *ca.* 0.5 kDa) of the resulting polyamide **56** and **58** . These oligomers are in the early stages of research and therefore further investigations are being carried out to improve the molecular weights which are currently fairly low. However, this method is a clever use of robust

organic chemistry to synthesise a novel terpenoid based polyamide, with a good control of stereochemistry.



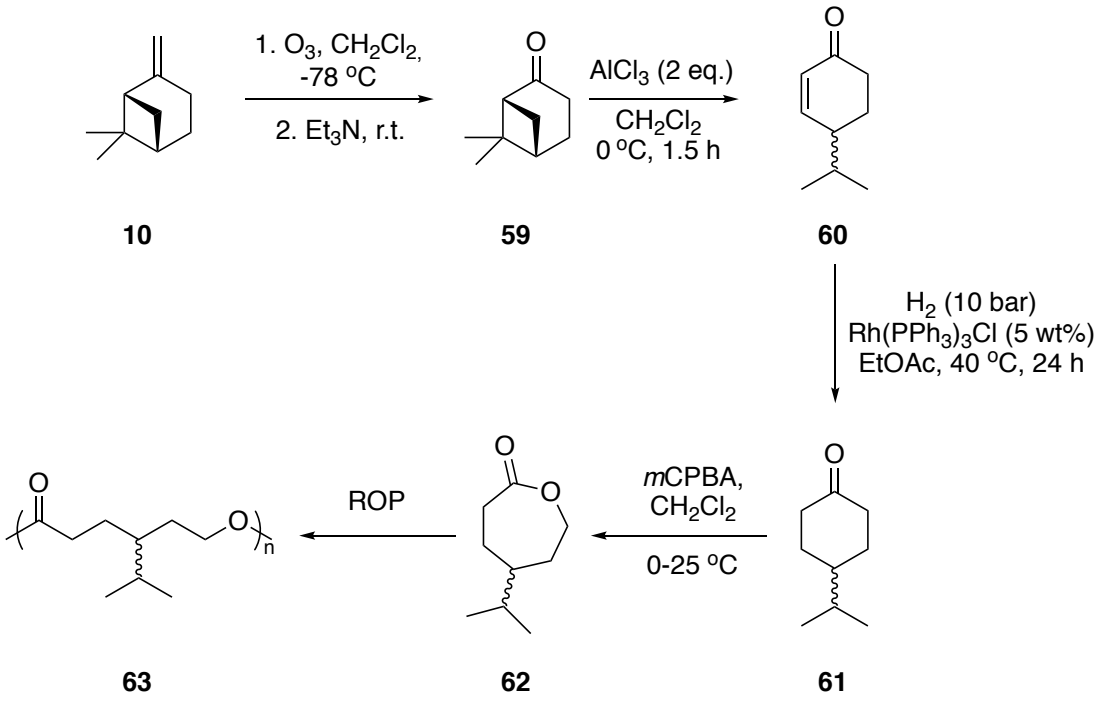
***Scheme 11**: Synthesis of polymers via lactams **55** and **57** obtains using the Beckman rearrangement.*[81]

Winnacker *et al.* has further developed these polymers through improved synthesis of the polyamide **58**.[82] This was achieved through a one pot synthesis of **57** from **50**, followed by the polymerisation using NaH as a base, a more convenient reagent than elemental potassium. These advances have led to the synthesis of **58** on a larger scale, and hence further analysis has been carried out. M_w 1-5 kDa were achieved with relatively high Đ (*ca.* 2). These polymers exhibit crystalline properties and have a high T_m 300 ^oC, making them promising for biobased versions of Nylon-6.

3.4. Pinenes

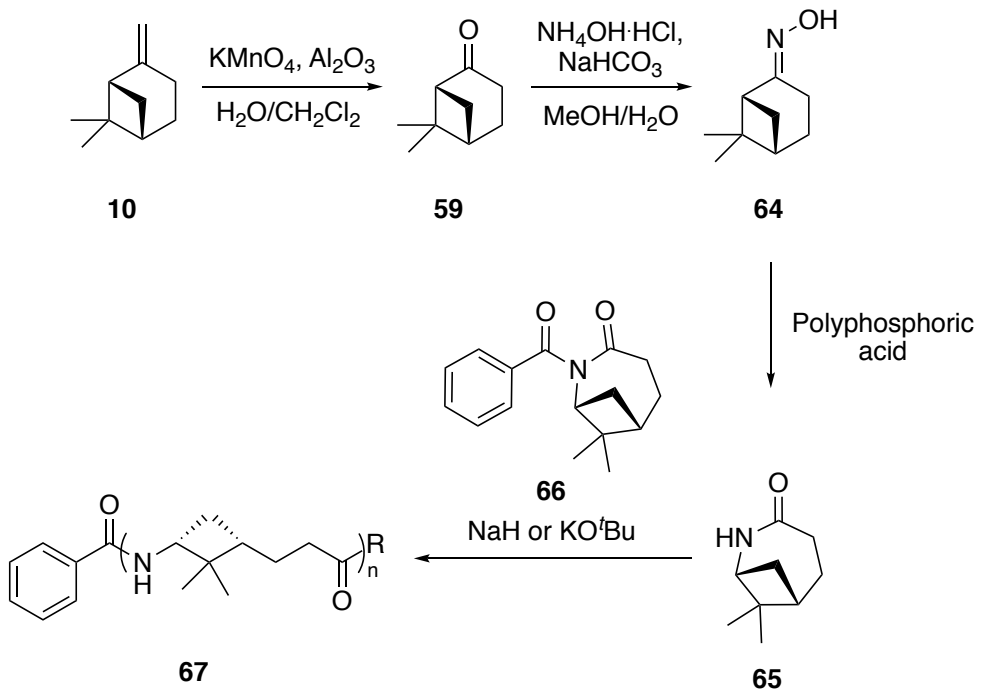
In order to circumvent the lack of reactivity of α-pinene (**11**) towards cationic and radical polymerisation Miyaji *et al.* used a visible light photo-oxidation to quantitatively convert **11** into pinocarvone.[83] Pinocarvone possesses an exocyclic double bond, which is conjugated to a ketone moiety, and can be homopolymerised through a radical ring opening process. The polymerisation was investigated in a number of solvents to yield polyketones with an M_n of 26 kDa and a fairly high T_g (162 ^oC). Both enantiomers of α-pinene (**11**) were used as starting materials in order to investigate the effect of chirality on the resulting polymer. The built in chirality is a very interesting aspect of using terpenes as monomers, and resulted in polymers with optical activities.

Following the success of the ROP of cyclic ester and amides derived from menthol (**49**) and carvone (**42**), work was done to expand the synthesis of lactones and lactams to the pinenes. Quilter *et al.* synthesised 4-isopropylcaprolactone (**62**) in four steps from β-pinene (**10**) which can be seen as a terpene derived ε-caprolactone (**Scheme 12**). The monomer was prepared on a multigram scale and was able to undergo ring opening polymerisation to give low T_g (-50 ^oC) bio-based alternatives to poly(caprolactone).



Scheme 12: *Functionalisation of β-pinene (**10**) to yield a cyclic ester capable of ROP*[84]

β-pinene (**10**) has also been modified by Winnacker *et al.* to produce bicyclic lactams which are able to undergo ROP *via* anionic or cationic polymerisations.[85] The lactam **65** is synthesised in four steps from β-pinene (**10**) which then can form a polyamide **67** *via* ROP (**Scheme 13**). The polyamides were synthesised with M_ns between 1.7 and 8.1 kDa and were found to be crystalline polymers with T_ms in the range of 300 °C. In addition to these thermal properties the polymers display optical activity and together this makes them very attractive for high performance polymers.



Scheme 13: *Synthesis and polymerisation of β-pinene (**10**) derived lactam (**65**)*

A recent collaboration between Howdle and Stockman has developed simple chemistry to modify terpenes and create new polymers.[86] Cheap and abundant terpenes, such as α-pinene (**11**), β-pinene (**10**) and limonene (**6**), were transformed into monomers by addition of acrylates and methacrylate functionality to create new monomers that can easily undergo free radical polymerisation (FRP).

A variety of terpene derived monomers have been synthesised (**Figure 7**). **10**, **11** and **6** were functionalised by use of a hydroboration then oxidation sequence in order to install a hydroxyl functionality. In the case of **42**, an alcohol was formed by reduction of the enone functionality with lithium aluminium hydride. The hydroxyl functionalised terpenes were esterified with acryloyl or methacryloyl chloride using Et_3N as a base.

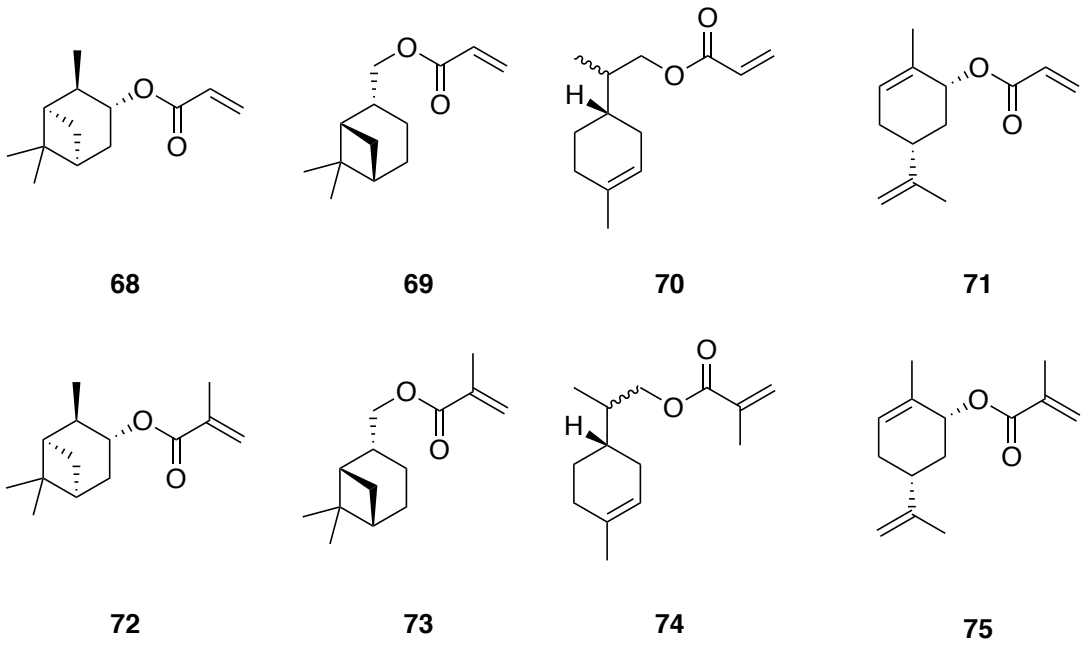
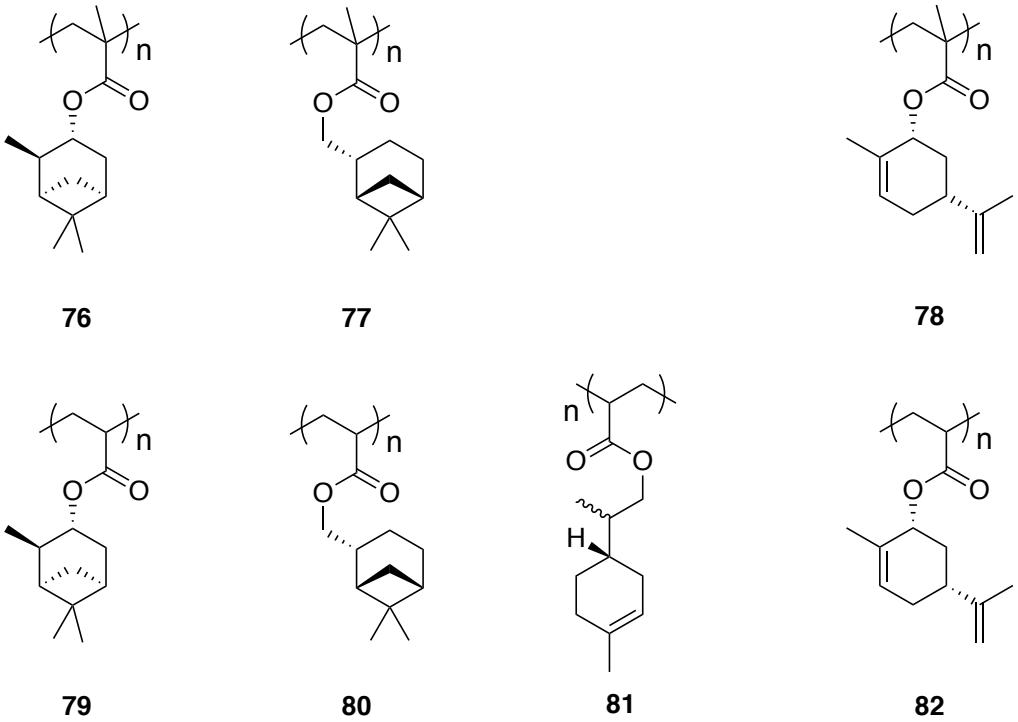


***Figure 7**: Monomers derived from terpenes*[86]

These new monomers **68-75** were polymerised through conventional FRP using azobisisobutyronitrile as an initiator. In most cases the polymerisations were successful yielding the polymers **76-82** (**Figure 8**). The polymerisations gave polymers with molecular weights up to 106 kDa with high conversions *ca.* 98 %. The Đ was high (1.3-2.2), as expected for FRP which do not use control agents. The polymers also displayed T_g values from -18 °C up to 142 °C, giving them the potential for many applications.



76 **77** **78**

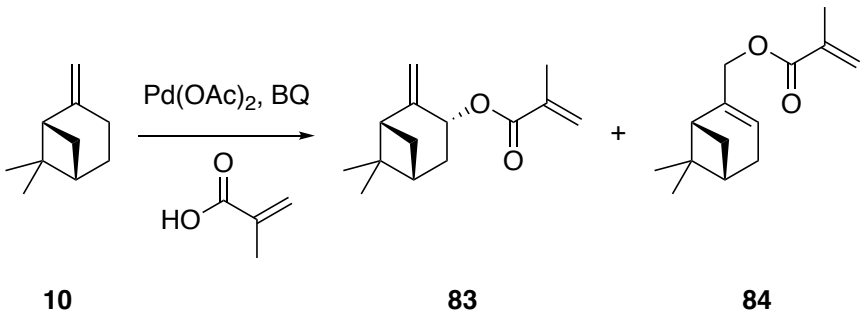
79 **80** **81** **82**

***Figure 8**: Polymers from acrylate and methacrylate monomers derived from terpenes*[86]

Varying the terpene and acrylic acid starting materials allows tuning of the properties of the resultant polymer, making them excellent candidates for commercially useful polymers from renewable resources. The above synthesis of the monomers is currently neither 'green' or sustainable. However, with the evidence of the useful properties of these polymers an effort can be made to optimise the conditions and develop improved routes for both the synthesis of the monomers and the polymerisation process.

With this in mind the synthesis was developed to move away from the toxic acryloyl and methacryloyl chloride and substituting with acrylic and methacrylic acid; both of which will become commercially available from renewable sources. A propyl phosphonic anhydride was introduced to promote ester coupling between terpene alcohols and acrylic acid, producing an environmentally benign water-soluble triphosphate by-product; considerably more sustainable than chloride in any waste stream.

Howdle, Stockman and co-workers looked into a more efficient one step synthesis of the monomers *via* C-H activation, which can be viewed as an efficient way of functionalising alkenes.[86] Methacrylic acid was added to **10** *via* catalytic C-H functionalisation using $Pd(OAc)_2$ as a catalyst (**Scheme 14**). Optimal conditions were found to be 2 mol% $Pd(OAc)_2$, 2 equiv. benzoquinone under an atmosphere of O_2 and using methacrylic acid as the solvent. The reaction was carried out at 50 °C for 16 h and produced two possible products in 82% (**83** and **84**) in a 10:1 ratio.



10 **83** **84**

***Scheme 14**: C-H activation of β-pinene (**10**) using a Pd catalyst to yield functionalised monomers.*[86]

C-H activation has been successful in improving the synthesis of acrylate and methacrylate functionalised monomers by reducing the number of steps from one to two, as well as producing new interesting monomers. Though this work is still ongoing, promising results have been demonstrated.

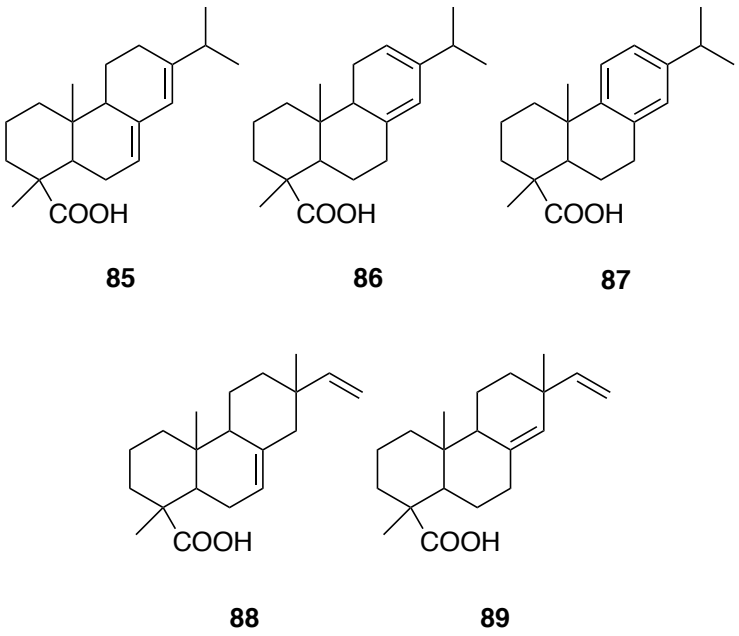
More recently Lima *et al.* used a similar approach to synthesise *trans*-sobrerol derived acrylates and methacrylates.[87] The secondary alcohol in *trans*-sobrerol was functionalised using acryloyl chloride and methacrylic anhydride respectively to produce monomers. These monomers were then reacted with unsaturated polyesters to produce resins with tunable thermomechanical properties. The sobreol-derived monomers have the potential to replace petrochemical derived styrene in formulations.

The research highlighted above really emphasises the benefits of collaboration within the scientific disciplines, here the convergence of polymer and organic chemistry has resulted in novel polymers with interesting and useful properties.

The polymers synthesised above are derived from renewable resources and possess required chemical properties which is crucial when developing new green and sustainable plastics. There are still problems to be solved, for example a renewable source of the acrylic and methacrylic acids is required. However, new processes are appearing, and synthetic biology looks set to create a 'toolbox' of platform chemicals that could be considered in the future.

3.5. Resin Acids

Gum rosin is the non-volatile fraction of pine resin obtained by tapping living pine trees and is the most common rosin. Production of rosin exceeds 1,000 KTA, consisting primarily of resin acids which include both abietic- and primaric type resin acids with characteristic hydrophenanthrecene structures (**Figure 9**).[36] The synthesis of polymers using rosin acids is a huge area of research and will not be covered in depth here, more comprehensive reviews have been published previously.[88,36]



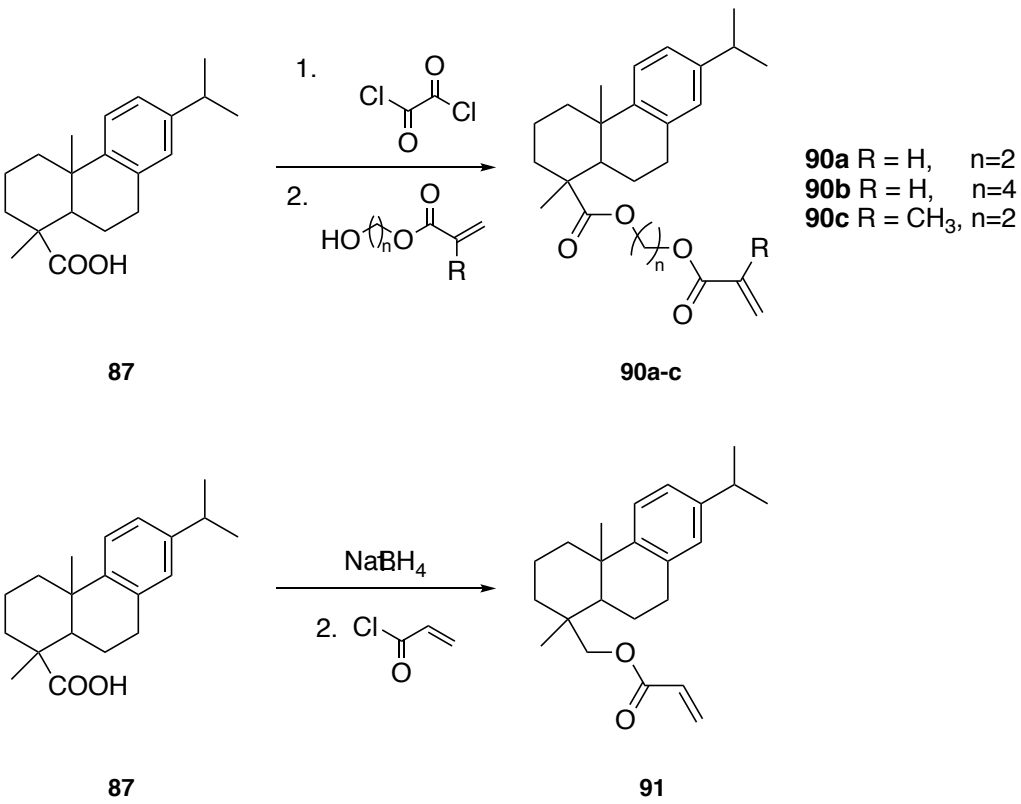
85 **86** **87**

88 **89**

***Figure 9**: Some common components of pine resin*

Main chain polymers derived from resin acids are most commonly polymerised by step growth polymerisation taking advantage of carboxylic acid functional groups. A range of functional monomers from resin acids have been synthesised using Diels-Alder reactions.[89] These monomers lead to the preparation of polyesters, polyamindes, polyamindeimides and polyester polyols.[90] Many of these main chain polymers have low molecular weights and this is due to steric hindrance of the bulky resin acids, monomer impurities and stoichiometric control.[88]

Resin acids have been converted into vinyl, acrylic or allyl ester groups that can undergo radical polymerisation (**Figure 15**).[91] Controlled radical polymerisation of monomers derived from gum rosin enables the preparation of well-defined polymers with high molecular weight and functionality, these could be developed into advanced materials such as thermoplastic elastomers and composites.



Scheme 15: *Conversion of dehydroabietic acid (**87**) to acrylates and meth(acrylates)*[91]

Tang and co-workers have developed a series of well-defined resin-containing (meth)acrylic polymers by controlled polymerisation.[91] The conversion of the carboxylic acid group of **87** to acrylate and methacrylate groups respectively resulted in the synthesis of monomers containing a vinyl group which was highly susceptible to radical polymerisation **90a-c** and **91**. ATRP was used to polymerise the (meth)acrylate monomers.

Acryloyloxyl dehydroabieticcarboxylate (ADA) (**91**) in which the dehydroabietic group is connected directly to the vinyl ester group, was prepared from acryloyl chloride and dehydroabietic alcohol, obtained by reduction of dehydroabietic acid (**87**) with sodium borohydride (**Scheme 15**). For monomers 2-methacryloyloxyethyl dehydroabieticcarboxylate (MAEDA) (**90c**), 2-acryloyloxyethyl dehydroabieticcarboxylate (AEDA) (**90a**), and 4-acryloyloxybutyl dehydroabieticcarboxylate (ABDA) (**90b**), dehydroabietic acid (**87**) was first converted

into an acyl chloride using oxalyl chloride followed by the in-*situ* esterification reactions with hydroxyl groups of corresponding (meth)acrylates.

Copper catalysed Atom transfer radical polymerisation (ATRP) of **91** was carried out to give polymers with a broad dispersity indicating the reaction was not controlled. This was most likely due to the dominating steric hindrance of the dehydroabietic moiety. For other acrylates, ATRP allowed the preparation of well-defined resin-derived polymers with low Đ and controlled molecular weight. The molecular weight of polymers ranged from 10 kDa to 100 kDa with Đ < 1.3. The higher molecular weight was consistent with the longer spacers between the rosin moiety and the vinyl group, further indicating the action of a steric effect. These polymers exhibited tunable thermal properties by simple manipulation of monomer structures and could show potential applications for thermoplastic elastomers or composites.

It is clear that the functionalisation of renewable feedstocks using green and sustainable methods is both an interesting and a commercially exploitable field of research. In particular the transformation of renewable feedstocks to yield small molecules containing functional groups which can be readily polymerised is a very promising area of research and development.[74] The terpenes are particularly interesting because of their wide range of functional groups and chiral centres. They present a significant opportunity in the search for 'green polymers' and up untill now it is the lack of a viable commercial scale route to new polymers that can compete with petrochemically derived commodity polymers that is holding back this potential.

4. Conclusions and Outlook

There is a long history of the polymerisation of monoterpenes, initially the most common polymerisation technique was to utilise the double bond for cationic polymerisation to produce homopolymers of α- and β-pinene.[37] Radical polymerisation has proven to be ineffective for the polymerisation of terpenes due to their high reactivity and ability to act as chain transfer agents.[67,68] The pinenes,

limonene and myrecene are the most abundant terpenes and therefore research has focused on these monoterpenes and is clearly reflected in the literature. The majority of this review focused on the functionalisation of terpenes prior to polymerisation, owing to the success of this approach over recent years. This method has allowed terpene derived monomers to be polymerised through methods other than cationic and radical polymerisation. Techniques such as, ring opening and condensation polymerisations have been utilised to produce novel, terpene derived polyesters, polyamides, polyurethanes and polycarbonates with a range of properties.

Terpenes are currently produced on the scale of 300 KTA with the potential to be produced on a larger scale from waste streams if the demand was high enough. Terpenes are produced by plants through metabolic pathways and as a result have inherent functionality and chirality. The present production of terpenes is not enough to manufacture a new plastic on a large commodity scale, but the functionalised nature of terpenes could enable the synthesis of low volume and valuable speciality materials derived directly from renewable feedstocks.[51]

This review has highlighted the present difficulties surrounding production of terpene homopolymers with useful properties and a range of inventive methods being employed by some research groups to overcome this problem. Most promising perhaps is the direct functionalisation of terpenes into monomers that can be "dropped-in" to established and efficient polymerisation processes. These approaches have the potential to produce sustainable polymers with valuable and tuneable properties, but to be successful the underlying chemistry by which the terpenes are modified needs to be efficient, green and sustainable. To achieve truly sustainable polymers with real world applications the development of collaborations across all scientific disciplines and industry is imperative.

Development of renewable small molecules as novel monomers is a large and ongoing area of research. Currently many renewable feedstocks rely on the allocation of arable land to grow crops specifically for extraction of the useful molecules; an ethically questionable practice comparable to that of the first generation biofuel production

processes. For the successful production of useful molecules from biomass the current extraction technology needs to be improved, or alternate carbon sources found. Of the currently available renewable polymers PLA has been the most successful, but only a small proportion of the plastics in the marketplace are developed from this and increasing capacity will rely upon more efficient routes to the continuous extraction of sugar from crops, and more energy efficient and optimised polymerisation processes.[3]

There is currently a trend towards sustainability both in research and in society. Consumers are more willing to pay extra for something that is perceived to be environmentally friendly and it now falls to the scientific community to ensure that there are suitable products on the market. In this review terpenes have been assessed for their potential as renewable monomers for polymer production.

5. Introduction to Polymerisations

Within the area of polymer science there is known to be two distinct types of polymerisation; chain growth polymerisation and step growth polymerisation. Chain growth polymerisation is one where the polymer chain grows quickly, and is initiated using a free radical initiator, cationic catalyst or an anionic catalyst. The cationic polymerisation of β-pinene is an example of this type of polymerisation (**Scheme 1**). In contrast during step growth polymerisation the polymer chain builds up slowly and undergoes only one reaction mechanism for the whole build-up of the polymer, i.e. there is not distinct initiation, propagation and termination reaction mechanisms.[92] These two mechanisms lead to two very different kinetic profiles for the polymerisation reactions **(Figure 10)**.

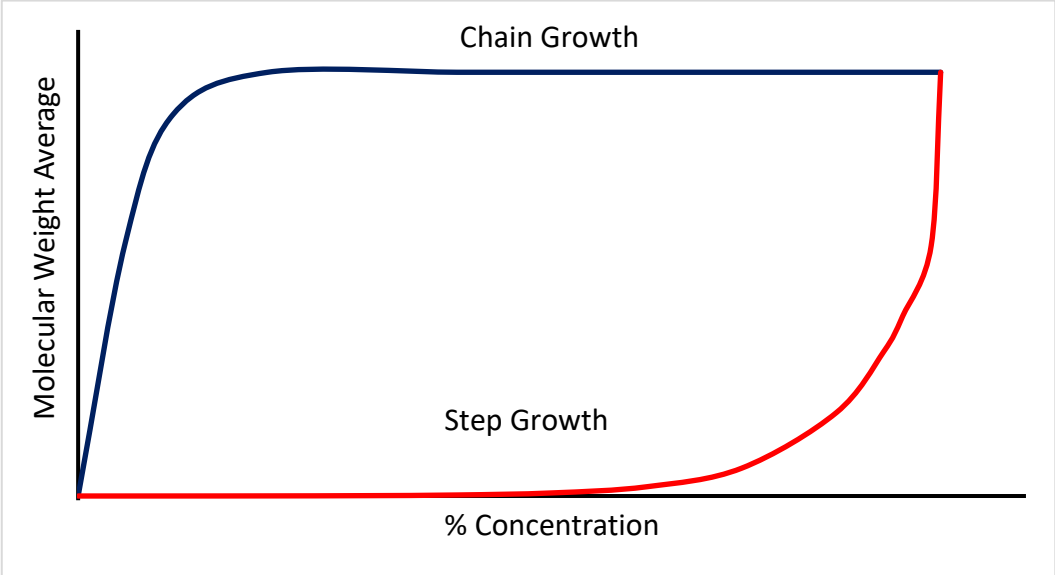


***Figure 10**: Graph displaying the relationship of conversion to the average molecular weight for step-growth and chain-growth polymerisation*

5.1. Step-Growth Polymerisation

Condensation polymers are formed, *via* the step-growth mechanism, from monomers bearing two or more reactive functional groups that can condense intermolecularly with the elimination of a by-product, usually water. As an example, polyesters are formed from hydroxy-acids by intermolecular esterification. A difunctional monomer or equimolar amounts of two different difunctional monomers are necessary at least to form a linear high molecular weight polymer. The polymerisation reaction proceeds by individual reactions of the functional groups on the monomers. Initially two monomers react to form a dimer which may now react with another dimer to produce a tetramer, or the dimer may react with more monomer to form a trimer. This process continues, the functional groups reacting essentially at the same rate until over a relatively long period of time, a high molecular weight polymer is obtained (**Figure 11**).[93,94]

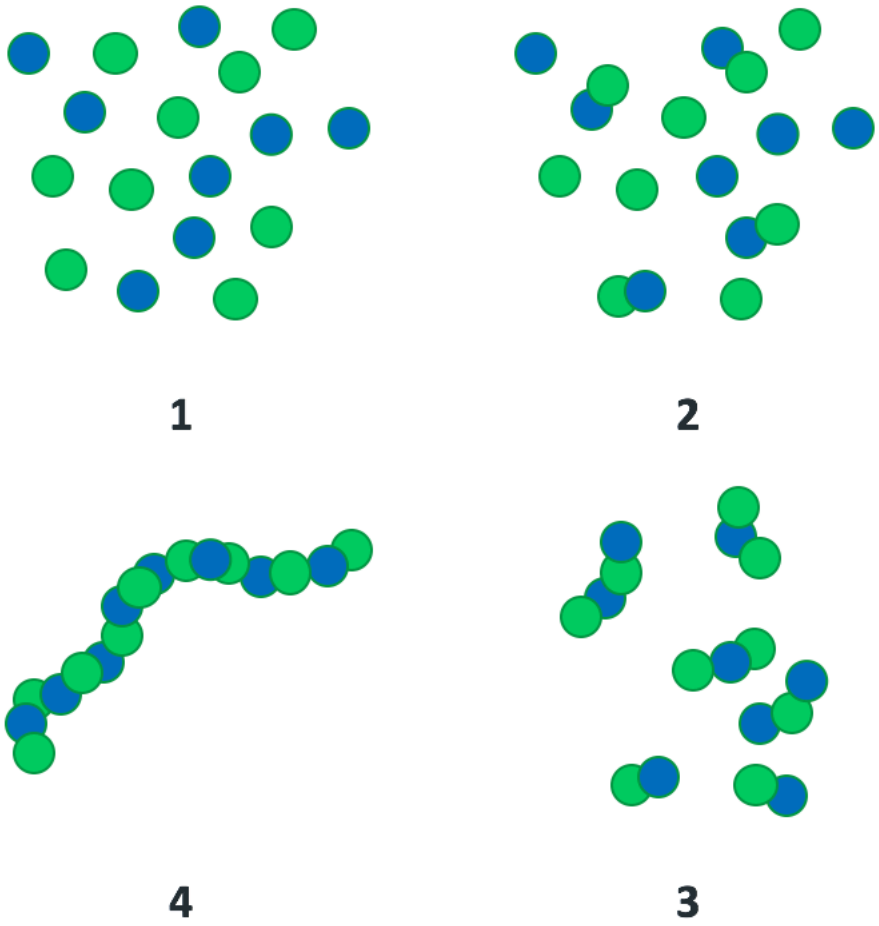


Figure 11: *Method of action of polycondensation polymerisation*

Polycondensation polymerisations are typically carried out using melt polymerisation techniques. These often involve high temperatures in order to ensure that both monomers are in the liquid phase, and in order to achieve high conversions and molecular weights it is crucial to drive the equilbirum to the right by continuously remove the condensate either using low pressures or by ways of a sparge.

5.2. Chain-Growth Polymerisation

This report will detail investigations into the synthesis of polymers *via* the ring opening polymerisation of cyclic esters. The ROP of lactones can be considered to go *via* a chain-growth mechanism however, there are subtle differences between the

formation of polyesters from lactones and the free radical polymerisation of vinyl groups.

For ROP the driving force is not the conversion of a multiple to a single bond but for most ROP the driving force is the ring strain and associated steric considerations. Additionally, there is the consideration of the ring chain equilibrium, unlike step-growth there is no formation of a small molecule which can be removed to drive equilibrium. This leads to the considerable influence of the initial monomer concentration and temperature on the microstructure of the products.[95]

Additionally, ROP is not aided by the enthalpy difference between a single and double bond, which counteracts the loss of entropy occurring as a consequence of polymerisation *vi*a chain polymerization. ROP have in common that the monomers are rings, irrespective of ring size, but the reason why polymerisation takes place can vary, and there are many factors that govern the formation of high molecular weight polymers.[96]

This research will investigate the polymerisation of terpenes derived monomers *via* both polycondensation polymerisation and ROP.

Chapter 1- Investigations into the Synthesis of Limonene Derived Monomers for Studies into Step-Growth Polymerisation

1. Introduction

1.1. Limonene (6) as a Waste Stream

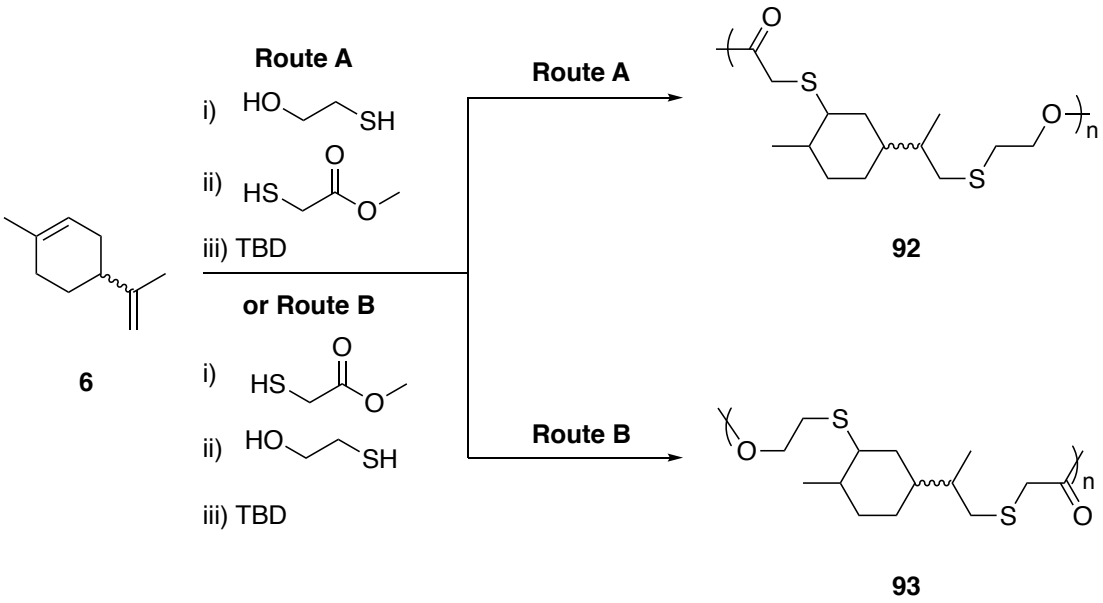
Limonene (**6**) is a terpene, containing both chiral centres and C=C bonds. It is obtained as a by-product of the citrus industry and is present in more than 300 plants.[62] Mostly extracted from waste citrus peel, (*R*)-limonene is a cyclic monoterpene used in many different industrial sectors. Limonene (**6**) is extracted *via* a steam distillation of orange oil derived by centrifugation of the oil−water emulsion (0.5−2% in oil).[97] **6** is a chiral molecule and its (*R*)-enantiomer is produced on a scale of over 70,000 tonnes per annum.[61] There is significant ambition to utilise **6** as a feedstock as currently it is an abundant waste stream with the potential to be employed in polymer chemistry.[69,70] With two alkenes that can be easily functionalised, the molecule has a broad and established organic chemistry, summarised by Thomas *et al*.[98] For the reasons discussed there is significant ambition to utilise limonene as a feedstock in polymer chemistry.[69,70,99]

1.2. Step Growth Terpene Polymers

There has been a high amount of attention in the literature around terpene based monomers, however there is a noticeable absence of terpene-dereived polymers synthesised *via* step-growth polymerisation.

One of the only step-growth polymers derived from limonene is synthesised by the Meier research group and utilised thiol-ene 'click chemistry'.[61] Thiol-ene additions are widely used as very efficient transformations as in many cases they display 'click-chemistry' reaction features.[100] Meier and researchers utilised the high atom efficiency of thiol-ene additions to introduce different functional groups to produce limonene based homopolymers.[61] Limonene (**6**) was reacted with both hydroxyl and methyl ester functionalised thiols to produce monomers which would be suitable for

polymerisation through polycondensation (**Scheme 16**). Limonene (**6**) has two C=C bonds, one of which is *exo* and the other is *endo*, both mono and diaddition products were obtained. The more reactive exocyclic double bond could be selectively functionalised due to the difference in reactivity of the two bonds. When a 1:1 ratio of terpene:thiol was used low conversions of the double bonds were achieved <50 %, the ratio was therefore increased to 1.2 equivalents of terpene to produce the highest yield of monosubstituted product ≈ 80%. Reactions were carried out at room temperature, in the absence of solvent and initiator, conditions which can be considered to be 'green'.

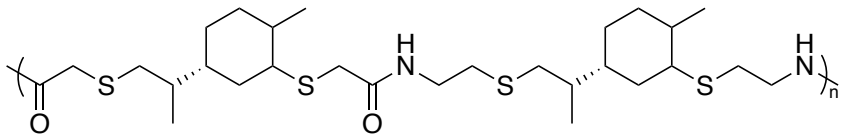


Scheme 16: *Synthesis of monomers from limonene (**6**) through thiol-ene click chemistry and the subsequent polyesters **92** and **93***

The disubstituted monomers were used for condensation polymerisation and 1,5,7-tri-azabicyclo[4.4.0]dec-5-ene (TBD) was chosen as a catalyst due to its high transesterification activity. The steric effect of the bulky cyclic structure of the terpene may have hindered the catalyst accessing reacting centres, resulting in the formation of mainly oligomers with the diester and diol despite the fact TBD has high activity. Polymerisation between two heterodifunctional monomers produced polymers **92** and **93** with molecular weights $\dot{M}_n$ = 8 kDa and 10 kDa and a Đs of 1.65 and 1.89 respectively.

It was discovered that high molecular weight polymers could be obtained from the diol or diester monomers with a spacer between limonene units to reduce the steric hindrance. The co-monomers were long-chain fatty acid-based diesters and diols derived from castor oil which can also be classed as a renewable monomer. Condensation polymerisation was carried out at 120 °C under vacuum using the same TBD catalyst. Crystalline polymers with a higher molecular weight ($\dot{M}_n$ = 9 kDa -25 kDa) were obtained, probably due to the reduction of steric hindrance from the long chain spacers. The T_gs of all polymers were ≈ −45 °C and the melting points varied from −15 °C to 50 °C.

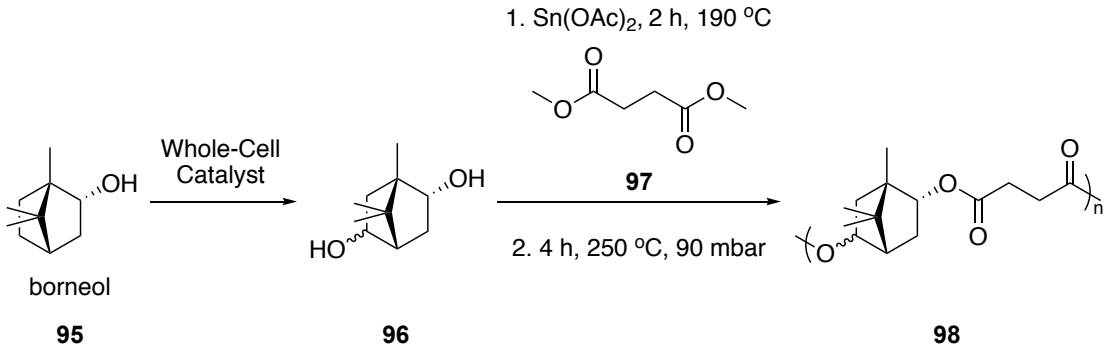
More recently the Meier group utilised the thiol-ene click chemistry to synthesise new renewable diamine monomers from (*R*)-(+)- and (*S*)-(−)-limonene (**6**).[101] In order to obtain renewable polyamides, the co-polymerisation of the synthesised diamines with different renewable diesters *via* polycondensation polymerisation was attempted (**Figure 12**). This method was also used to obtain isocyanate-free polyurethanes.



94

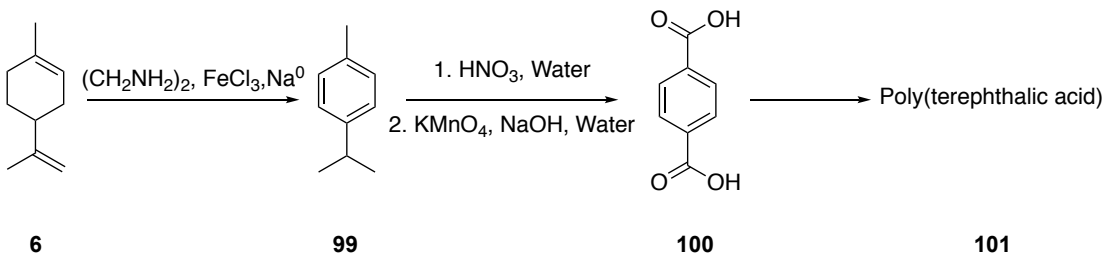
Figure 12: *Polyamide (**94**) synthesised from limonene (**6**)*[101]

The synthesis of renewable polyamides **94** with molecular weights up to $\dot{M}_n$ = 12 kDa were obtained *via* the selective combination of thiol modified limonene. Work by Meier and co-workers also demonstrates the potential for elegant and efficient chemical functionalisation of renewable monomers.[61,101] The functionalisations were carried out at room temperature without the presence of solvents. However, the use of thiols in polymers can be seen as undesirable because of potential discolouration and bad odours; both are important considerations when developing polymers for commercial applications.



Scheme 17: *Biotransformation of borneol (**95**) to 5-hydroxyborneol (**96**) using an engineered whole cell catalyst, and subsequent polymerisation with dimethylsuccinate*[102]

Another example of terpene derived step-growth polymerisation comes from Roth *et al.* who used biotechnology to synthesise a borneol derived diol **96** suitable for step-growth polymerisation (**Scheme 17**).[102] Using a cytochrome P450, which had been engineered to perform a whole cell catalytic transformation, a hydroxyl group was inserted into **95** producing 5-hydroxyborneol (**96**). **96** subsequently underwent a polycondensation reaction with dimethyl succinate (**97**) to produce polyesters **98** with the bicyclic structure incorporated into its backbone. The resulting polymer exhibited a high glass transition temperature of around 70 °C and a molecular weight in the range of 2-4 kDa. This work demonstrates how chemical biology can be used in collaboration with polymer chemistry to allow access to interesting new bio-based monomers.



Scheme 18*: Synthesis of PTA (**101**) from limonene (**6**)*[103]

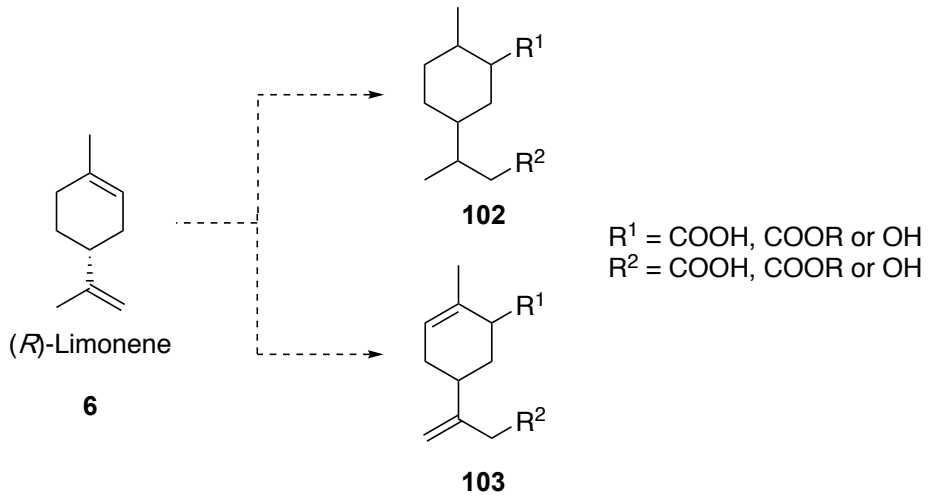
Commodity monomer terephthalic acid (**100**) was synthesised from limonene (**6**) (**Scheme 18**) in order to form poly(terephthalic acid) (PTA) (**101**).[103] This is an example of a biobased version of a plastic which is already in use and therefore has properties

which are desirable. However, this is a very expensive synthesis of PTA and the method used cannot be described as green. Thus, merely using a renewable alternative as a starting material for a polymer does not necessarily result in a sustainable or commercially viable route to a polymer. There must be a synergistic relationship between the development of sustainable synthetic methods and the advances of novel and imaginative biomaterials.

2. Aims and Objectives

The overall aim of this research programme is to synthesise novel and useful polymers derived partially or entirely from renewable feedstocks. Terpenes will be the bio-feedstock of choice throughout this project, specifically limonene (**6**) and α-pinene (**11**), with this chapter focusing on limonene (**6**). This research aims to synthesise small molecules, derived from terpenes, containing handles for polymerisation reactions. Ideally, these syntheses should be performed in a sustainable manner, and will aim to minimise adverse effects on the environment.

This project will build on, and draw inspiration from, work previously carried out by Howdle and Stockman and co-workers. However, it will move away from chain growth polymers with all-carbon backbones.[86] The aim is to synthesise novel polyesters incorporating the functionalised terpene into the backbone of the polymer, which differentiates this work from previous approaches within the University of Nottingham.



Scheme 19**: Proposed structures of limonene (**6**) derived monomers **102** and **103

The terpenes will be converted into monomers containing either two or three functional groups, including; carboxylic acids, alcohols and esters (**Scheme 19**). These precursors will then have the potential to either homopolymerise or co-polymerise with other bifunctional molecules for the synthesis of polyesters. The low cost, synthesis efficacy, ease of isolation and reduction of waste materials in the terpene polymer production will be the major foci of this research.

The project will be split into two main areas:

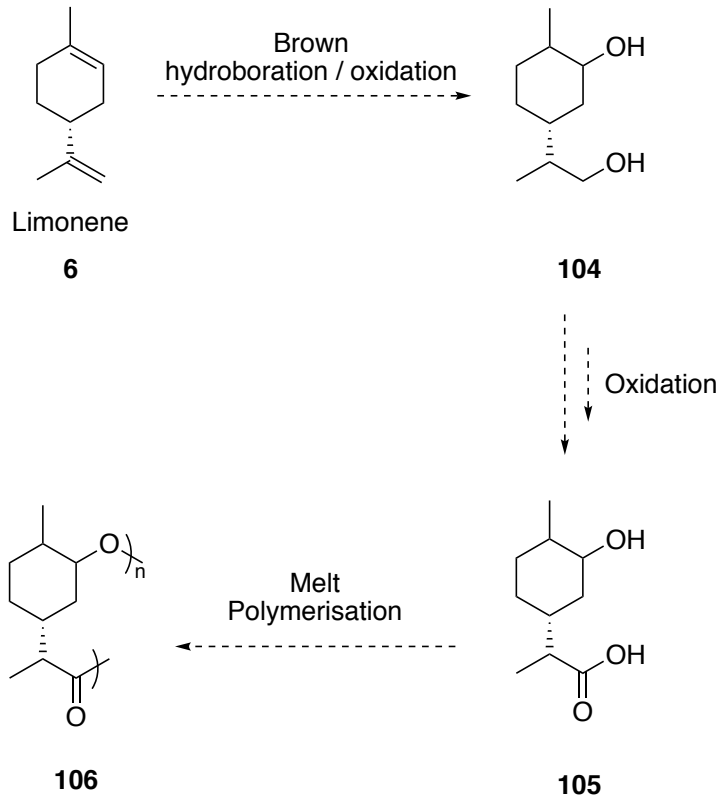
1. The sustainable synthesis of monomers, from naturally occurring terpenes, which are suitable for polymerisation.
2. Investigations into the polymerisation of the functionalised terpenes under various conditions, including metal and organic catalysts.

As this project is centred around the synthesis of potentially degradable polyesters the end of life strategy for these polymers will also be investigated.

The polyesters synthesised in this project will be novel and it is therefore desirable to aim for polymers which exhibit a range of properties (e.g. a range of M_ns and T_gs). This will allow a large space to be targeted with respect to applications. The project will also explore the application of a variety of polymerisation techniques.

3. Results and discussion

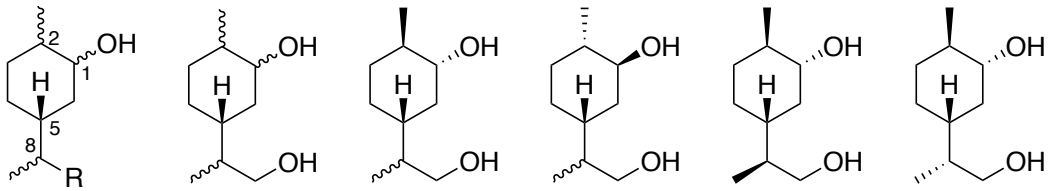
3.1. Synthesis of Limonene Derived Hydroxy-Acid (105)



Scheme 20: *Proposed synthesis and polymerisation of hydroxy-acid (**105**)*

It was desirable to investigate the formation of a limonene (**6**) derived monomer that could homo-polymerise, and it was proposed that the hydroxy-acid **105** could serve as a monomer for the polymerisation to polymer **106**. 100% of the carbon atoms in the backbone of **106** would originate from a terpene and to the best of our knowledge a material of this nature is yet to be reported from step-growth polymerisation. Step-growth polycondensation of hydroxy-acids is well known, however there are few examples where a (carbocyclic)ring is incorporated into the backbone of the polymer. It was proposed that this feature would impart structural rigidity and perhaps lead to desirable properties such as a high T_g.

Explanation of Numbering System



104 **104a** **104b** **104a'** **104a''**

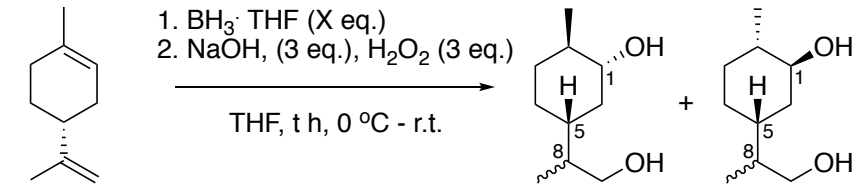
Figure 13: *Example numbering for the different diastereomers of* ***104***

Throughout this report compounds are synthesised as mixtures of diastereomers, the following numbering system has therefore been devised to aid the reader. When a compound is referred to by number only (**104**) it is referring to the general compound as a mixture of diastereomers. When the number is followed by a letter (**104a**) this is referring to a *cis* or *trans* relationship between positions C1 and C5 with a mixture of epimers at the C8 position. When a number followed by a letter which subsequently has ' or '' attached (**104a'**) it is referring to a single epimer at the C8 position (**Figure 13**).

3.1.1. Synthesis of limonene diol intermediate 104

It was proposed that **105** could be accessed *via* a diol intermediate **104**. Using the Brown hydroboration / oxidation conditions, **104** was synthesised from limonene (**6**) (**Table 1, Entry 1**).[104] Analysis using mass spectrometry confirmed the presence of the desired product however, it was shown to be impure by ^{1}H NMR analysis, **104a** and **104b** were isolated after purification by column chromatography in a 72% yield.

***Table 1**: Optimisation of the synthesis of diols **104a** and **104b** from limonene (**6**)*



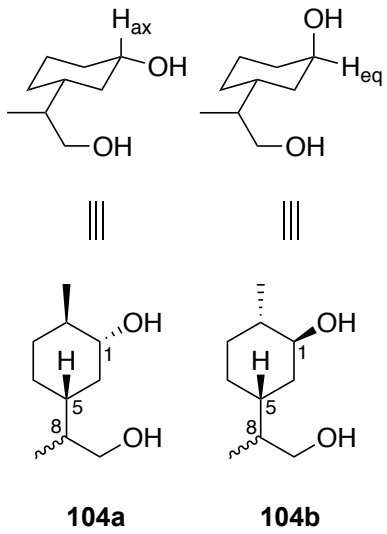
Limonene

6 **104a** **104b**

Entry	Borane:C=C (X eq.)	Order of Addition	t (h)	Yield (%)	104a:104b
1	2:1 (4)	Limonene to Borane	4	72	73.27
2	1:2 (1)	Limonene to Borane	4	53	76:24
3	1:2 (1)	Borane to Limonene	4	76	69.31
4	1:2 (1)	Borane to Limonene	16	97	71:29
5[a]	1:2 (1)	Borane to Limonene	5	27	100:0

[a]Thexyl borane was used as the borane source (**Scheme 22**).

Protons in axial and equatorial positions on a cyclohexane ring are known to give resonances from ^{1}H NMR spectroscopic analysis which have a difference of up to 0.5 ppm due to anisotropic effects.[105,106] Heteronuclear Multiple-Quantum Correlation (HMQC) NMR analysis was used to probe the stereochemical outcome of the reaction and indicated the presence of both **104a** and **104b** as the 1,5-*cis* and 1,5-*trans* diol derivatives (**Figure 14**). This can be deduced from the presence of resonances at 3.10 ppm and 3.62 ppm which correspond to the protons *alpha* to the secondary alcohol in the axial and equatorial positions respectively (**Figure 15**). The ^{13}C NMR analysis also confirms that there are four diastereoisomers present in the mixture both **104a** and **104b** exist as 1:1 epimers in the C8 position.



104a **104b**

Figure 14: *3D representation of the products synthesised from the Brown hydroboration / oxidation of limonene (**6**)*

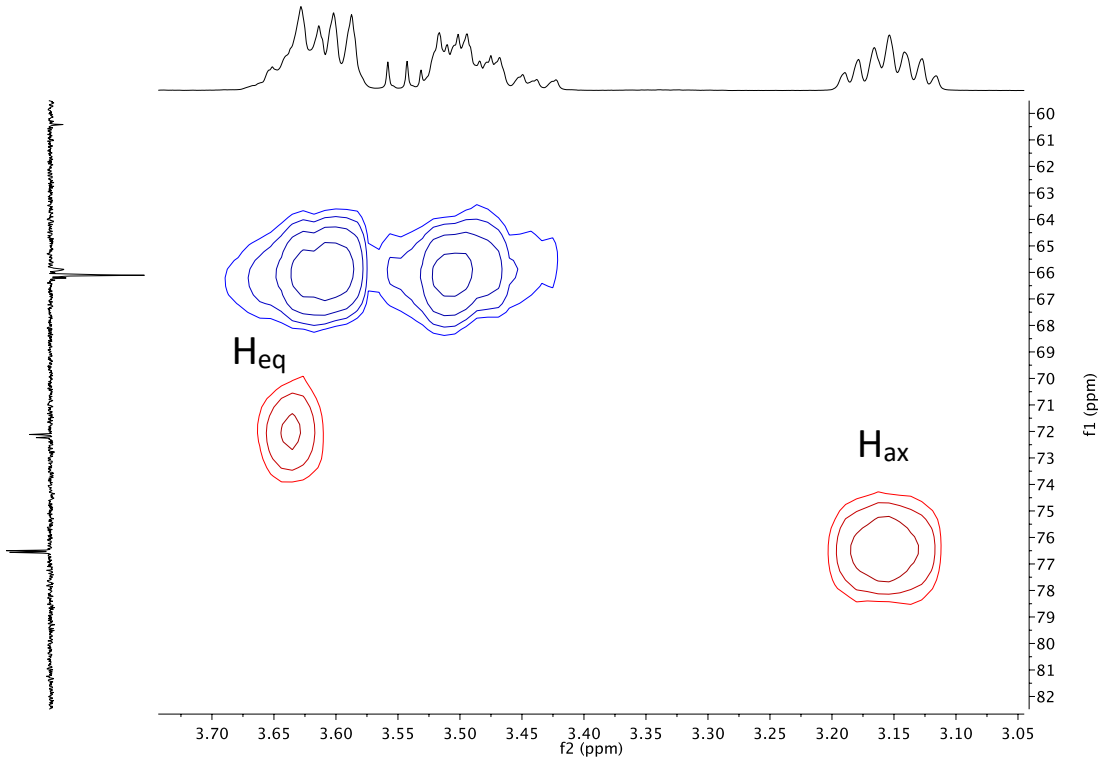
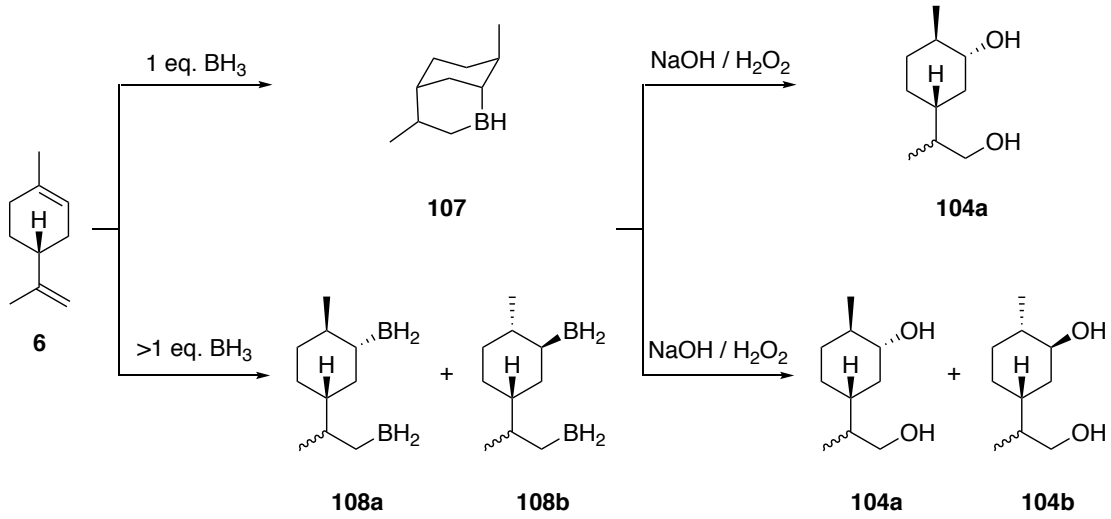


Figure 15*: HMQC spectrum of **104a** and **104b***

In an attempt to influence the stereoselectivity of the reaction the equivalents of borane and order of addition were varied (**Table 1**). It is proposed that the reaction goes through the cyclic intermediate **107** in order to favour product **104a**, however

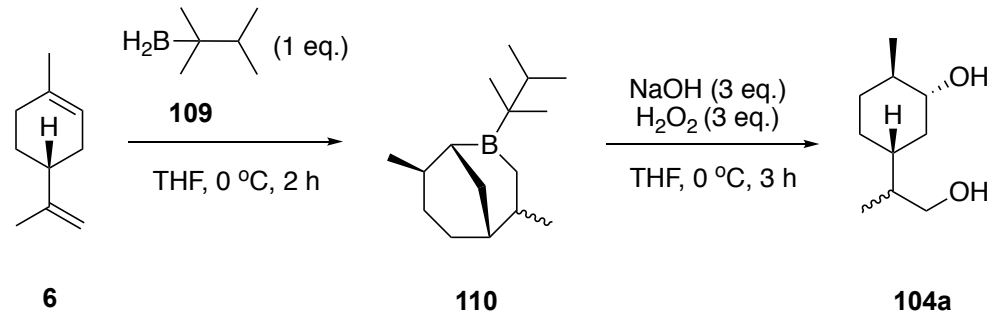
depending on the equivalents of borane used there is also the potential to go through intermediates **107** or **108** (**Scheme 21**). If there is more than one equivalent of BH_3 there is a higher potential for **108a** and **108b** to form. Reaction conditions were varied in order to encourage the formation of cyclic intermediate **107** to optimise the formation of **104a**.



***Scheme 21**: Proposed intermediates for the synthesis of **104a** and **104b** from limonene (**6**).*

The equivalents of borane were reduced from 4 to 1, in an effort to encourage the formation of cyclic intermediate **107** (**Table 1**, **Entry 2**). This resulted in a small increase in the yield of **104a** however the overall yield was significantly reduced (53% *vs* 72%). The order of addition was also changed and the borane was added to the limonene, again to encourage the formation of **107** (**Table 1**, **Entry 3**). Surprisingly this slightly reduced the ratio of **104a** to **104b** (69:31) however the yield was increased to 76%. As the ratios differed only slightly between the reactions it was decided to attempt to increase the yield while still keeping the equivalents of borane low. The reaction was attempted a final time for a longer period of time (16 h) and pleasingly the yield of **104** was increased to 97% (**Table 1, Entry 4**). This represents an approximate 25% increase in the yield from the literature synthesis, and also the first time ^{1}H NMR analysis has been used to probe the stereochemical outcome of the reaction.

In a further effort to synthesise exclusively **104a** it was proposed to use conditions developed by Brown *et al.* (**Scheme 22, Table 1**, **Entry 5**) utilising thexyl borane (**109**) for the hydroboration of limonene (**6**).[104] This is a bulky reagent and encourages intramolecular cyclisation by hindering the attack of a second molecule of **6**, and instead reacting intramolecularly with the second double bond of limonene (**6**) first to synthesise **110**. **110** can then be isolated and oxidised to form exclusively **104a** over **104b**.



***Scheme 22**: Synthesis of **104a** as a single 1,5, 'cis' diastereomer*

In order to isolate the cyclic boron species **110**, the crude reaction mixture was distilled under vacuum. The distillate was then submitted to standard oxidation conditions ($NaOH/H_2O_2$) to yield **104a** as a colourless oil in a 27% yield.

^1H NMR analysis was used to investigate whether the *cis* isomer **104a** had been isolated. Previous reactions using BH_3 yielded a mixture of **104a** and **104b** (**Table 1**). Heteronuclear single quantum correlation (HSQC) spectroscopy was used to probe the presence of the equatorial proton *alpha* to the secondary alcohol in **104b**. The product isolated from the oxidation of the cyclic boron species **104a** has an absence of the signal at ~3.65 ppm which is indicative of the *trans* isomer **104b** not being present.

Upon storage of **104a** at -20 °C for 16 h a white solid precipitated. This was analysed using ^1H and ^{13}C NMR spectroscopy which indicated that the solid constituted an enriched sample of either **104a'** or **104a''.**

The enantiomers of **104a'** and **104a''** (**ent-104a'** and **ent-104a''**) have been previously synthesised and characterised by Harrowven *et al.*[107] The assignments for **104a'** and **104a''** were compared to the literature values for the enantiomers and were found to correspond leading to the assignment of the major diastereomer in the enriched sample as **104a'**.

Upon recrystallisation a single crystal was obtained from the enriched sample and after analysis using single crystal X-ray diffraction spectroscopy the structure was elucidated as **104a'** (**Figure 16**). This confirmed the *cis* relationship between the C1 and C8 substituent. The recrystallised sample was analysed using ^{13}C and ^{1}H NMR spectroscopy and indicated that it was a further enriched sample of **104a'**, implying that the single crystal was representative of the bulk of the recrystallised sample.

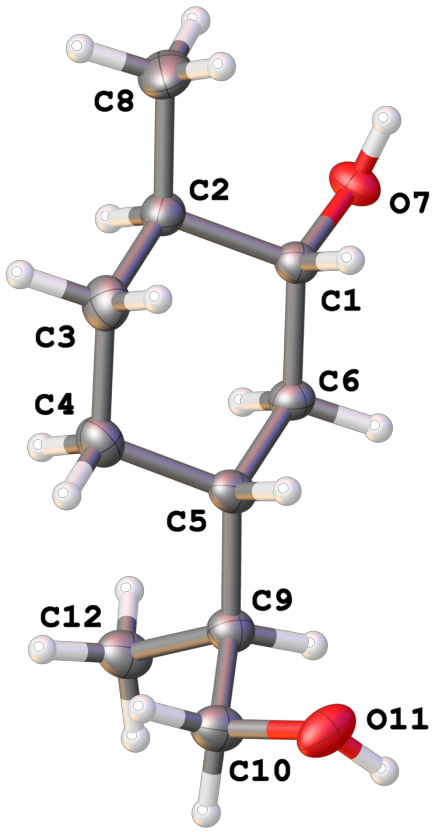
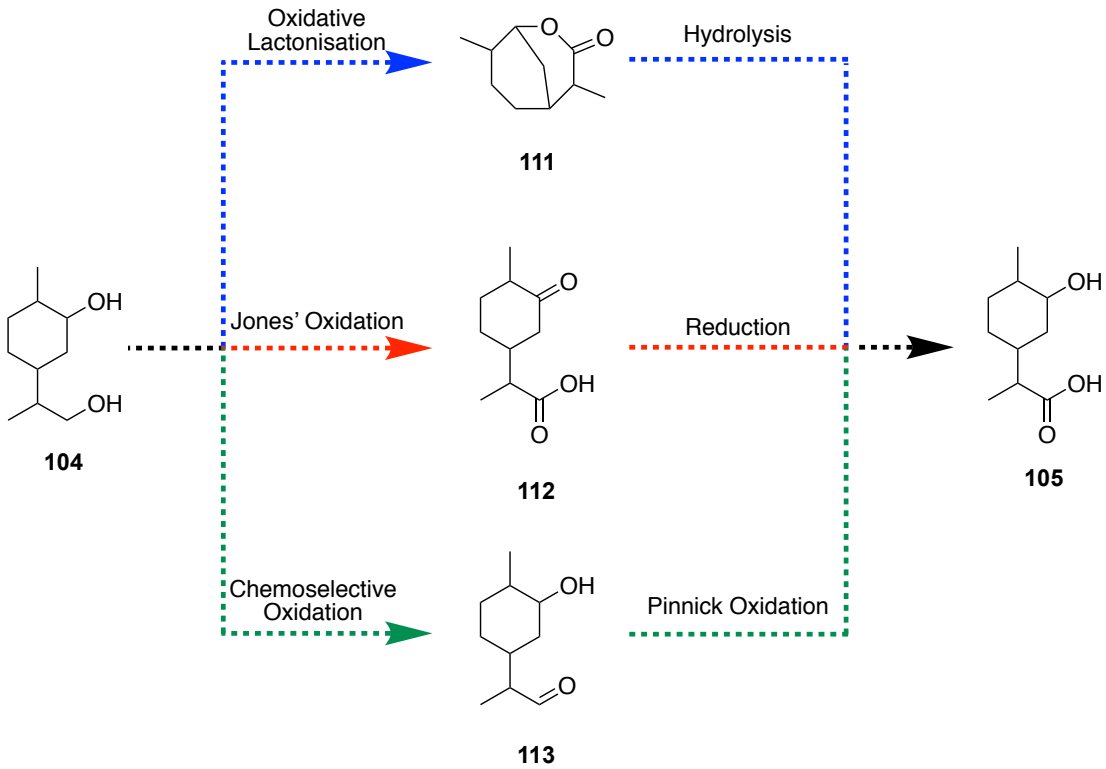


Figure 16: *Molecular structure of* ***104a'***

Although the synthesis of **104a** was successful the yield was significantly lower than that of the synthesis of **104** as a mixture of diastereomers (27% *vs* 97%) and for this reason it was decided to use the diol **104** as a mixture for subsequent experiments. The optimised synthesis of **104** was performed up to a 100 mmol scale, to yield 16.7 g of diol **104**, and with this key intermediate in hand the synthesis of hydroxy-acid **105** could be investigated.

3.1.2. Investigations into the Optimal Synthesis of Hydroxy-Acid 105

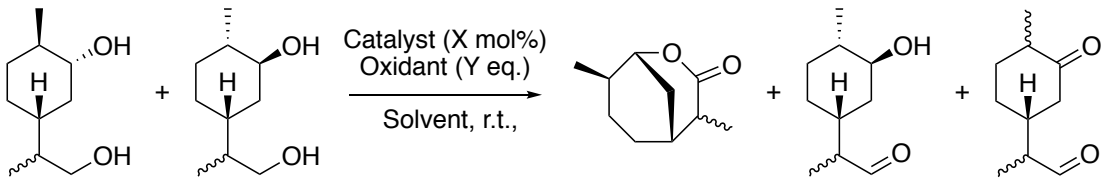
Three synthetic routes for the synthesis of **105** from **104** were proposed, the optimised two-step routes were compared in terms of yield, operational simplicity and sustainability (**Scheme 23**).



Scheme 23: *Three proposed synthetic routes for the synthesis of hydroxy-acid* ***105***

The first route comprises an oxidative lactonisation followed by hydrolysis, opening lactone **111** to yield hydroxy-acid **105**. Using conditions reported by Forsyth *et al.* lactone **111** was synthesised with a 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) / Bis-acetoxyiodobenzene (BAIB) system.[108] TEMPO was chosen as there is precedent for the chemoselective oxidation of primary alcohols in the presence of secondary alcohols.[109] The synthesis of **111** was optimised to improve the yield and reduce the number of side products formed (**Table 2**).

Table 2: *Optimisation of the synthesis of lactone* ***111***



104a **104b** **111** **113b** **114**

Entry	Catalyst/Oxidant	X	Y	Time	Solvent	Product (Isolated Yield of 111)
1[a]	TEMPO/BAIB	20	3	20 h	DCM	**111** + **113b**
2	TEMPO/BAIB	20	3	5 h	DCM	**111** + **113b**
3	TEMPO/BAIB	20	3	24 h	MeCN/H_2O 1:1	**111** + **113b**
4	TPAP/NMO	10	3	5 h	DCM	**114**
5	TEMPO/BAIB	40	5	48 h	DCM	**111** (28%)
6[a,b]	TEMPO/BAIB	40	5	24 h	DCM	**111** + **113b**
7[c]	TEMPO/BAIB	40	3	48 h	DCM	**111** (33%)
8	TEMPO/BAIB	40	3	96 h	DCM	**111** (27%)

[a]Purification was attempted however **111** was not separated from **113b**, [b]**104** was not purified prior to use, [c]104 mmol scale

The synthesis of **111** was attempted using conditions reported (**Table 2**, **Entry 1**).[110] ^{1}H NMR analysis showed formation of lactones **111** however following purification a mixture of **111** and **113b** was obtained. **113b** was identified as the *trans* isomers of the aldehydes formed from the oxidation of **104** which could not cyclise due to the relative position of the 1,5 substituents on the ring. Quantitative ^{1}H NMR analysis

indicated the yields of the impure material were poor often < 20%. In part this was due to the presence of the unwanted by-products aldehydes **113b** (**Table 2**, **Entries 1-2**). The solvent system was changed to water/acetonitrile (**Table 2**, **Entry 3**) this solvent system is common throughout the literature for TEMPO/BAIB oxidations.[111] However a pure product was not obtained and ^{1}H NMR analysis indicated the amount of **111** in the crude material was low.

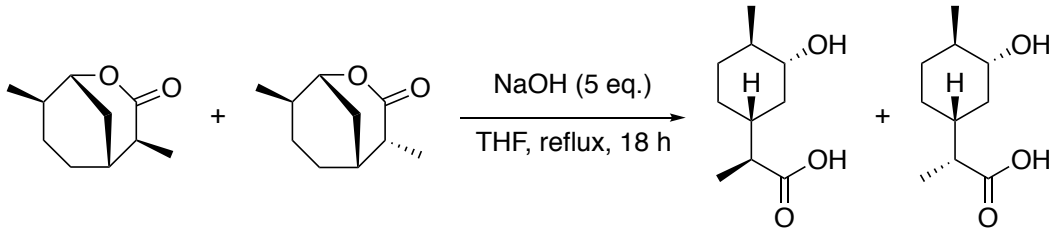
TPAP/NMO systems have been shown to oxidise 1,5 diols to lactones, and it was therefore attempted to change the oxidation system from TEMPO/BAIB to TPAP/NMO (**Table 2**, **Entry 4**).[112] The reaction was attempted using conditions from Bloch *et al.* TLC analysis showed that the starting material was consumed completely after 5 h. ^{13}C NMR analysis of the crude material indicated that **111** had not been formed and in fact the secondary alcohol had also been oxidised to form the ketone **114**.

Higher equivalents of the catalyst (TEMPO) and terminal oxidant (BAIB) were used (**Table 2**, **Entry 5**). Following column chromatography, the fractions were analysed using ^{1}H NMR spectroscopy as TLC and mass spectrometry analysis was found to be unsuitable. This resulted in the first isolation of lactones **111** in a 28% yield as a mixture of epimers at the C8 position.

The poor efficiency of the purification was resulting in a low isolated yield, however lactones **111** and aldehydes **113** have almost identical R_f values which proved to be a difficult separation. In order to reduce the amount of purification steps a telescope reaction was attempted using crude **104** to synthesise **111** (**Table 2**, **Entry 6**). However, the separation proved too difficult to isolate a high yield of **111**.

It was hypothesised that the yield and the purification could be improved by using **104a** (the *cis* isomer of the diol) as the starting material in order to increase the yield of **111**, which can only be formed *via* the ring closure of the *cis* diol **104a**. With **104a** in hand (from the synthesis of **104** using thexyl borane (see above)) the oxidative lactonisation was attempted. ^{1}H NMR analysis, however indicated that the yield was still low (>20%) and not worth the extra steps required to synthesise **104a**. Using the

cis diol as the starting material had not significantly improved the yield and therefore despite the low yield, it was decided to scale up the catalytic lactone synthesis. The synthesis of **111** was scaled up to 20 g (**Table 2, Entry 7**) to give **111** in a 33% yield.

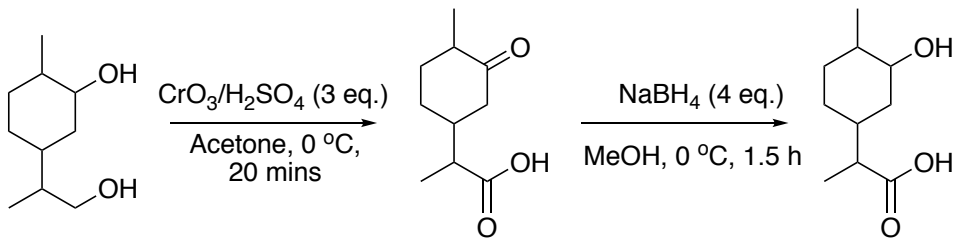


111a' **111a''** **105a'** **105a''**

Scheme 24**: Synthesis of **105a'** and **105a''

It was envisaged that **105a'** and **105a''** could be accessed *via* a hydrolysis to open the ring of **111a**. This strategy would yield two diastereomers (**105a**), making the analysis of both the monomer and polymer easier. The reaction was attempted on a 5.5 mmol scale to yield **105a** in a 98% yield. Subsequent recrystallisation from hot EtOAc afforded a single diastereomer **105a'** or **105a''** which was isolated for analytical purposes.

The second proposed route (red) (**Scheme 23**) uses Jones's reagent to perform a global oxidation of **104**, followed by a selective reduction of the cyclohexanone moiety to yield the hydroxy acid **105** (**Scheme 25**).



104 **112** **105**

Quantatative 38%

Scheme 25**: Oxidation of **104** and subsequent reduction for the synthesis of **105

The oxidation of **104** went smoothly and was finished in 20 min (indicated by a colour change from red to green) to yield the keto-acid **112** in a quantitative yield, which was used without further purification. Sodium borohydride was used to selectively reduce the ketone moiety to give the desired product **105**. The oxidation of **104** created a ketone removing the stereocentre at the C1 position of the molecule. Upon the non-stereoselective reduction, C1 again became a stereocentre, resulting in a total of 8 different diastereomers (**105a**-**d**) (**Figure 17**).

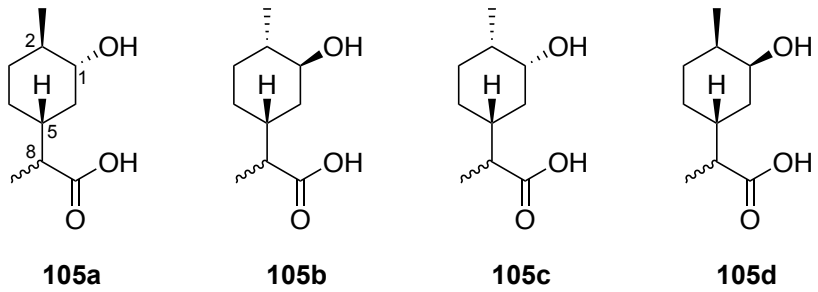
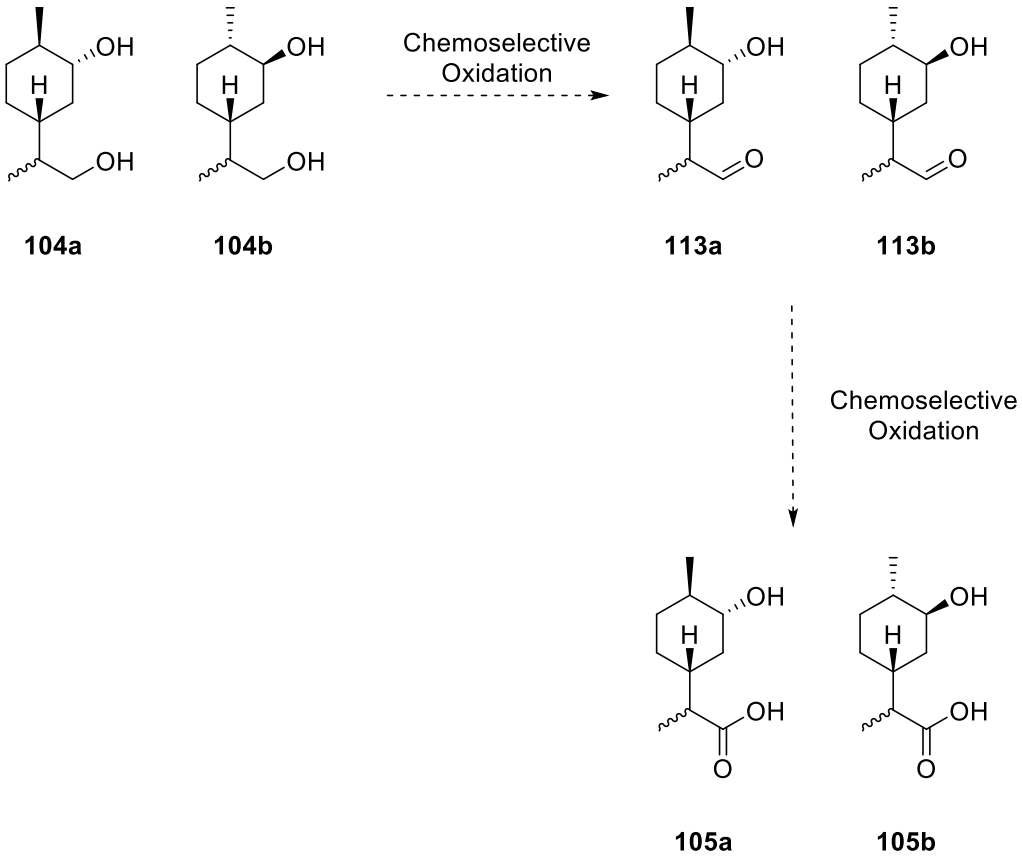


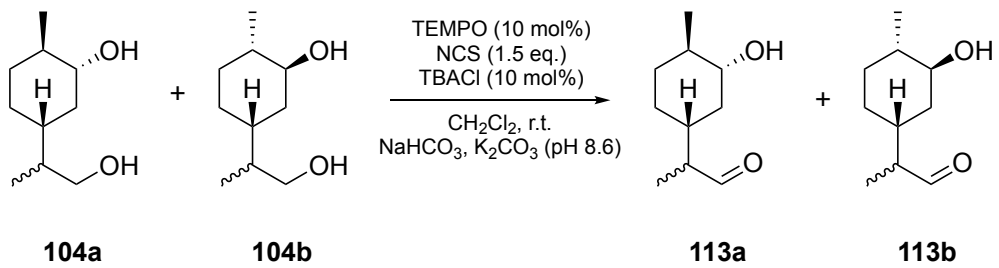
Figure 17*: Eight diastereomers arising from the reduction of* ***112****. Each one is an epimer at the C8 position.*

The third route investigated utilised a chemoselective oxidation of the primary alcohol of **104** over the secondary alcohol to obtain the hydroxy-aldehydes **72**. The aldehydes **72** could be sequentially oxidised to the desired hydroxy-acids **69** *via* a second chemoselective oxidation of the aldehyde over the alcohol (**Scheme 26).**



***Scheme 26**: Proposed synthesis of **105** via* sequential oxidations

TEMPO is able to selectively oxidise primary over secondary alcohols due to the steric bulk of TEMPO and therefore it was chosen as the catalyst for the transformation of **104** to **113** (**Scheme 27**).[111] Conditions developed by Einhorn *et al.* were employed and these used catalytic amounts of TEMPO (10 mol%) and *N*-chlorosuccinamide (NCS) as the stoichiometric oxidant.[113]

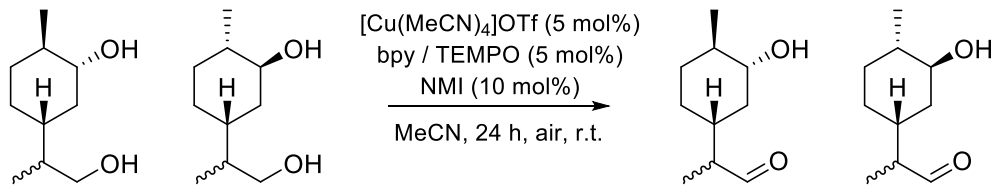


Scheme 27**: Synthesis of **113

The reaction was carried out on a small scale (1.74 mmol) at room temperature and was kept at approximately pH 8.6 using a buffer solution. The reaction was monitored by TLC analysis and was shown to be complete after 1.5 h to yield the required hydroxy-aldehydes **113a** and **113b**, in a 40% yield, as a mixture of four diastereomers **113a'/a''** and **113b'/b''** (d.r. 3:1).

The reaction was scaled up in order to acquire enough **113** to investigate the oxidation of aldehydes **113**. The reaction was repeated on a 34 mmol scale to afford 1.6 g of aldehydes **113** after purification in a 32% yield.

In order to investigate the properties of a monomer, a large amount of material is needed. A 32% yield of the aldehydes **113** after scale up is low and would require a large amount of starting material to synthesise enough monomer. It would also be desirable to replace NCS with oxygen as the stoichiometric oxidant, reducing the amount of waste generated in the synthesis of aldehydes **113**.



104a **104b** **113a** **113b**

***Scheme 28**: Synthesis of **113** using catalytic reagents*

Using conditions developed by Hoover *et al.* aldehydes **113** were synthesised using oxygen from the air as the terminal oxidant (**Scheme 28**) .[114–116] This approach requires the addition of no stoichiometric reagents and therefore generates less waste than the previous synthetic method. The synthesis of **113** was initially trialled on a small scale (2.9 mmol), to yield aldehydes **113** in a 42% yield (d.r. 3:1). The reaction was scaled up (29.1 mmol) and **113** was isolated in a 77% yield (d.r. 3:1).

The two methods highlighted above were compared in order to decide the most appropriate for large-scale synthesis of **113** (**Table 3**).

Table 3**: Table for the comparison of the two methods for the synthesis of **113

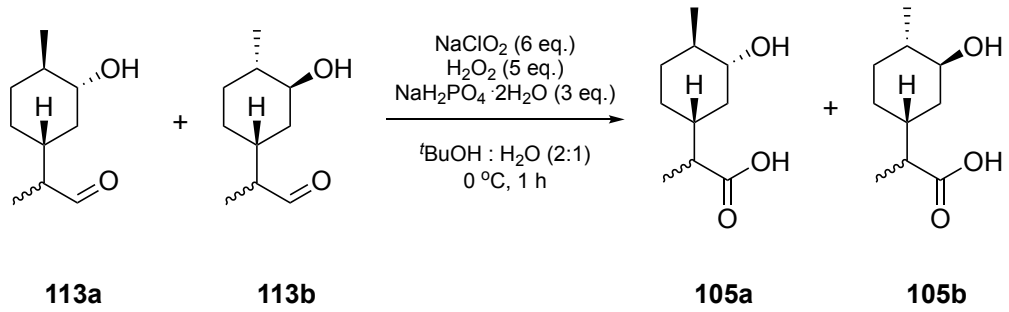
Entry	Catalysts	Mol% of catalysts	Terminal Oxidant	Scale (mmol)	Yield (%)	E-Factor
1	TEMPO / TBACl	20	NCS	34	32	9.7
2	TEMPO/ $[Cu(MeCN)_4]OTf$/ bpy/NMI	20	O_2 (From Air)	29	77	0.6

E-factor is a measure of how efficient a reaction is and is often used as a metric in green chemistry (**Equation 1**).

$$\mathrm{E-Factor} = \frac{\text{Total waste (g)}}{\text{Total product (g)}} \qquad \text{(Equation 1)}$$

The lower the value of the E-Factor, the less waste the reaction generates. Comparison of the E-Factor for the two synthetic methods for the synthesis of **113** indicated that the second method generates less waste. This is primarily due to the use of air as the terminal oxidant (**Table 3**, **Entry 2**). Sheldon *et al.* state that for the synthesis of bulk chemicals the E-factor should be between 1-5 and therefore the copper catalysed oxidation has an extremely low E-factor (0.6).[117] The yields of the scaled-up reactions were also compared and the second method was found to have a much higher yield (77% *vs* 32%) (**Table 3**). Taking these results into consideration it was concluded that future synthesis of the aldehyde **113** should be carried out using the conditions which gave the highest yield and lowest E-Factor (**Table 3**, **Entry 2**).

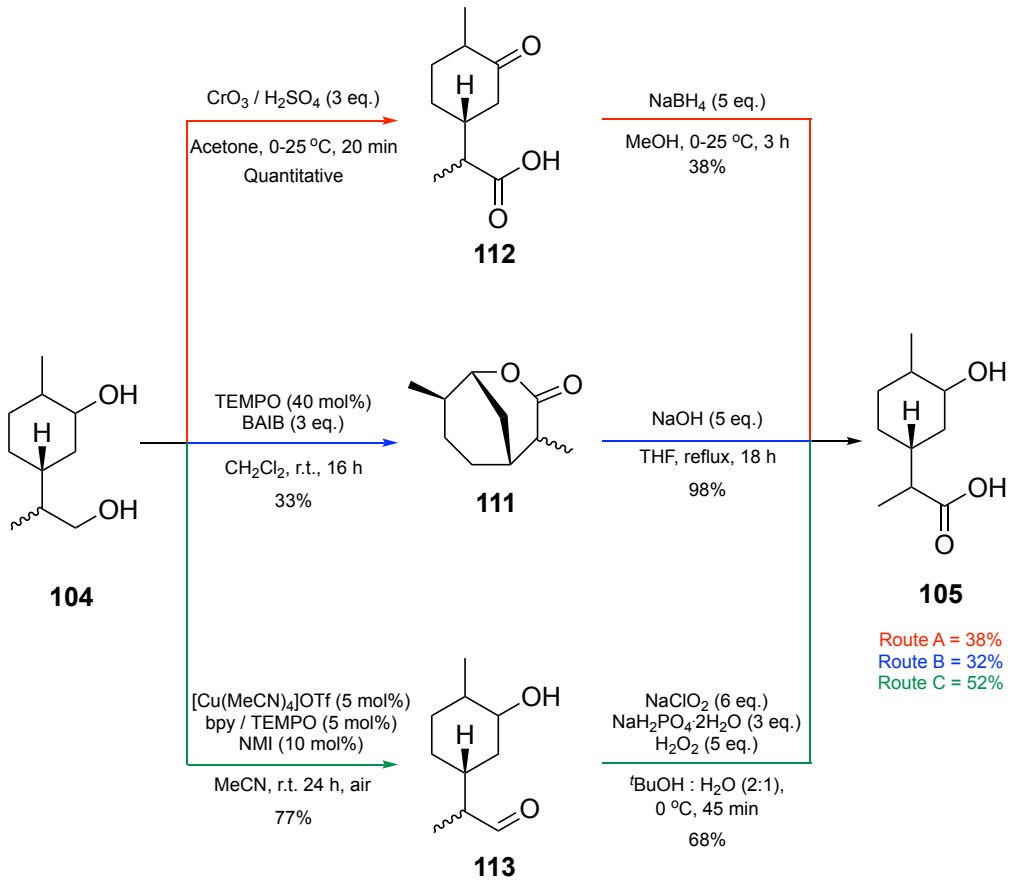
With aldehydes **113** in hand they could now be oxidised to the hydroxy-acids **105**. A Pinnick oxidation was chosen for this transformation as it uses mild conditions which should not oxidise the secondary alcohol (**Scheme 29**).[118,119]



113a **113b** **105a** **105b**

Scheme 29: *Pinnick oxidation of **113** to **105***

A common scavenger used in the Pinnick oxidation is hydrogen peroxide, it was hypothesised that the by-products of the reaction using this scavenger would all be water soluble and therefore would not be isolated. The reaction was repeated using hydrogen peroxide as the scavenger to yield **105a** and **105b** in a 60% yield (d.r. 3:1). The reaction was scaled up (17.5 mmol) to yield the hydroxy-acids **105** in a 68% yield, without the need for further purification.



Scheme 30**: Comparison of three routes for the synthesis of **105

Route A comprises global oxidation followed by ketone reduction, Route B involves oxidative lactonisation and subsequent hydrolytic ring opening, and Route C comprises a two-step chemoselective primary alcohol to carboxylic acid oxidation (**Scheme 30**). The optimised two-step routes were compared in terms of yield, operational simplicity and sustainability (as judged using the metric tool Green Motion™) (**Figure 18**).[120]

One benefit of Route A is its operational simplicity; the synthetic sequence could be carried out in a single working day, without the need for purification of the products using column chromatography. This route did however require the use of super-stoichiometric Jones' reagent, which apart from being toxic, produced a mixture of eight diastereomers, complicating analysis of the reaction mixtures considerably. Route B had a similar overall yield to Route A (38% vs 32%), however purification of the lactone **111** *via* chromatography was required and each step took longer than a

day for completion. Route C was the highest yielding, affording the hydroxy-acid **105** in 52% over two steps (as opposed to 32% and 38% for Routes A and B respectively). Other benefits to Route C are the incorporation of a catalytic protocol for aldehyde formation that utilises molecular oxygen as the terminal oxidant and the mild conditions employed for the Pinnick oxidation. One drawback of this route was that it required purification of **113** using silica gel chromatography.

The tool Green Motion™ was used to evaluate each route with respect to overall sustainability, the lower the impact the environment the higher the rating (100 being ideal). The metric combines the twelve principles of green chemistry with a penalty point system. The use of the toxic Jones' reagent in route A resulted in a score of zero with respect to hazard and toxicity and subsequently the lowest overall score of 38. Route B scores a slightly higher 41 however falls down due to the use of halogenated solvents for the oxidative lactonisation. 53 was the highest score coming from Route C, which scored high due to the use of a catalytic protocol and benign reagents.

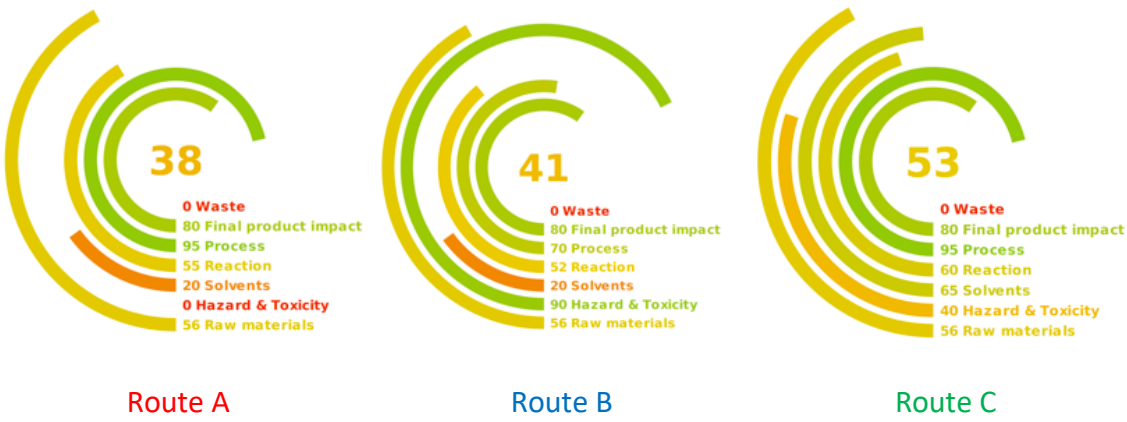


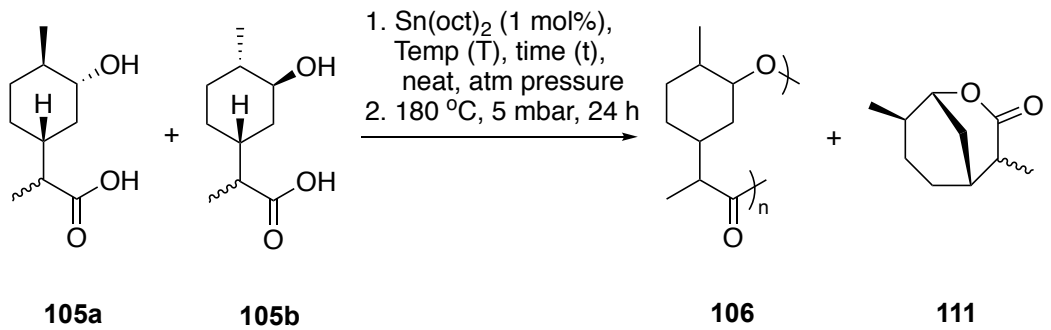
Figure 18: Analysis of the three routes using the metric tool Green Motion

Overall, it was concluded that Route C constitutes a robust and environmentally benign synthesis of **105**, proceeding in reasonable yield over two steps. This route had been scaled up for the synthesis of 2.2 g of monomer **105** which was enough to start the investigation of the polymerisation of **105**. With approximately 3 g of monomer

105 (from the various syntheses of **105**) in hand some initial studies of the polymerisation could be carried out.

3.2. Polymerisation Studies of Hydroxy-Acid 105

Table 4**: Polymerisation studies of hydroxy-acid **105



105a **105b** **106** **111**

Entry	T (°C)	t	M_n (kDa)	Đ	T_g (°C)
1	180	24 h	2.6	1.4	44
2[a]	180	24 h	0.3	1.1	N/A
3	120	24 h	1.2	3.5	-
4	120	1 month	2.2	2.4	44

[a]Reaction performed using **105a** only

The polymerisation was attempted using a two stage method which is commonly used in the literature for the direct condensation of alcohols with carboxylic acids.[8] $Sn(oct)_2$ was used as a catalyst at 180 °C under an inert atmosphere and was then put under vacuum for the second stage of the polymerisation (**Table 4**). ^{1}H NMR analysis of the reaction mixture indicated that initially **105** formed primarily lactones **111** (20 min and 3 h) (**Figure 19**). After 24 h, the concentration of **105b** had started to decrease and a polymer peak at approximately 4.7 ppm had appeared. After 24 h vacuum was applied and the ^{1}H NMR analysis suggested that lactones **111** had been mostly removed under reduced pressure. This left polymer **106**, indicated by the broad peaks at approximately 4.5 and 4.7 ppm. It was hypothesised that these two distinct peaks could be due to the axial and equatorial protons *alpha* to the oxygen in the ester bond (represented by the pink circle (**Figure 19**)). The polymer was analysed using GPC to probe the molecular weight. The analysis showed a broad peak typical of step growth

polymerisation, with molecular weights up to 2.6 kDa. The broad peak and the relatively low molecular weights can be attributed to the sterically hindered nucleophilic secondary alcohol which acts to propagate the reaction.[121] The thermal properites of the polymer were also investigated, dynamic mechanical analysis (DMA) was used to probe the T_g. The analysis showed the polymers has a T_g of 44 °C, this T_g is relatively high despite the polymers being of low molecular weight. It was theorised that this high T_g arose from the *p*-menthane derived backbone, which pleasingly aligned with the original hypothesis.

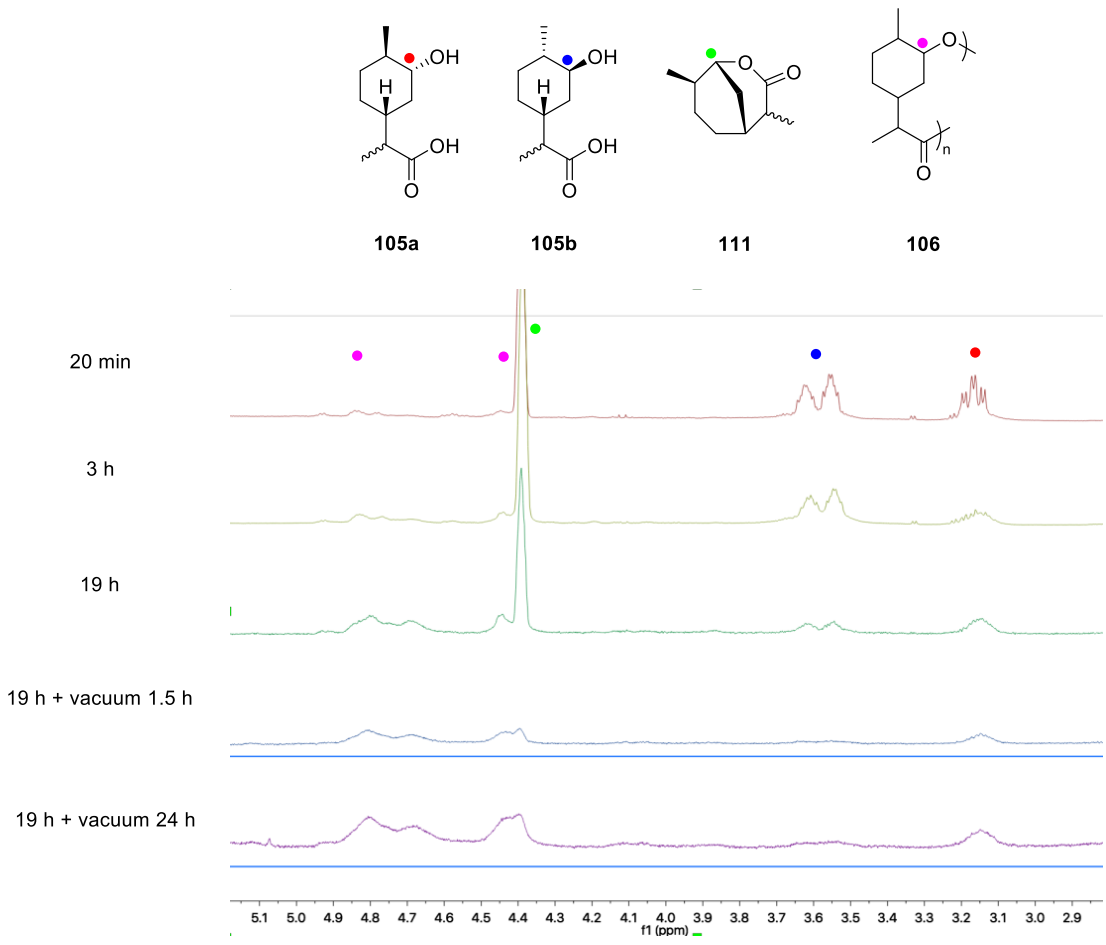
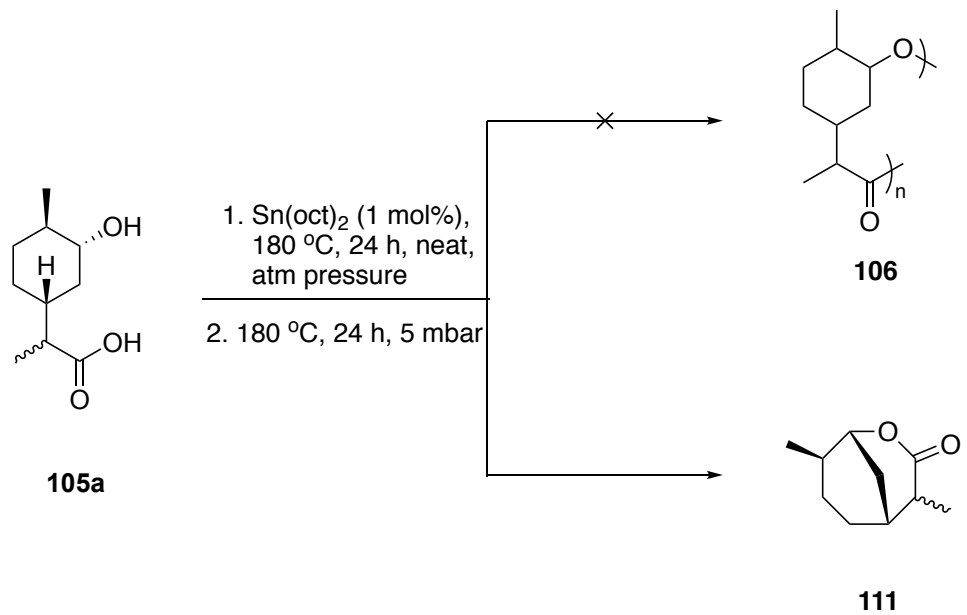


Figure 19**: [1]H NMR analysis of the polymerisation of **105a** and **105b

A di-functional hydroxy-acid is not sufficient to assure formation of polymer, the reaction may proceed intramolecularly with the formation of cyclic products. For example, hydroxy-acids form either (or both) lactone or linear polymer.[96] If the ring size is less than five atoms, or more than seven, open-chain polymer will be almost exclusively formed under ordinary conditions. If a five membered ring can be formed, this will be the single product. If six or seven membered rings can be formed, either, or both, ring and chain polymer are likely to be formed. It was hypothesised that the lactonisation of **105** was only possible for the *cis* isomer **105a,** through the disfavoured 1,5-diaxial conformer of **105a**. Whereby the close proximity of the *endo*-alcohol functionality with the carboxylic acid is sufficient to allow lactonisation and It was speculated that the same is not true for **105b***.* To test this hypothesis hydroxy-acid **105a** (accessed through the hydrolysis of **111**) were subjected to the polymerisation conditions (in the absence of **105b**) (**Table 4**, **Entry 2**). Quantitative conversion to the lactone **111** was observed (^{1}H NMR analysis), with no sign of polymeric species being detected somewhat supporting the theory that **105a** is forming lactone **111** in the polymerisation mixture.



Scheme 31: *Attempted polymerisation of* ***105a***

In an effort to minimise the cyclisation of **105a**, the polymerisation was repeated at 120 °C (**Table 4**, **Entry 3**) as it was hypothesised that a lower temperature would favour the formation of linear polymers over the intramolecular cyclisation. However, analysis using GPC showed that the material was mainly composed of low molecular weight oligomers. Since the lower temperature may be contributing to a slower rate of reaction, the reaction was subsequently repeated for a longer period of time (1 month) (**Table 4, Entry 4)**. ^{1}H NMR analysis suggested that the reaction had gone to full conversion, and the absence of the monomer was confirmed using mass spectrometry analysis.

GPC analysis was used to compare the molecular weights of the three polymerisation attempts (**Figure 20**). As previously mentioned the traces show broad distributions with distinct peaks arising from the step-growth nature of the polymerisation. The traces show a high molecular weight region at approximately 10 minutes retention time. The red trace has a distinct peak at 10 minutes corresponding to an M_n of ~2.6 kDa at a lower temperature of 120 °C it is clear there is a lower proportion of high molecular weight species present after 24 h (green trace). It is however clear that upon leaving the reaction for a longer period of time (1 month) the mixture again contains higher molecular weight species of approximately 2.4 kDa (blue trace). DMA was used to investigate the thermal properties of the polymer resulting from the reaction at 120 °C and 1 month and it was observed to have a similar T_g as the previously analysed polymer (44 °C). Pleasingly both polymers showed high molecular weights of 2.4-2.6 kDa, albeit with high distributions, and T_gs of 44 °C. This T_g is high for an aliphatic polyester obtained from renewable resources, and it is hypothesised this is due to the cyclohexane ring present in the backbone of the polymer.

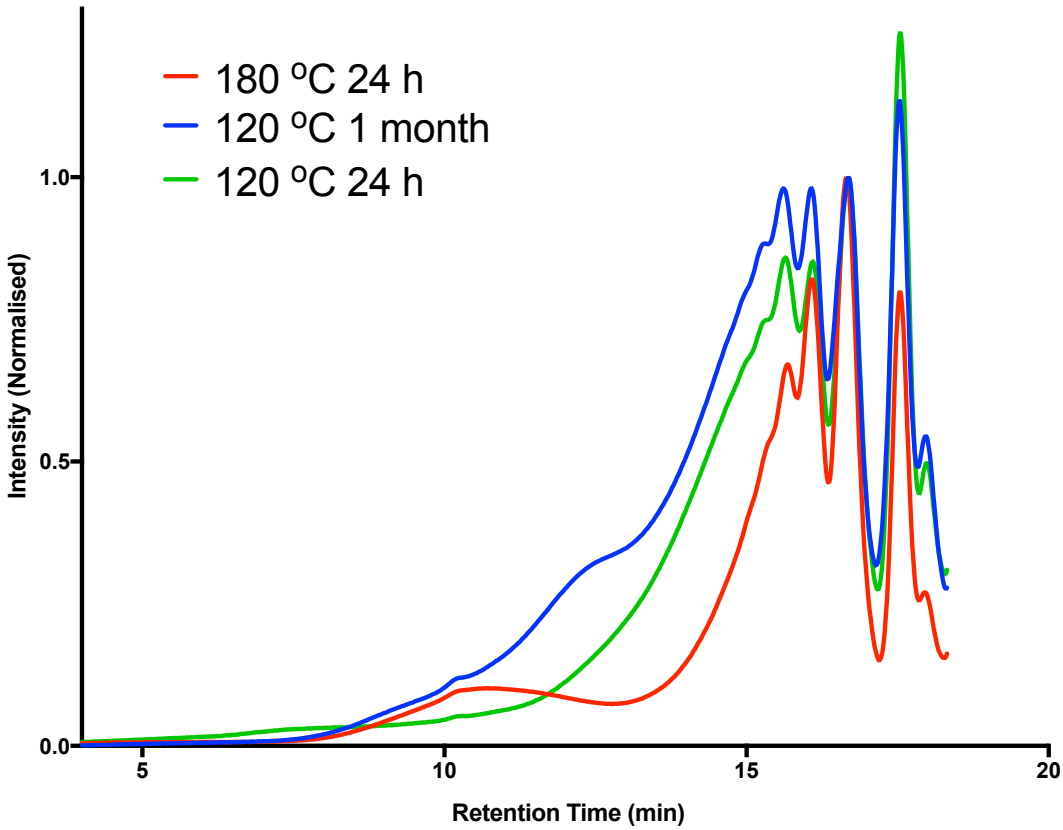


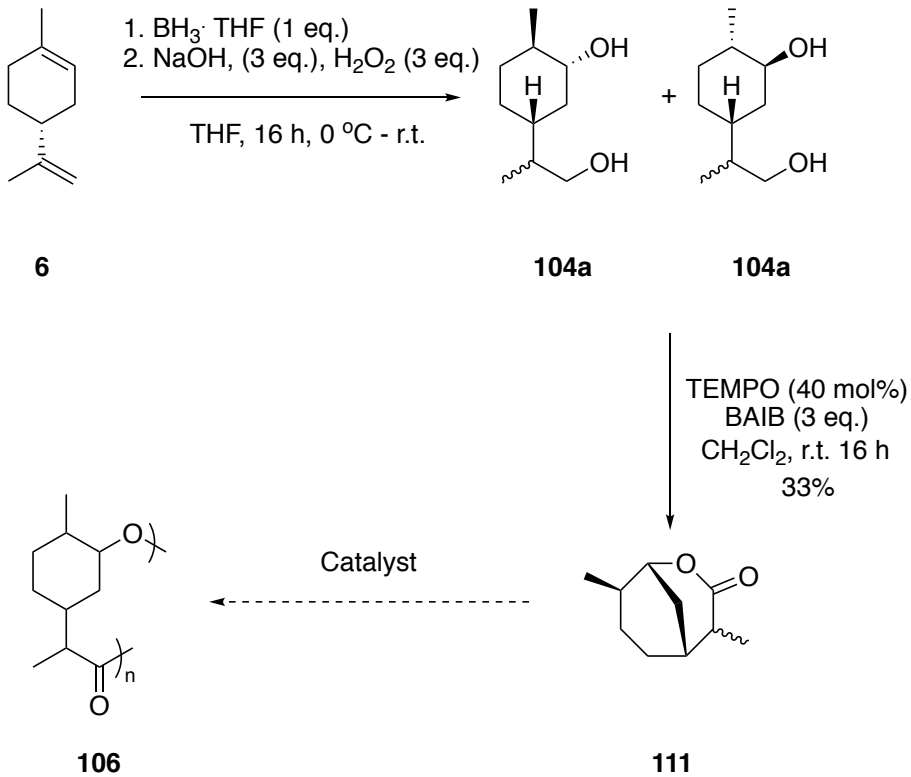
Figure 20**: GPC analysis of the polymerisations of **105

One potential explanation for the slow rate of polymerisation observed with the hydroxy-acids **105a** and **105b** is the somewhat sterically hindered environment of the secondary alcohols. Using DFT analysis it could be inferred that the formation of the lactone *via* **105a** was favoured (ΔG = - 8.3 kcal/mol) over homopolymerisation (ΔG -0.9 kcal/mol) or copolymerisation with **105b** (ΔG = as low as -3.9 kcal/mol). The polymerisation of **105b** is marginally favoured thermodynamically (ΔG = between -0.8 and -1.9 kcal/mol depending on the conformation(s) of **105b** units in the polymer linkage – e.g. axial/axial, equatorial/equatorial, axial/equatorial or equatorial/axial). This somewhat explains the long reaction times and low molecular weights obtained from the polymerisation of **105a** and **105b**. One potential solution to this is to utilise **105a** and **105b** as comonomers in the synthesis of copolyesters.

The renewable polymer **106** was synthesised from the hydroxy-acid **105** to yield a polyester which contains 100% of its carbons from limonene. This is the first example of a terpene-derived polyester, synthesised through step growth polymerisation and containing an exclusively terpene derived backbone. The molecular weights were low (2.6 kDa) however the polyester displayed high T_gs making it an interesting low molecular weight polymer for applications requiring a high glass transition temperature.

3.3. Polymerisation of the Limonene Derived Lactone 111

We were also intrigued to investigate whether the lactone **111**, which had served as an intermediate in the synthesis of **105a,** could itself be utilised as a monomer for synthesis of polyester **106** *via* ring opening polymerisation (ROP).



Scheme 32**: Proposed synthesis and polymerisation of lactone **111

When investigating ROP it is important to take into account the ring strain in the monomer candidate. It is well known that six membered rings are typically stable to ring opening due in part to low ring strain.[122] It is also acknowledged that substituents on the ring decreases the equilibrium monomer conversion. This is especially true for lactones substituted in the *alpha* and *delta* positions.[123,124] The terpene derived lactone **111** is a six membered ring and is substituted in both the *alpha* and *delta* positions meaning that it could be thermodynamically unfavourable for ring opening polymerisation. However, **111** is also a bridged bicyclic system and it was theorised that this would provide the added ring strain needed to facilitate opening of the ring.

3.3.1. DFT Studies of the Lactone 111

DFT calculations were conducted by Antoine Buchard at The University of Bath to probe the potential of **111** for ROP.

Density functional theory (DFT) calculations on **111** were used to probe the thermodynamics of the ring opening of **111** (protocol rM062X-D3/6-311++g(2d,p)/cpcm=ethylethanoate). DFT analysis indicated that the most stable conformation of **111a'** and **111a''** occurs when the cyclohexane ring is in a chair conformation (**Figure 21**).

The driving force for most ROP is the release of ring strain. The enthalpy of polymerisation (ΔH) can be used as a measure of the ring strain, and for polymerisation to be favourable $\Delta H < 0$.[95] The ring strain for the predicted structure was calculated to be at least -6 kcal/mol which implied that polymerisation may be enthalpically favourable. However, the overall ΔG of the polymerisation was calculated as at best +0.6 kcal/mol. This could indicate that the entropic factor of the ROP may counteract the ring opening, although the calculated value of ΔG was in the margin for error for DFT.

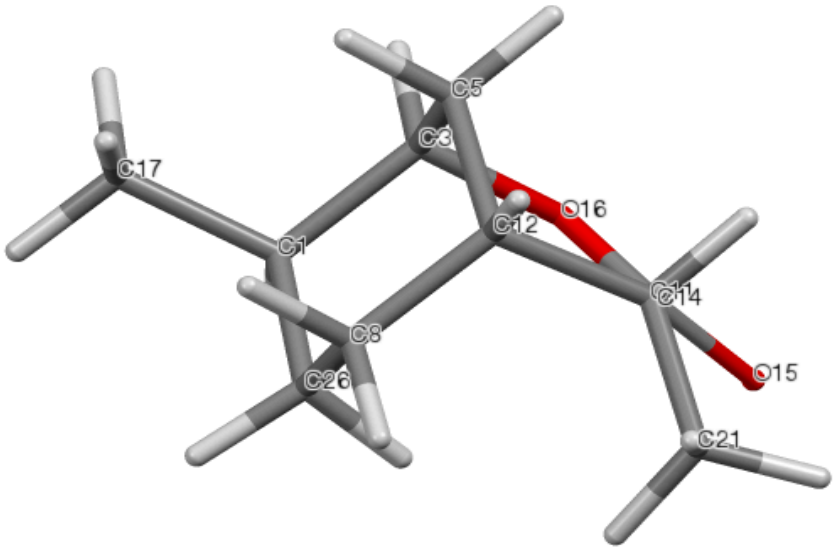


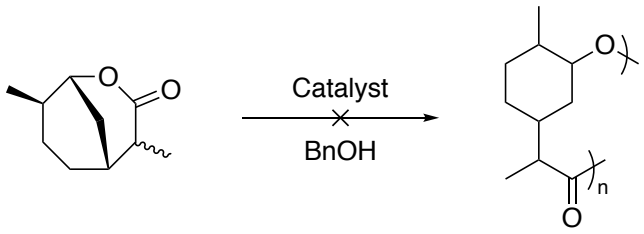
Figure 21: *Calculated favourable conformation of* ***111a''***

To achieve high conversion of a cyclic ester to a polymer it is crucial to minimise the equilibrium monomer concentration. For this reason, low concentrations and temperatures were attempted to favour the equilibrium towards the opened form.[125] After DFT studies indicated that the ROP of **111** could be favourable, It was decided to attempt some polymerisation studies using conditions known to be good for polymerisation of substituted six membered lactones.

3.3.2. Investigations into the ROP of 111

A range of catalysts with literature precedent for the ROP of 6 membered rings were investigated in the synthesis of polymer **106**, included Brønsted acids, Lewis acids, Lewis bases and metal alkoxides (**Table 5** and **Table 6**).

Table 5: *Investigations into the polymerisation of lactones* ***111*** *using different catalysts*



111 **106**

Entry	Catalyst	Cat (mol%)	BnOH (mol%)	Concentration	Time	Temp (ºC)	Polymer
1	$HCl.Et_2O$	1.80	0.6	0.4 M	4 days	25	No
2	$HCl.Et_2O$	1.80	0.6	0.4 M	7 days	100	No
3	$Sn(oct)_2$	0.20	2	Neat	7 days	100	No
4	$Sn(oct)_2$	1	2	Neat	1 month	120	No
5	$Sn(OTf)_2$	0.04	1.2	Neat	6 days	25	No
6	$Sc(OTf)_3$	0.04	1.2	Neat	6 days	25	No

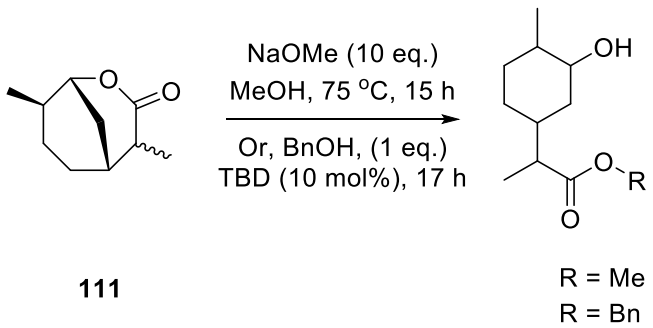
Initial polymerisations were conducted using a Brønsted acid catalyst (**Table 5**, **Entries 1** and **2**) using conditions taken from Lou *et al.*[126] The reaction was carried out at room temperature for four days; however, ^{1}H NMR analysis indicated that the monomer remained intact. The reaction was also repeated at 100 ^{o}C for 7 days. However this also did not lead to a polymer.

$Sn(oct)_2$ is commonly used to perform ring-opening polymerisation of lactones (**Table 5**, **Entry 3**). The conditions were taken from a paper by Cooper *et al.* in which an *alpha* substituted six membered lactone was opened to form a polymer.[127] After 7 days, ^{1}H NMR analysis showed that the monomer had not opened to form a polymer. The reaction was repeated at a higher temperature, however the ring was still left intact, even after 1 month (**Table 5**, **Entry 4**).

Transition metal triflates can be used to open substituted lactones and form polymers, $Sn(OTf)_2$ and $Sc(OTf)_3$ were used (**Table 5, Entries 5** and **6**).[127] These catalysts also proved unsuccessful with the monomer yet again remaining intact. These reactions were also probed using gel permeation chromatography which also confirmed that there were no species of high molecular weight in the reaction mixture. Analysis of the reaction mixture from all of these conditions indicated that not only was a polymer not being formed but also benzyl alcohol was not initiating the reaction.

3.1.1. Initiation and Propagation studies of 111

Polymerisation studies (**Table 5**, **Entries 1**-**5**) were analysed using ^{1}H NMR analysis and it was clear that initiation using benzyl alcohol was not taking place. However DFT suggested that there is enough ring strain in **111** for the ring to open. It was hypothesised that the electrophilic centre of the cyclic ester was sterically crowded which would make it difficult for nucleophiles to attack and open the ring. Control reactions were designed to investigate the ring opening of the lactone using various nucleophiles (**Scheme 33**).



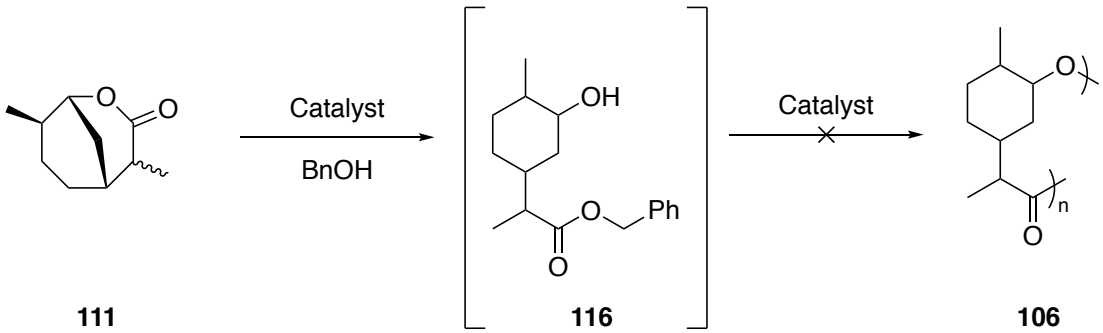
***Scheme 33**: The opening of **111** using NaOMe or BnOH*

Lactone **111** was opened using sodium methoxide indicating that there is enough space for a small nucleophile to attack the carbonyl of **111** (**Scheme 33**). After the successful synthesis of ester **115** it was decided to model the initiation of the polymerisation using benzyl alcohol (**Scheme 33**). After 17 h the reaction was worked up and analysed using ^{1}H NMR spectroscopy which showed that benzyl ester **116** had

been synthesised, however there was also a small amount of starting material **111** still present. This suggested that benzyl alcohol was a good enough nucleophile to open **111** however it is slow.

The synthesis of esters **115** and **116** indicated that it was possible to open the ring of **111** with nucleophiles. After the success of using TBD and BnOH to open **111** further ROP studies were conducted using these conditions, as TBD is a catalyst known for its high activity with respect to ring opening polymerisations.[128,129]

Table 6: *Investigations into the polymerisation of lactone* ***111*** *using a catalyst that induced initiation*



111 **116** **106**

Entry	Catalyst	Cat (mol%)	BnOH (mol%)	Concentration	Temp (ºC)	Result		
						18 h	7 days	6 months
1	TBD	10	1	Neat	25	Initiation only	Initiation only	Initiation only
2	TBD	10	1	Neat	0	Initiation only	Initiation only	N/A
3	TBD	10	1	Neat	120	Initiation only	Initiation only	N/A
4	$Sc(OTf)_3$	10	1	0.9 M	25	Initiation only	Initiation only	Initiation only
5	TBD	100	1	Neat	25	Initiation only	Initiation only	Initiation only
6	DABCO	10	N/A	Neat	25	-	-	-
7	DABCO	10	N/A	Neat	100	-	-	-

10 mol% and 100 mol% of TBD was used to catalyse the ROP of lactone **111** (**Table 6**, **Entries 1**,**2 and 5**). ^{1}H NMR analysis after 18 h revealed that initiation using benzyl alcohol had taken place. The reaction was also repeated at 0 ^{o}C and 120 ^{o}C (**Table 6, Entries 2 and 3**), again ^{1}H NMR analysis detected **116** indicating initiation had taken place. $Sc(OTf)_3$ was used again as a catalyst (**Table 6**, **Entry 4**) as a solution in toluene, this reaction initiated after 18 h with ^{1}H NMR analysis revealing that the benzyl alcohol had been completely consumed.

The reactions in which the polymerisation had initiated were analysed again using ^{1}H NMR after an extended duration (7 days). ^{1}H NMR analysis revealed that the reaction had stopped after initiation and there was no sign of polyesters being formed.

Polymerisations of substituted lactones can often be slow and therefore the three reactions where the polymerisation was initiated were repeated (**Table 6**, **Entries 1**, **4** and **5**) and left for a long period of time (6 months). ^{1}H NMR analysis showed that even after 6 months there was no sign of propagation of the polymerisation, and no high molecular weight polymers present. The complete lack of low molecular weight esters synthesised reinforces the idea that the secondary alcohol cannot propagate the polymerisation and that even after long periods of time the steric factors are the dominating factor preventing polymerisation.

Diazabicyclo[2.2.2]octane (DABCO) is a nucleophilic organocatalyst and It was hypothesised that this could catalyse the ROP of **111**. DABCO is a bulky but highly nucleophilic amine and acts to activate the ester towards nucleophilic attack. It was hypothesised that the sterically hindered, nucleophilic secondary alcohol could react with the acyl ammonium species due to its highly activated nature. The reaction was attempted using 10 mol% of DABCO at 25 and 100 ^{o}C (**Table 6**, **Entries 6** and **7**), however ^{1}H NMR analysis indicated that the monomer remained intact.

The synthesis of **116** suggested that **111** is able to be opened by oxygen based nucleophiles. However, the stalling of the ROP after initiation indicates that propagation by the resulting alcohol **116** is unfavourable. One hypothesis is that the

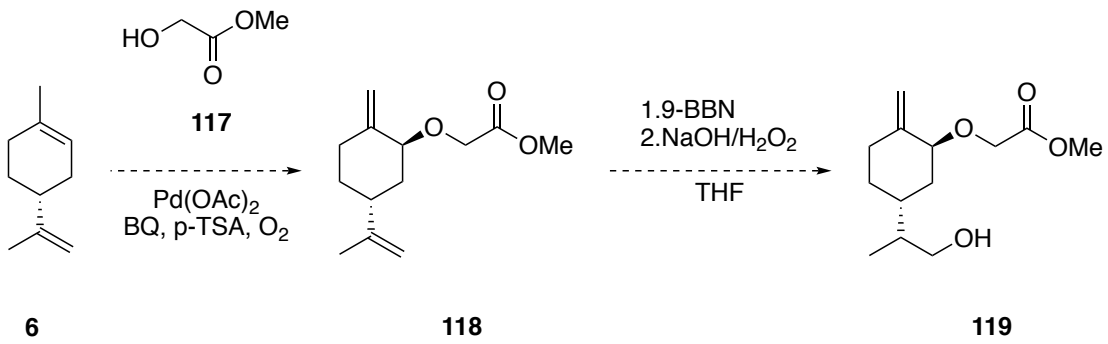
secondary alcohol of **116** was too sterically hindered for the successful approach on the already hindered carbonyl of **111**.

3.2. Conclusions from the Synthesis and Polymerisation of 111

A limonene-derived lactone monomer **111** was synthesised and ROP to form a terpene-derived homopolymer **106** was investigated. The monomer **111** was synthesised directly in two steps from limonene. The second step was optimised to give a moderate yield of 65% over two steps. Monomer **111** was further used for polymerisation studies. Investigation into the ROP revealed that it was unable to form a homopolymer of **111** due to issues in the propagation step of the polymerisation.

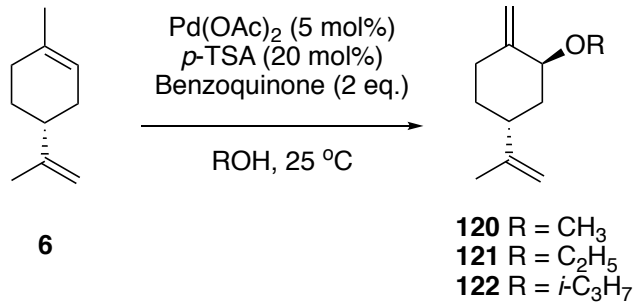
3.3. Towards the Synthesis of a Limonene Derived Hydroxy-Ester

It was proposed that a hydroxy-ester (**119**) could be accessed using palladium catalysis followed by a Brown hydroboration oxidation. This would give a di-functional molecule suitable for step-growth polymerisation, and in this case the monomer would possess a primary alcohol group, meaning that it would be less sterically hindered for the attack on the ester. The monomer would also be less likely to undergo an intermolecular cyclisation due to the resulting ring size being disfavoured (nine membered ring).



Scheme 34: *Proposed synthesis of hydroxy-ester* ***119***

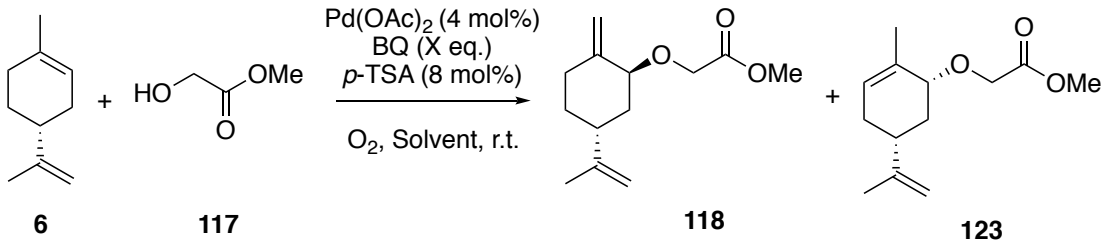
Recent literature published by Gonçalves *et al.* reported the alkoxylation of limonene using various alcohols (**Scheme 35**).[130]



Scheme 35:*The alkoxylation of limonene (**6**) using a $Pd(OAc)_2$ catalyst*[130]

This reaction could introduce a handle for polymerisation such as an ester or carboxylic acid. It was decided to adapt the conditions to synthesise the monomer precursor **118**. In order to synthesise a small molecule capable of participating in polymerisation reactions an ester or carboxylic acid group needed to be introduced into limonene, and it was proposed to be done using the conditions reported by Gonçalves *et al.* (**Table 7**).

Table 7: *Solvent screen for the synthesis of* ***118***



6 **117** **118** **123**

Entry	Solvent	Time (h)	BQ (eq.)	117 (eq.)	Yield 123 (%)
1	THF	6	1	2	0[a]
2	Ethyl Acetate	6	1	2	0[a]
3	Toluene	20	1.6	1	11
4	Toluene	6	1	2	15[a]
5	THF	20	1.6	1	0
6	Ethyl Acetate	20	1.6	1	0

[a] Yields were calculated using quantitative ^{1}H NMR techniques and pyrazine as an internal standard.

To investigate the synthesis of **118** a small initial solvent screen was carried out, using solvents with a range of polarities and properties (**Table 7**).

THF and EtOAc were investigated as solvents, after six hours the crude reaction mixtures were analysed using quantitative ^{1}H NMR with pyrazine as an internal standard (**Table 7, Entries 1-2**). ^{1}H NMR analysis showed starting material remaining.

The reaction was investigated in toluene for 20 h (**Table 7, Entry 3**) and ^{1}H NMR analysis indicated formation of a new product. Purification using silica gel chromatography gave **123** in a 11% yield.

The reaction time was decreased to 6 h (**Table 7, Entry 4**). ^{1}H NMR analysis of the crude mixture from the reaction in toluene showed some starting material remained, however also the appearance of a potential product with an ^{1}H NMR yield of 15%.

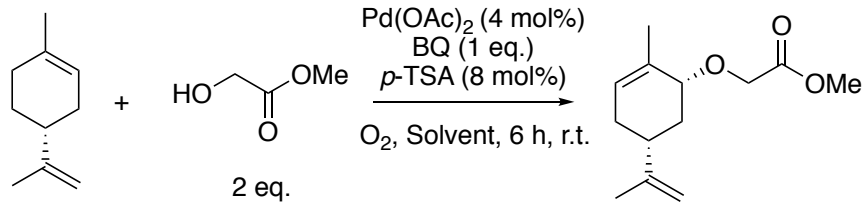
The reaction was repeated for a longer amount of time, (20 h) to investigate whether a longer reaction time would result in full consumption of a starting material (**Table**

7, Entries 5 and **6**). The results were very similar for the reaction at 20 hours and 6 hours, ethyl acetate and tetrahydrofuran both yielded only starting material.

^{1}H NMR analysis of the pure product revealed that methyl glycolate (**117**) had attacked the limonene (**6**) in a different way than was anticipated. The predicted peak for the two vinylic protons on the exocyclic double bond attached to the cyclohexane ring were not present, and instead there was a peak at 5.65 ppm. When integrated this corresponded to one proton and the structure **123** (**Table 7**) was proposed.

It was proposed that **116** could be further functionalised in a selective hydroboration oxidation sequence to synthesise a monomer with the potential to undergo stepwise polymerisation. With this in mind the reaction for the synthesis of **123** was optimised. A more comprehensive solvent screen was carried out (**Table 8**).

Table 8**: Optimisation of the synthesis of **123



6 **117** **123**

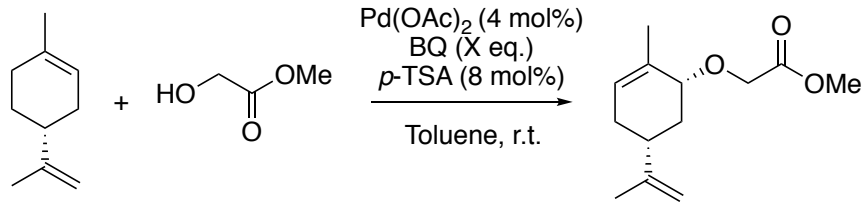
Entry	Solvent	Yield (%)[a]
1	Acetonitrile	Trace
2	DMSO	Trace
3	DMF	Trace
4	Hexane	11
5	Toluene	15

[a]Yields were calculated using quantitative ^{1}H NMR techniques and pyrazine as an internal standard.

The only reactions to produce a clear amount of **123** were those using hexane or toluene (**Table 8**, **Entries 4** and **5**) to give **123** in 11% and 15% yields respectively. Of the six solvents screened only toluene and hexane yielded the desired product **123**,

indicating that non-polar solvents are the most effective. Further optimisation used toluene as the solvent as this had given the best yield (**Table 9**).

Table 9: *Further optimisation of the synthesis of* ***123*** *using toluene as the solvent*



6 **117** **123**

Entry	Time	Temperature (°C)	BQ (eq.)	Atmosphere	117 (eq.)	Yield (%)
1	18.5 h	25	1.6	O_2	1	17[a]
2	18.5 h	25	1.6	O_2	1.5	19
3	18.5 h	25	1	O_2	2	11
4	18.5 h	25	1	O_2	1	18
5	1 week	25	1.6	O_2	1	0
6	51 h	25	1.6	O_2	4	26
7	6 h	50	1.6	O_2	1	0
8	6 h	25	1.6	Air	1	0
9	2 h	25	1	O_2	2	10
10	16.5 h	25	1.6	O_2	1	28

[a]Isolated yield

The initial parameter changed was the equivalents of the reagents **(Table 9, Entries 1-4**). The equivalents of **117** were increased and the equivalents of BQ were decresed as it is a very toxic reagent and either has to be removed by column chromatography or washed with copious amounts of sodium dithionite. These changes didn't seem to influence the yield significantly, giving **123** in yields of 11-19%.

The reaction time was increased to one week (**Table 9, Entry 5**) After one week there was no product observed in the ^{1}H NMR spectrum indicating that longer reaction times does not lead to full consumption and potentially leads to degradation.

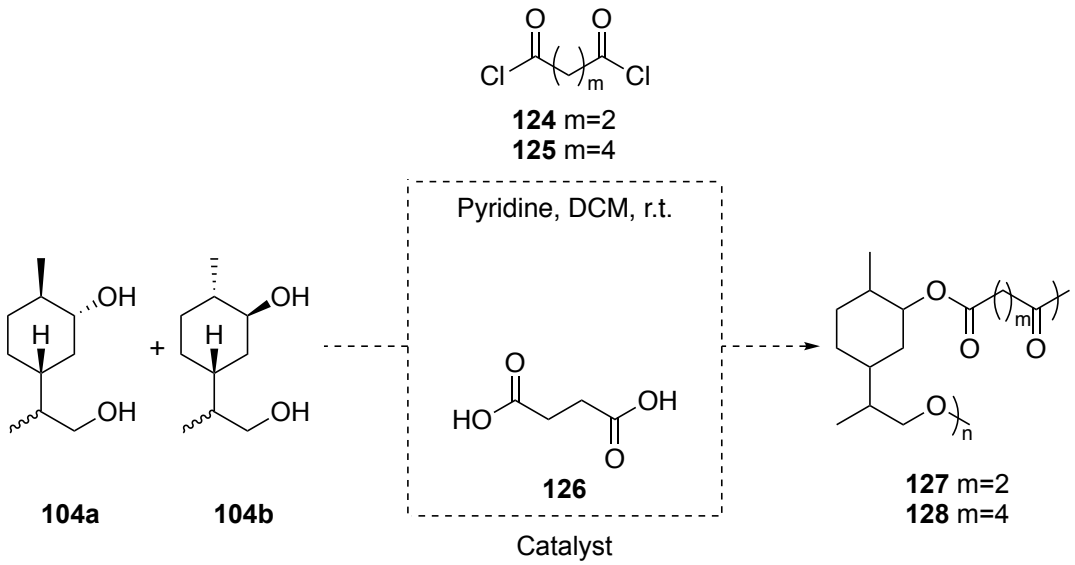
The conditions used by Gonçalves *et al.* the alcohol as both the reactant and the solvent which ensured there was multiple equivalents of the reagent in the reaction, therefore the equivalents of **117** were increased to 4 (**Table 9, Entry 6).** This gave a reasonable yield of 26% however this reaction also had a longer reaction time, (51 h) and the high yield observed could be due to this.

It was hypothesised that heating the reaction could promote full consumption of the starting material, the reaction was heated to 50 ^{o}C (**Table 9, Entry 7**). ^{1}H NMR analysis indicated no formation of the desired product **123** and furthermore no remaining starting material **6**, signifying decomposition during high temperatures. The reaction was carried out in air instead of an atmosphere of oxygen, however showed no formation of the desired product **123**, and only degradation was observed using the ^{1}H NMR analysis (**Table 9, Entry 8**).

The highest yield achieved for this reaction was 28% (**Table 9, Entry 10)**, using the conditions reported by Gonçalves *et al.* with a reaction time of 16.5 hours. However this yield was not deemed to be high enough for a synthetic step in monomer synthesis and for this reason no further investigations into this functionalisation were carried out.

3.4. Synthesis of Polymers from Limonene Diol (104)

Limonene diol **104** was synthesised previously and used as an intermediate in the synthesis of hydroxy-acid **105**, however it was hypothesised that it could be used as a comonomer in the synthesis of polyesters (**Scheme 36**).

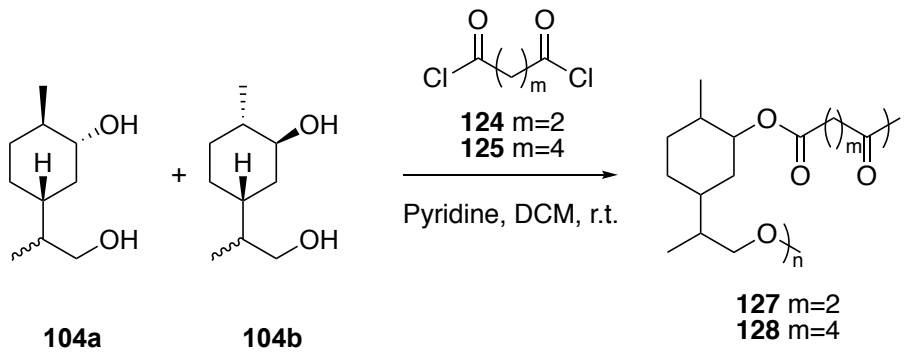


Scheme 36: *Proposed synthesis of polyesters **127** and **128***

3.4.1. Investigations into the synthesis of polymers 127 and 128 using solution polycondensation

It was proposed that the synthesis of polymers **127** and **128** could be accessed through solution condensations with a diacyl chloride or in the melt using a dicarboxylic acid. Adipoyl chloride (**125**) and succinyl chloride (**124**) were investigated to probe the effect of linker chain length on the properties of the polymer.

Table 10: *Investigations into the solution polycondensation of* ***104a*** *and* ***104b***



Entry	Monomer	Time (h)	Py:104	Concentration	Purification	M_n (kDa)	Đ	T_g (°C)
1	**M=4**	16.5	17:1	0.23 M	Organic workup	1.8	2.6	-23.3
2	**M=4**	72	17:1	0.23 M	Organic workup	5.8	3.6	-17.5
3	**M=2**	48	5:1	0.7 M	Precipitation in MeOH	7.2	2.2	11.2
4	**M=4**	48	5:1	0.7 M	Precipitation in MeOH	10.3	3.0	-17.0

Succinyl chloride **124** and adipoyl chloride **125** were chosen as co-monomers because of their relatively short chain lengths (C4 and C6 respectively) in an attempt to make a fairly rigid polymer. Pyridine was selected as the proton trap due to its prevalence in literature for being a good amine for the synthesis of high molecular weight polymers.[131] Gandini and co-workers reported that temperature had little effect on the properties of the resulting polymer and therefore the reaction was carried out at room temperature (~25 °C).[131] 1.1 equivalents of **124** and **125** were used to account for any hydrolysis of the acid chlorides to carboxylic acids which are unreactive under the conditions of the polymerisation. The polymerisations were initially attempted using a low concentration of diol (0.23 M) and a high excess of pyridine (17:1 w.r.t. diol) (**Table 10**, **Entries 1 and 2**). The workup procedure involved washing with $NaHCO_3$, then $CuSO_4$, followed by drying the organic layer over $MgSO_4$, removal of the solvent in *vacuo* to give the polymer which was analysed without further purification. ^{1}H NMR showed evidence that a polymer had formed however, traces of pyridine were still present in the polymer. Hence it was decided to slightly alter the conditions

of the solution polycondensations. The concentration of the diol was increased to ~ 0.7 M and the equivalents of pyridine lowered to a 50% molar excess with respect to the HCl generated (2.5 eq.) (**Table 10**, **Entries 3 and 4**). The polymer was then isolated through precipitation in MeOH to give a pure polymer with no trace of pyridine by ^{1}H NMR (**Figure 22**).

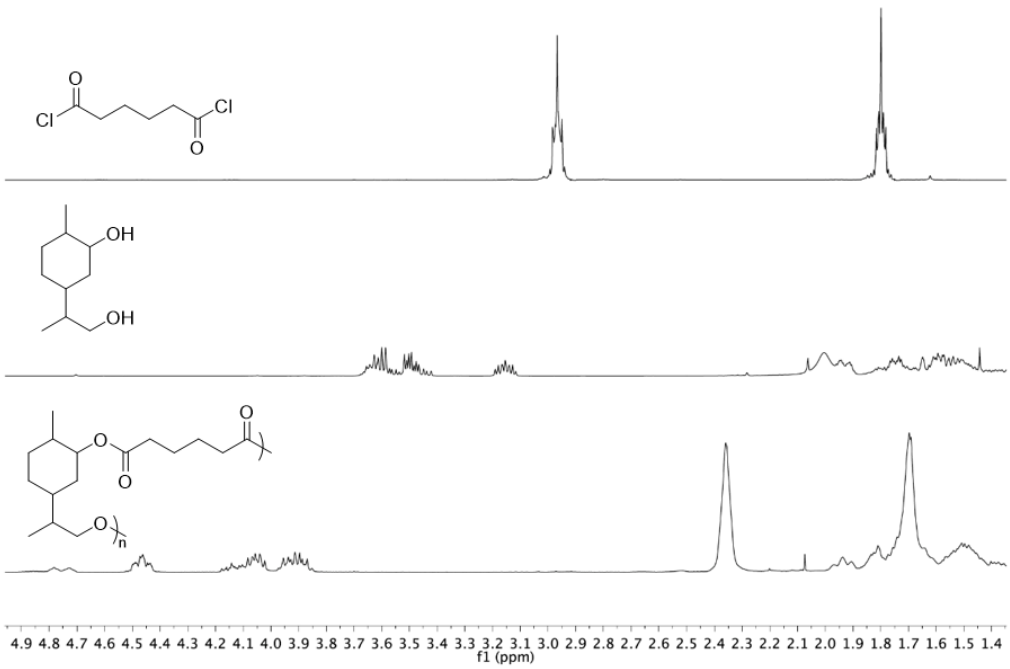


***Figure 22**: From top to bottom, ^{1}H NMR spectra of the acyl chloride, monomer **125** and polymer **128**. The shift in resonances from ~3.5 ppm - ~4.2 ppm is indicative of the formation of ester bonds.*

The polymers were analysed by ^{1}H NMR to probe the consumption of the monomer. ^{1}H NMR of all synthesised polymers displayed no peaks corresponding to any starting monomers indicating that all monomers had reacted. ^{1}H NMR spectra of all reactions using **4** showed a shift in the peaks for the protons at 3.63-3.36 ppm and 3.10 ppm which correspond to the protons *alpha* to the hydroxyl groups, suggesting that all the hydroxyl groups of monomer **104** reacted with **124** or **125** to form esters (**Figure 22**). The ^{1}H NMR shows the formation of the polymer as the peaks c and d (from the acyl chloride) have shifted downfield compared to the monomer indicating the ester has been formed, the peaks have also broadened which is further evidence the polymer has been formed.

Analysis using GPC confirmed the successful synthesis of polymers, which have eluted at times between 6.5 and 8.5 min. The polymers synthesised using solution polycondensations followed by precipitation in methanol gave the highest molecular weights, 7-10 kDa **(Table 10**, **entries 3** and **4**). This suggested that the best conditions for solution polycondensation are a high concentration of diol, a ratio of pyridine to diol of 4:1 and isolation through precipitation in MeOH. These should be further investigated and optimised, potentially by changing the time, the temperature or the concentrations of reagents. Molecular weights of between 7.2 and 10.3 kDa are promising starting points for the synthesis of high molecular weight polymers and clearly demonstrates synthesised diol **104** can be used to produce polyesters derived from terpenes (**Figure 20**).

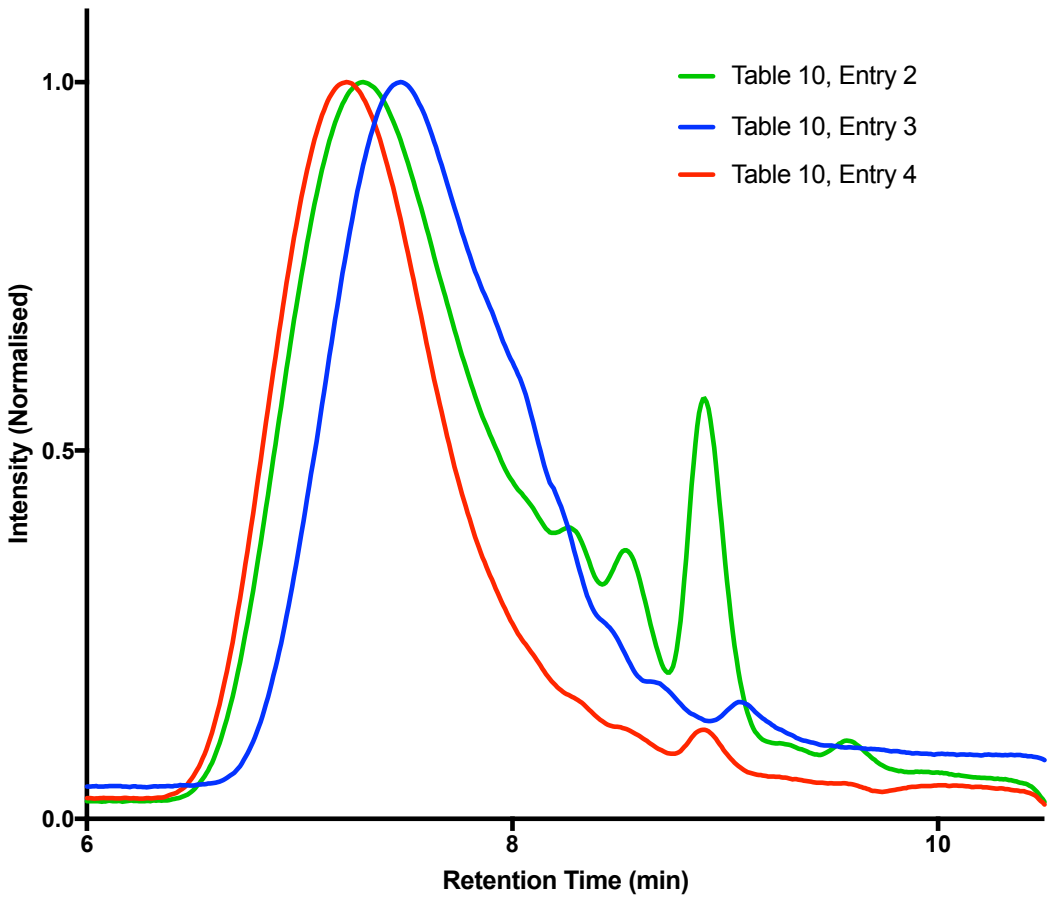
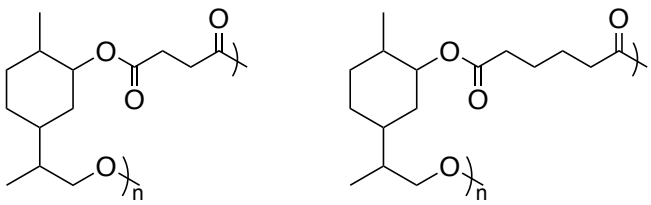


***Figure 23**: GPC traces for the solution polycondensation of **104** with adipoyl chloride (**125**) and succinyl chloride (**124**)*

DSC was employed to conduct thermal analysis of the polymers produced using solution polycondensation reactions, and this allowed the calculation of T_gs for polymers with an M_n of or above 1 kDa (**Table 10**). The highest T_gs (11.2 ^oC) were those with the highest molecular weights and the shortest linker which is usually the general trend for polymers.[132] The polymers using **124** had a higher T_g than those which contained **125** as their co-monomer. This is believed to be due to the longer carbon chain length, which gives the polymer a higher degree of flexibility and therefore a lower T_g. The polymers synthesised all had fairly low T_gs (below room temperature) and this indicated the potential for uses in coating applications due to their high flexibility.

The polymers were analysed using matrix assisted laser desorption ionisation (MALDI) spectrometry. The MALDI spectra of polymers **127** and **128** (**Table 10**, **Entries 2** and **3**) show a pattern common with polymers of a certain repeating unit (**Figure 26**). The MALDI spectrum of polymer **127**, has a repeating unit of 254 mass units which is equal to one molecule of **104** coupled with one molecule of **124**, (**Figure 24**).



127 **128**

***Figure 24**: From left to right repeating units of **127** and **128** confirmed by MALDI spectrometry.*

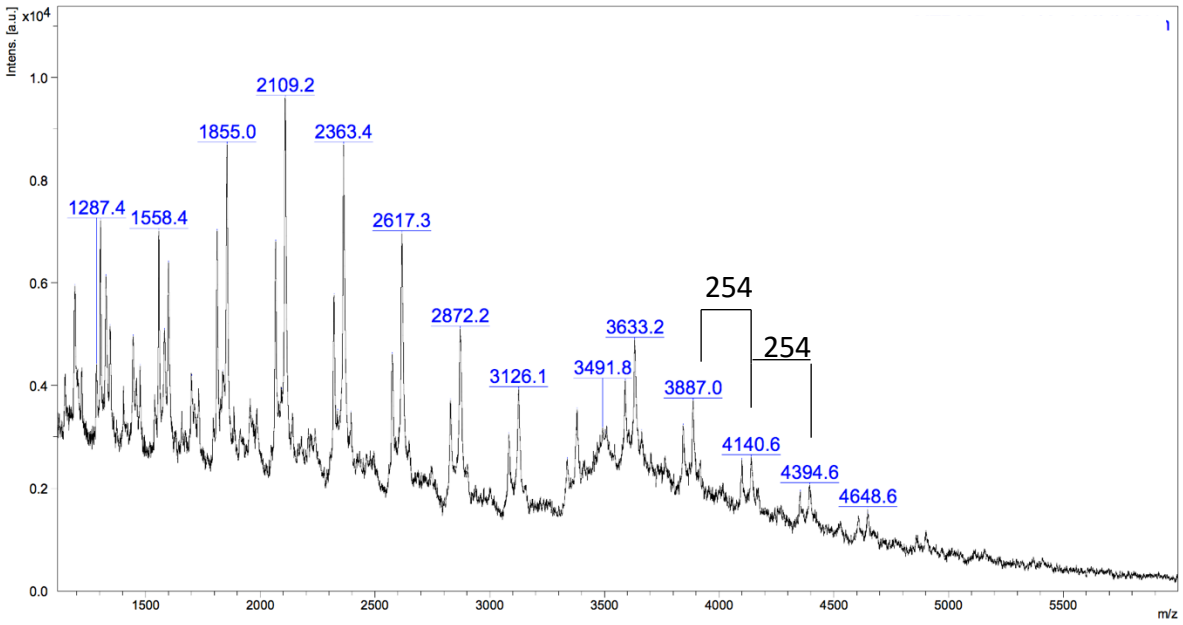


Figure 25: *MALDI spectrum of* ***127****.*

MALDI spectrometry analysis of **128**, indicates a repeating unit of 282 mass units (**Figure 26**). This is consistent with the structure drawn, suggesting the repeating unit is one molecule of **104** coupled with one molecule of **125**.

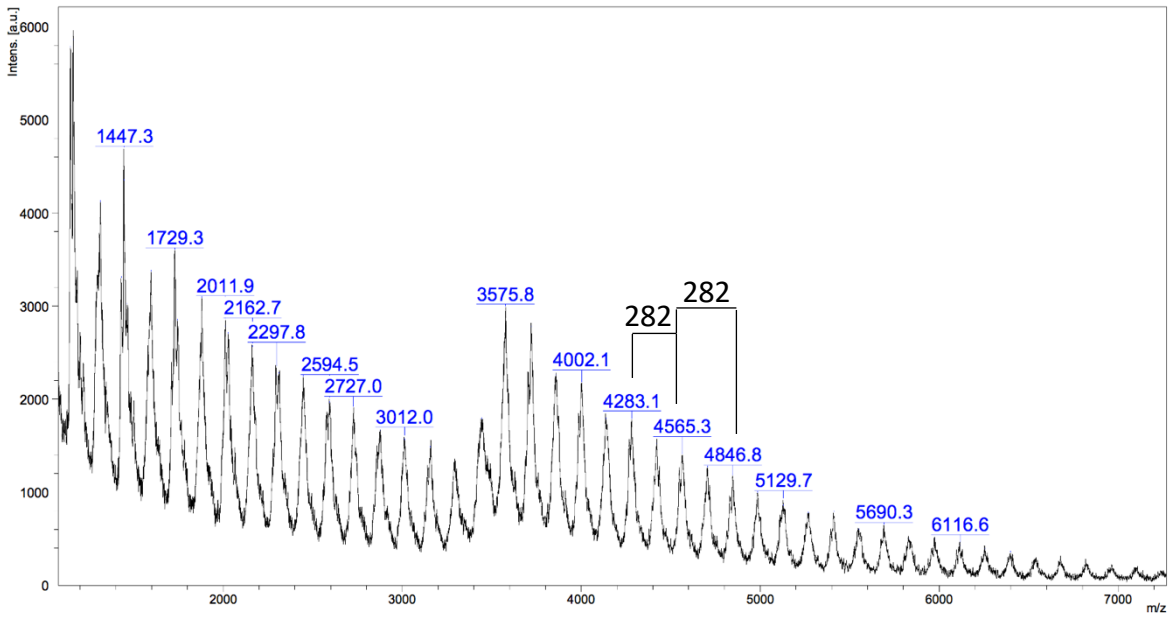


***Figure 26**: MALDI spectrum of **128**.*

The MALDI spectra of both polymers (**127** and **128**) display two distinct sets of polymers, this could be due to different end groups, for example it is expected that the polymers could be capped with either acid of alcohol end groups.

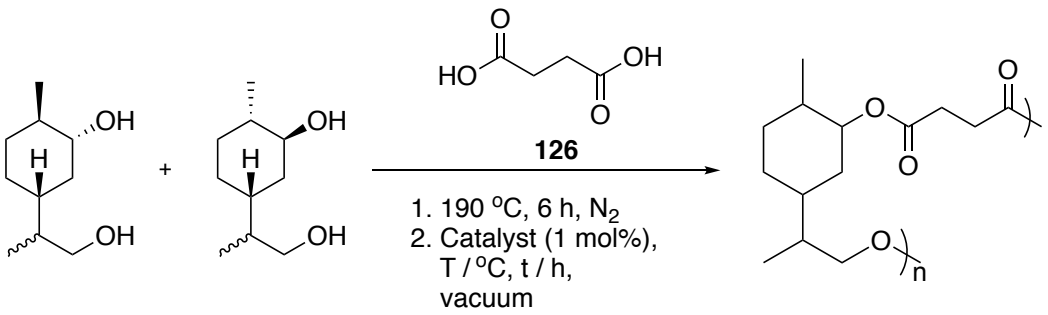
3.4.2. Investigations into the synthesis of polymer 127 using melt polycondensation

The previously discussed solution polycondensations had produced polymers with moderate molecular weights, however it was desirable to attempt to push the molecular weights higher. Melt conditions are well known in the literature for the direct synthesis of polyesters from diols and diacids. High temperatures and low pressures are used to help to push the equilibrium of the polymerisation and achieve high molecular weights. It can also be seen as beneficial from a green chemistry perspective as it doesn't require chlorinated solvents and uses a renewable diacid as a comonomer (as opposed to an acyl chloride which currently cannot be accessed from biomass). Succinic acid (**126**) was selected as co-monomer due to its established availability from renewable resources[133]; it was envisaged that co-polymerisation of **104** and **126** would yield the entirely bio-based polyester **127** (**Table 11**). Conditions

precedented for the melt polymerisation of diols and diacids were initially selected (**Table 11**).

The polymerisations were initially performed using a two-step method where the diol and diacid were heated under a flow of nitrogen for 6 hours at 190 °C, $Sn(oct)_2$ was then added and the reaction was put under vacuum for 24 h (**Table 11**, **Entry 2**). The polymerisation was analysed using ^1H NMR spectroscopy and the resulting spectrum showed the same resonances as the polymer previously synthesised using solution polycondendsation and this indicated that again the polymer **127** had been synthesised. The polymer was also analysed using GPC to elucidate the molecular weight. The molecular weight was found to be 20.7 kDa, which is a significantly higher than any of the molecular weights achieved using solution polycondensation. The thermal properties were analysed using DMA and the T_g was found to be 21 °C again this is higher than those synthesised previously and this is presumably due to the increase in molecular weight.

***Table 11**: Investigations into the melt condensation of diol **104** with succinic acid*



104a **104b** **127**

Entry	Catalyst	T2 /°C	t2 / h	M_n / kDa	T_g / °C	Đ
1	$Ti(OBu)_4$	190	24	18.4	6	2.4
2	$Sn(oct)_2$	190	24	20.7	21	2.5
3	N/A	190	24	9	-7	1.7
4	$Ti(OBu)_4$	230	24	11.2	4	1.5
5	$Sn(oct)_2$	230	24	10.1	15	1.5
6	N/A	230	24	9.2	19	1.4
7	$Ti(OBu)_4$	230	3	30.4	16	2.5
8	N/A	230	3	9.3	6	1.3
9	$Sn(oct)_2$	230	3	28.3	23	2.3

One of the major challenges dealt with in polymer syntheses is undoubtedly the use of renewable resources which supports the sustainability of the process, however simply using renewable starting materials is not enough. It is also important to consider the greenness of the process by developing convenient synthetic pathways, avoiding hazardous and toxic substances and using more eco-friendly conditions.[6,134] Finding a replacement for highly efficient tin containing polymerisation catalysts is a prevalent area of research. One of the most commonly employed catalysts for condensation polymerisation is $Sn(oct)_2$, however the use of this species raises concerns with respect to sustainably. One class of catalysts that can be considered a greener alternative are the titanium alkoxide complexes,[8,135] whose environmental benefits arise predominantly from the fact that titanium is generally non-toxic and earth abundant.[136] The polymerisation of **104a** and **104b** with succinic acid was investigated using $Sn(oct)_2$ and $Ti(OBu)_4$ as catalysts and the results were compared by GPC analysis. The polymerisation using the catalyst $Sn(oct)_2$ was compared to using $Ti(OBu)_4$ and a control reaction which was catalyst free (**Table 11**, Entries 1-3). The polymerisations using the different catalytic systems were compared using ^{1}H NMR and GPC analysis. ^{1}H NMR analysis indicated that all three systems had gone to full conversion from the complete disappearance of the monomer. GPC analysis was used to probe the molecular weights and pleasingly comparable results were achieved using both $Sn(oct)_2$ and $Ti(OBu)_4$ (**Figure 27**).

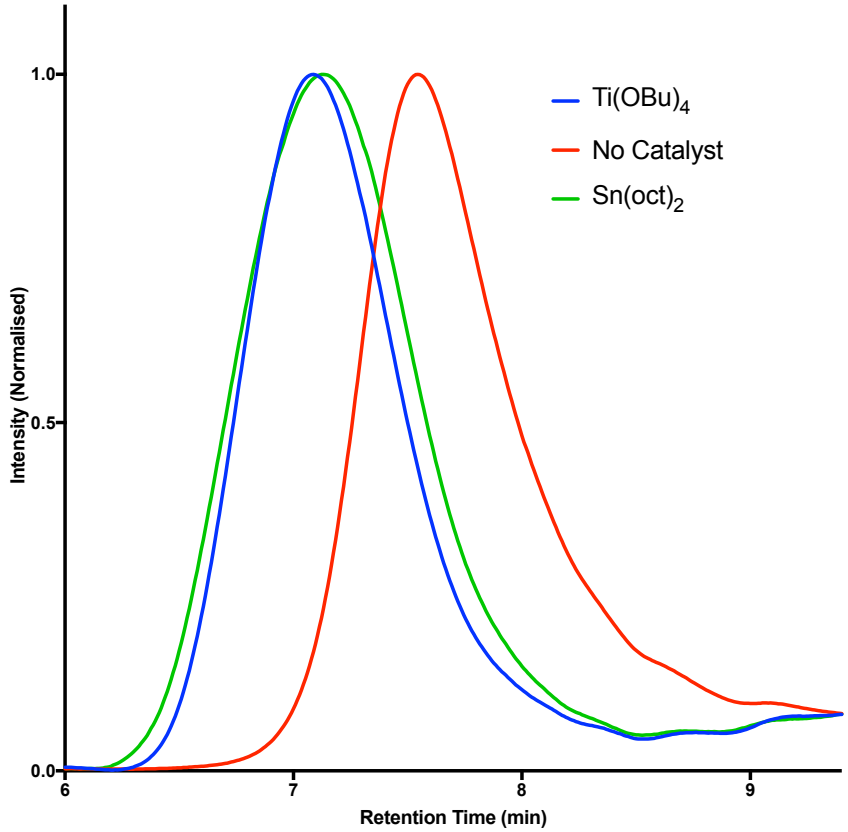


***Figure 27**: GPC traces of the polymerisation of **104** and **126** using different catalytic systems*

The systems using both $Sn(oct)_2$ and $Ti(OBu)_4$ both resulted in polymers of similar molecular weights (18-20 kDa). The system which didn't use a catalyst resulted in a polymer of a lower molecular weight (9 kDa) which is to be expected when the system doesn't have a metal catalyst, however polymers with a molecular weight of 9 kDa are desirable especially when there isn't a need for a metal catalyst in the reaction. DMA was used to probe the T_gs of the polymers (**Table 11**) and the T_gs were found to be below room temperature (-7-21 ^oC). These results indicate that these polymers are able to be synthesised using either a tin or titanium catalyst, which from a sustainability perspective is promising.

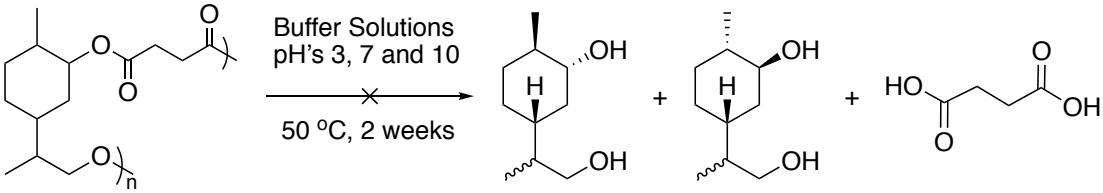
The reaction temperature was increased to 230 ^oC in order to study the effect of tempertature on the resultant polymers. It was hypothesised that a higher temperature could facilitate the synthesis of higher molecular weight polymers (**Table 11**, **Entries 4-6**).

The polymerisations conducted under higher temperatures were found to be of a lower molecular weight than the previously synthesised polymers (9-11 kDa) it was hypothesised that this could be due to the polymer being heated above its ceiling temperature for an extended period of time. The reactions were subsequently repeated for a shorter period of time at the elevated temperature (**Table 11**, **Entries 7-9**). GPC analysis indicated that the polymers synthesised under these conditions using $Sn(oct)_2$ or $Ti(OBu)_4$ had high M_ns of between 28-30 kDa. These were the highest achieved for the polymerisation of diol **104** and succinic acid (**126**), again the system not using a catalyst achieved molecular weights of ca. 9 kDa. These molecular weights are the highest achieved for the polymerisation of **104** and **126** indicating that the optimised conditions for this system is to perform the polymerisation at 230 ^{o}C for the shorter period time of 3 h.

The polymerisation of the limonene derived diol **104** with succinic acid (**126**) were successful and yielded novel aliphatic polyesters with reasonably high molecular weights (up to 30 kDa). Succinic acid (**126**) can be derived from renewable resources and therefore the polyester synthesised can be classed as coming from 100% renewable biomass, with a large percentage of the polymer arising from terpenes.

3.5. Investigations into the Degradation of Polymer 127

End of life solutions are an important and often overlooked area of polymer research. As the prevalence of plastics in our environment increases it is becoming more and more critical for chemistry to design end of life solutions into polymers.[137] It was therefore decided to investigate the potential for polymer **127** to degrade. Initially the polymer **127** was investigated for hydrolytic degradation.



127 **104a** **104b** **126**

***Scheme 37**: Attempted degradation of polymer **127** under hydrolytic conditions.*

Polyesters have ester linkages along the backbone, and these bonds are known to be susceptible to hydrolysis. This means that in theory the bonds could be broken and the monomers reclaimed. The hydrolysis was attempted under acidic, neutral and basic conditions using buffer solutions (**Table 12**).

Table 12**: Hydrolytic degradation studies of **127

Entry	Buffer	pH	Degradation
1	Citric acid	2.5	No
2	Phosphate	7	No
3	Sodium carbonate	10.7	No

The polymer was weighed into a vial and solubilised in CH_2Cl_2, the solvent was then allowed to evaporate leaving a disc in the vial, which was then dried to constant weight under vacuum. The buffer solutions were then added, and the solutions heated to 50 °C for 2 weeks. The polymers were analysed using ^{1}H NMR spectroscopy and GPC, to probe for the existence of high molecular weight species. After two weeks the aqueous solution was decanted off and the remaining solid dried under vacuum to a constant weight. The solid was found to be the same weight as it was before being submitted to the degradation studies. The solid was analysed using ^{1}H NMR, the peaks between 4.8 and 3.9 ppm (representing the proton *alpha* to the ester bond) indicate that the ester bonds in the polymer remained intact (**Figure 28**).

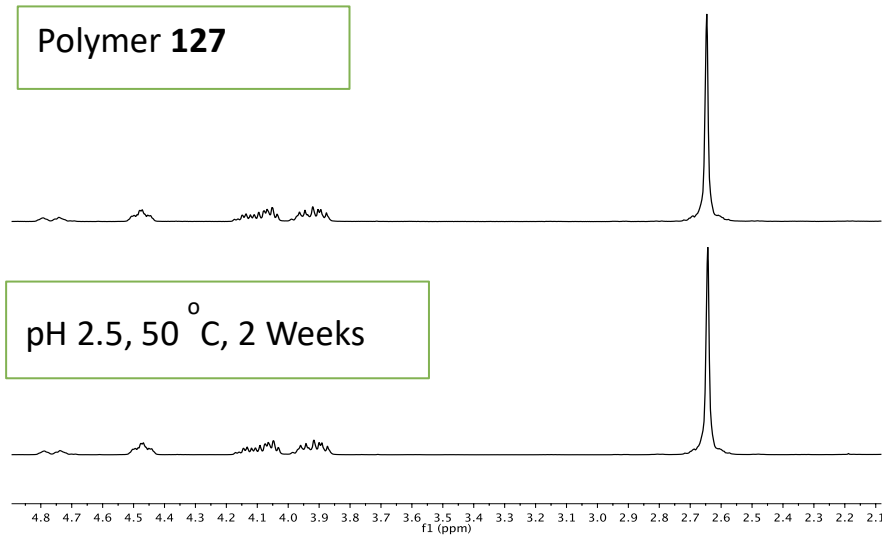


Figure 28: *^{1}H NMR analysis of **127** before and after degradation experiments.*

The remaining solid was also analysed using GPC, as it was hypothesised that a small amount of hydrolysis could have taken place, which would be undetectable using ^{1}H NMR spectroscopy however there could be a decrease in the molecular weight. The three samples were analysed against the original polymer and the traces indicated that the polymers had remained intact. The original polymer showed a retention time of ~16 min and this was also the case for the polymers after hydrolytic degradation studies (**Figure 29**).

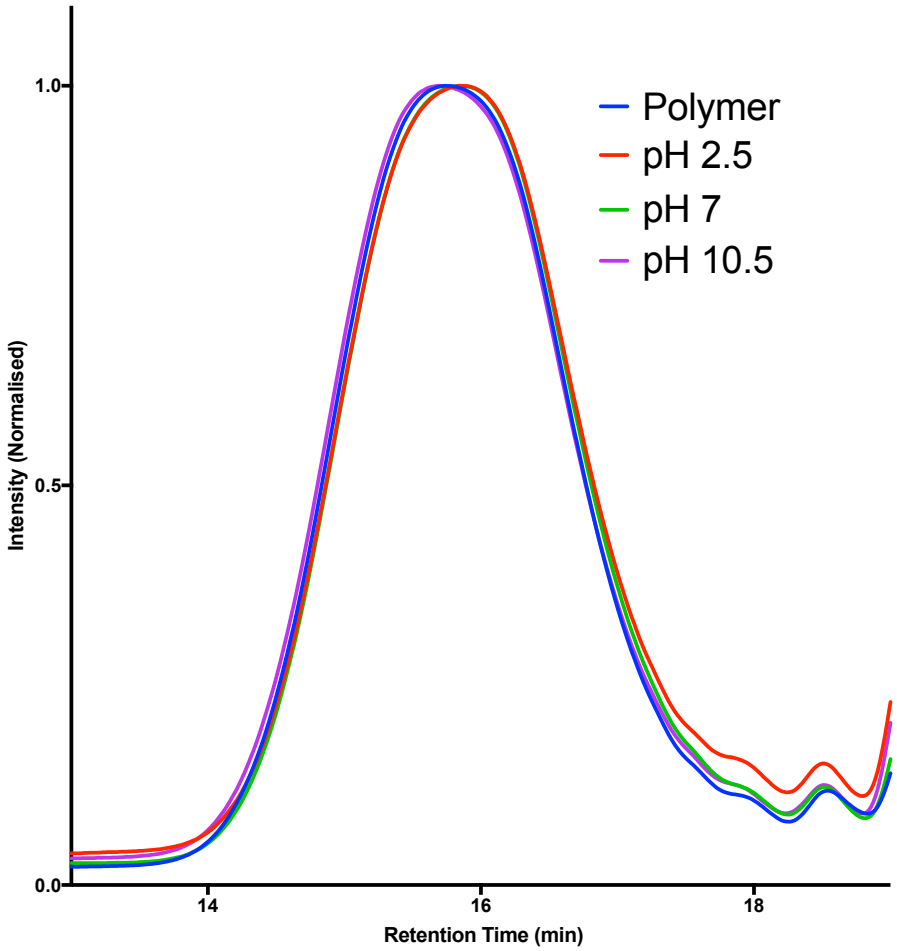
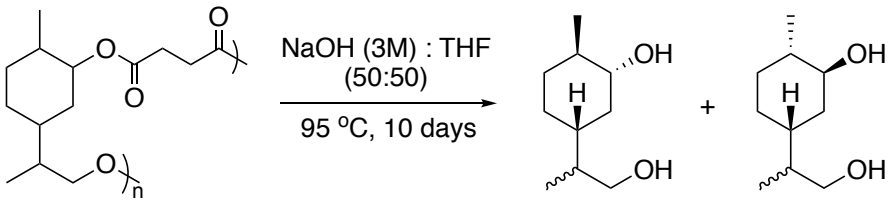


Figure 29: GPC analysis of **127** before and after hydrolytic degradation experiments

It was theorised that the polymers were not degrading due to poor solubility in the aqueous media. It was therefore decided to attempt the degradation study again using a mixture of aqueous and organic solvents (**Scheme 38**).



127 **104a** **104b**

Scheme 38**: Degradation studies of **127

The degradation was attempted again under basic conditions using sodium hydroxide (3 M) in THF (1:1). The reaction was heated to 95 °C for 10 days, the THF was removed under reduced pressure and the mixture subjected to an acid wash followed by an extraction.

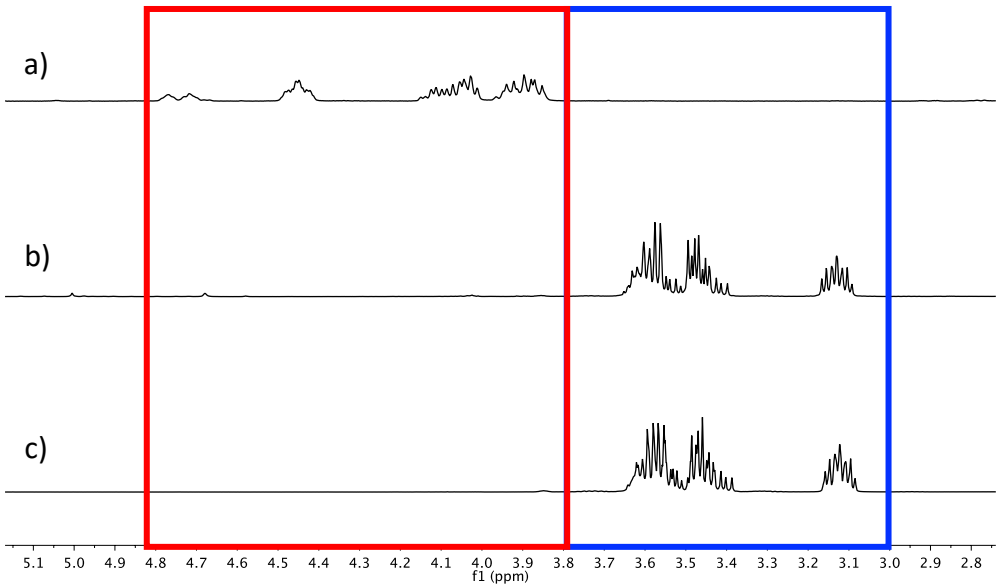


Figure 30: *^{1}H NMR analysis of the decomposition of polymer of **127** using NaOH : THF (1:1). a) Polymer **127** b) monomer **104** c) Polymer after degradation experiment.*

The crude residue was analysed using ^{1}H NMR spectroscopy. The polymer has resonances between 4.8 and 3.8 ppm corresponding to the proton *alpha* to the ester bond (**Figure 30**, Spectrum a), after the degradation experiment the ^{1}H NMR shows no resonances in the region of 4.8 and 3.8 ppm, indicating the ester bonds have broken. The analysis of the crude residue indicated that not only had the polymer degraded but in fact the monomer had been reclaimed to the same purity as the monomer when it was used for the polymerisation (**Figure 30**, Spectra b and c). The monomer **104** was recovered in excellent purity by simple extraction into CH_2Cl_2. This opens up the potential to recycle the polymer **127** and create a closed, circular system. GPC analysis also indicated that the polymer had degraded, the disappearance of the peak at a retention time of ~30 min indicates there is a loss of high molecular weight species (**Figure 31**).

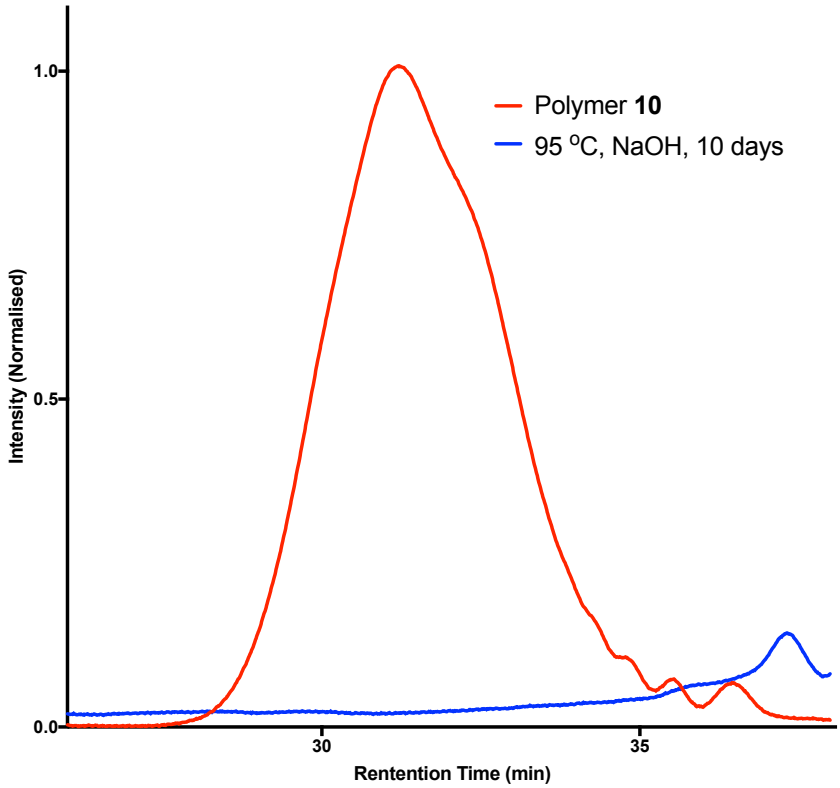
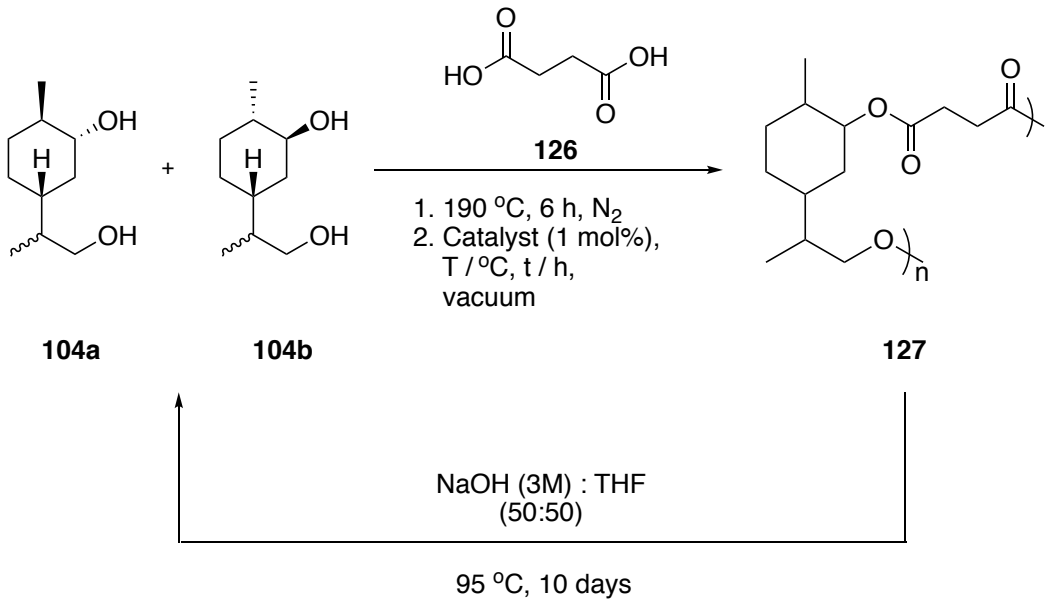


Figure 31: *GPC analysis of the degradation of* ***127***

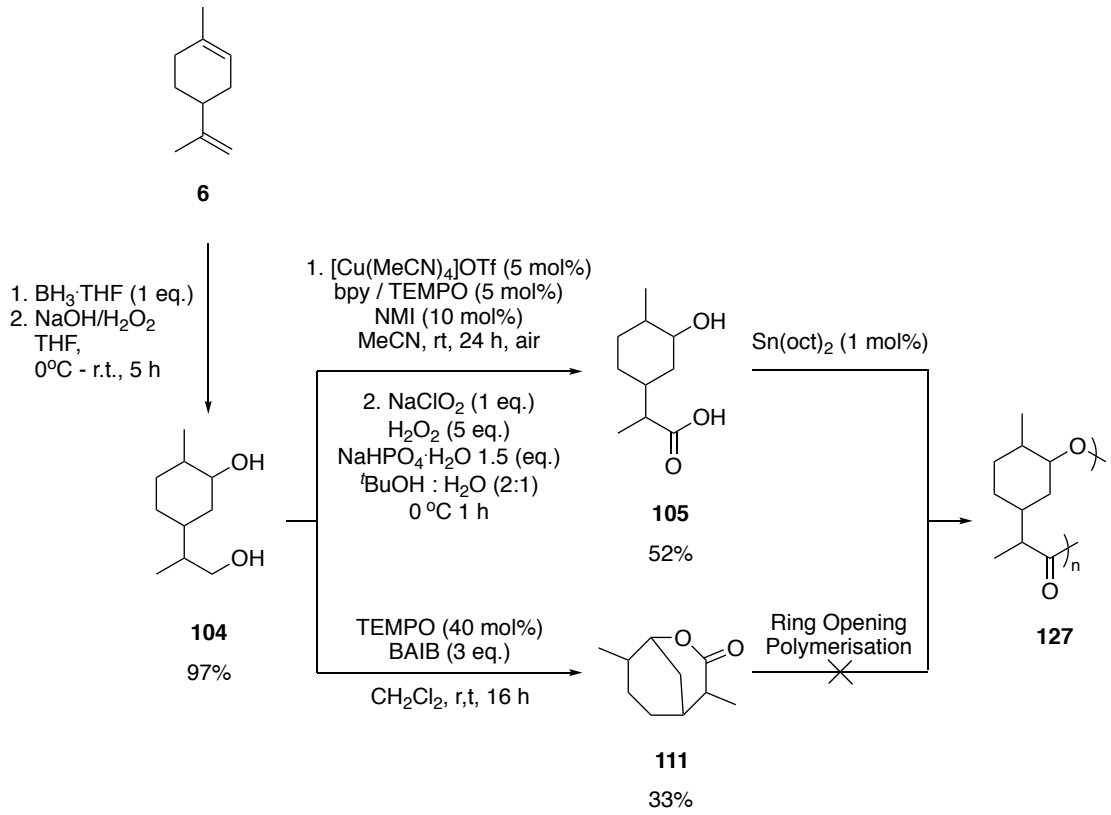
The limonene diol **104** can be accessed, in one step from limonene (**6**), in an almost quantitative yield of 97%. This has been shown to act as a co monomer with a bio based diacid, succinic acid (**126**) to produce polyesters with high M_ns (up to 30 kDa). Furthermore upon exposure to basic conditions the polyester can degrade and the diol monomer **104** can be reclaimed with excellent purity. This indicates that the terpene-derived polymer **127** has the potential to be circular.



Scheme 39: *Synthesis and subsequent degradation of polymer* ***127***

4. Conclusions and Future Work

Two terpene derived monomers (**105** and **104**) have been synthesised from limonene (**6**) and their polymerisation potentials investigated (**Scheme 40**).[138] The unusual bridged bicyclic lactone **111** was also studied both experimentally and computationally but was observed not to undergo ring opening polymerisation. Polymerisation of the hydroxy-acid **105** using a polycondensation technique yielded low molecular weight polymers (M_ns *ca*. 2.6 kDa) with T_gs of *ca.* 44 °C. However, co-polymerisation of the diol **104** and succinic acid produced the novel polyester **127** with considerably higher M_ns of up to 30 kDa. This material is derived completely from renewable resources and a high percentage of its carbon content can be sourced from terpene waste streams. Finally, the polymer **127** was shown to degrade under basic conditions into its substituent monomer **104**, opening up a significant opportunity for recycling.



Scheme 40: *Synthesis and polymerisation attempts of* ***105*** *and* ***111***

Future work involving these terpene-derived monomers could include some further exploration into the recyclability of the system. The current degradation procedure uses harsh conditions and long time scales. It would be desirable to shorten the degradation times and to lower the concentration of base used. It was also be interesting to make the system fully recyclable through the re-polymerisation of the terpene derived monomer **104** for the synthesis of the polymer **127**. This could be studied by re-submitting the reclaimed **104** to the polymerisation conditions to probe the recyclability of the monomer **104** and investigating the properties of the polymer synthesised using the recycled monomer.

5. Experimental

5.1. General Experimental

BnOH was distilled from CaH_2 and 2,3-dimethyl-2-butene was distilled onto molecular sieves prior to use; THF was freshly distilled from sodium metal and benzophenone; water was deionised before use. All other reagents were purchased from a chemical supplier and used without further purification. TLCs were performed on silica gel on aluminium and were visualised using a potassium permanganate or phosphomolybdic acid or vanillin dip. Experiments carried out under inert atmosphere used argon or nitrogen, and glassware was flame dried prior to use. All solutions are saturated unless stated otherwise.

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, $(CD_3)_2SO$ or CD_3OD at ambient temperature using Bruker DPX400 (400 MHz), AV400 (400 MHz), AV3400HD (400 MHz), AV3400 (400 MHz) and AV3500 (500 MHz) spectrometers. Data are expressed as chemical shifts in parts per million (ppm) relative to the residual solvent signal of $CHCl_3$ (δ_H = 7.27) or $CDCl_3$ (δ_C = 77.0 as the internal standard. The following abbreviations are used to designate the multiplicity of each signal; s, singlet; d, doublet; dd, doublet of doublets; dddd, doublet of doublet of doublet of doublets; t, triplet; dt, doublet of triplets; ddt, doublet of doublet of triplets; q, quartet; m, multiplet; app, apparent; br, broad. Coupling constants *J* are given in hertz (Hz).

Size exclusion chromatography (SEC) was performed using an Agilent 1260 Infinity Series HPLC (Agilent Technologies, USA) in THF (HPLC grade, Fisher Scientific) as eluent at room temperature using two Agilent PL-gel mixed-E columns in series with a flow rate of 1 mL min^{-1}. A differential refractometer (DRI), was used for sample detection. Or using an Agilent 1260 Infinity Series HPLC (Agilent Technologies, USA) in Chloroform (HPLC grade, Fisher Scientific) at room temperature using two Agilent PL-gel 5 µm mixed-C columns (300 x 7.5 mm) in series with a PL-gel 10 µm Guard Column (50 x 7.5 mm). A flow rate of 0.5 mL min^{-1} was used. A PMMA column calibration was

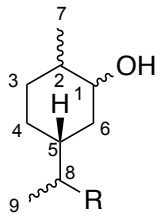
used alongside a differential refractometer (DRI, Wyatt) for sample detection and analysis.

Infra-red spectra were recorded using a Bruker Tensor 27 FT-IR spectrophotometer using either an ATR attachment or a solution cell using $CHCl_3$ as the solvent and their peaks are quoted as υ_{max} in cm^{-1}. High-resolution mass spectra were obtained using a Bruker MicroTOF mass spectrometer operating in electrospray ionisation (ESI) mode. MALDI-TOF analyses were performed using Bruker UltraFlex III. The matrix used was trans-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) with sodium (Na^+) and potassium (K^+) as cations. Into the analysis were applied the reflection mode and ~ 15% of laser intensity. The MALDI-TOF sample consists in 10 µl of polymer sample in methanol (10 mg ml^{-1}) mixed with 20 µl of DCTB solution in acetonitrile (10 mg ml^{-1}). Afterwards, 1 µl of this mixture is spotted into the target plate and left to dry at room temperature.

Dynamic mechanical analysis (DMA) was used to determine the T_g of the polymers. Measurements were performed on a Triton Technologies DMA (now Mettler Toledo DMA1) using the powder pocket accessory. The sample (40 mg ± 5 mg) was weighed into a powder pocket. Samples were measured at 1 and 10 Hz in single cantilever bending geometry between -100–100 °C. The value of the T_g was taken as the peak of the tan delta (tan δ) curve.

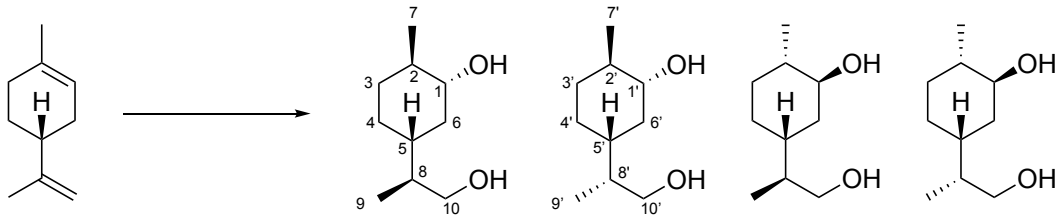
Differential scanning calorimetry (DSC) was performed using a DSC Q2000 from TA-instruments. The measurements were carried out from -100 to 250 ^oC with a heating and cooling rate of 10 ^oC/min under a nitrogen flow of 50 mL/min. The T_gs were obtained from the inflection point in the curve recorded during the second heating run.

5.2. Experimental Procedures for Monomer Synthesis



Throughout the experimental procedures it is assumed that the compounds are a 1:1 mixture of epimers at the C8 position. Where known, the ratio of diastereomers at the C1 position relative to the C5 position will be quoted in the experimental text.

Synthesis of (1*R*,2*R*,5*R*)-5-(1-hydroxypropan-2-yl)-2-methylcyclohexan-1-ol (104a) and (1*S*,2*S*,5*R*)-5-(1-hydroxypropan-2-yl)-2-methylcyclohexan-1-ol (104b)

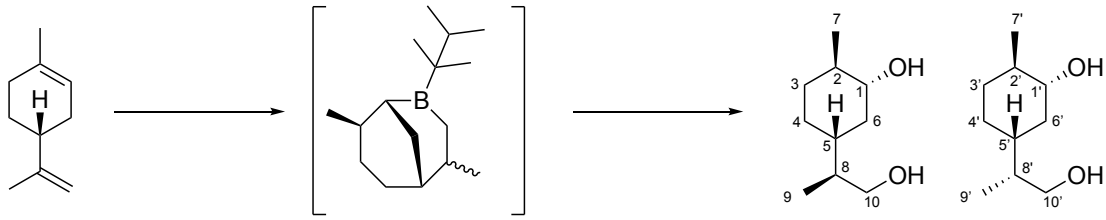


6 **104a'** **104a"** **104b'** **104b"**

To a solution of limonene (16.1 mL, 100 mmol) in THF (30 mL) cooled to 0 °C was added borane (100 mL, 100 mmol, 1 M in THF) dropwise over 25 min. Once the addition was complete the reaction was allowed to warm to room temperature and stirred (2 h). The reaction was cooled to 0 °C, a solution of $NaOH_{(aq)}$ (350 mL, 350 mmol, 1 M) was added followed by H_2O_2 (34 mL, 350 mmol, 30% w/v in H_2O). The reaction mixture was allowed to stir at 0 °C (30 min) and then at room temperature (30 min). EtOAc (400 mL) was added to the reaction mixture and the organic layer separated and washed with H_2O (200 mL), $Na_2CO_{3(aq)}$ (200 mL), $NaCl_{(aq)}$ (200 mL). Dried over Na_2SO_4 and concentrated under reduced pressure to give a yellow oil. Purification by silica gel chromatography (40% EtOAc in petroleum ether) afforded the title compound as a mixture of four disastereomers **104a'/a''** and **104b'/b''** (3:1) (16.7 g, 97.0 mmol, 97%) as a pale yellow oil.

FTIR (ATR) ν_{max} 3604, 3449, 2940, 2867, 1653, 1183; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 3.67-3.54 (m), 3.53-3.37 (m), 3.19-3.07 (m), 1.96-1.85 (m), 1.81-1.62 (m), 1.61 -1.41 (m), 1.28-1.15 (m), 1.03-0.93 (m), 0.93-0.85 (m); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{20}NaO_2$ $[M + Na]^+$ 195.1361 found 195.1366.

Synthesis of (1*R*,2*R*,5*R*)-5-((*S*)-1-hydroxypropan-2-yl)-2-methylcyclohexan-1-ol (104a') and (1*R*,2*R*,5*R*)-5-((*R*)-1-hydroxypropan-2-yl)-2-methylcyclohexan-1-ol (104a'')



6 **110** **104a'** **104a''**

For the synthesis of a 0.5 M solution of thexylborane in THF. To a solution of borane (100 mL, 100 mmol, 1 M in THF) at 0 ^oC was added 2,3-dimethyl-2-butene (100 mL, 1 M in THF) dropwise and stirred (1 h). To dry THF (20 mL) thexylborane (200 mL, 100 mmol, 0.5 M in THF) and limonene (16.1 mL, 100 mmol) in THF (35 mL) was added simultaneously dropwise over 40 min. The reaction mixture was allowed to stir (1 h) at 0 ^oC and then at room temperature (1 h). The THF was removed under reduced pressure and the crude residue was distilled under vacuum to yield the cyclic boron intermediate **110** which was used without further purification.

To a solution of **110** (2.19 g, 9.31 mmol) in THF (10 mL) cooled to 0 ^oC, was added $NaOH_{(aq)}$ (32.5 mL, 32.5 mmol, 1 M), followed by H_2O_2 (3.70 mL, 32.5 mmol, 30% w/v in H_2O). The reaction mixture was allowed to stir at 0 ^oC (30 min) and then at room temperature (30 min). EtOAc (30 mL) was added to the reaction mixture and the organic layer separated and washed with H_2O (10 mL), $Na_2CO_{3(aq)}$ (10 mL), $NaCl_{(aq)}$ (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to give a yellow oil. Purification by silica gel chromatography (10-100% EtOAc in petroleum ether) afforded the title compounds as a mixture of two epimers **104a'** and **104a''** as

a pale-yellow oil (440 mg, 2.56 mmol, 27%). Upon cooling to -20 °C a solid crystalline sample enriched with **62a'** was obtained. After the assignment of the ^{13}C NMR spectra of **62a'** the ^{13}C NMR spectra of the mixture of **104a'** and **104a''** was used to identify the peaks for **104a''** (Data in agreement with literature values)[107]

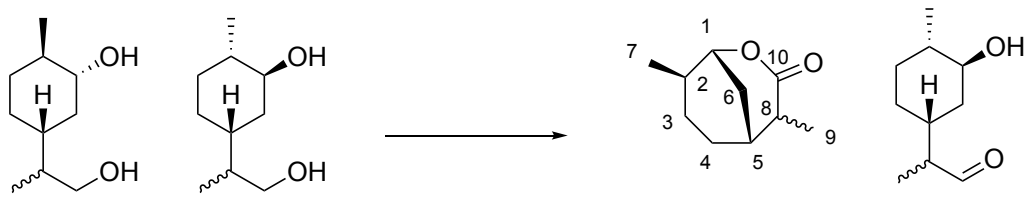
104a'

FTIR (ATR) ν_{max} 3316, 3307, 2954, 2923, 2872, 1036; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 3.60 (dd, *J* = 10.5, 5.7 Hz, 1H, H-10), 3.53-3.43 (m, 1H, H-10), 3.20-3.08 (m, 1H, H-1), 1.97-1.86 (m, 1H, CH_2), 1.78-1.65 (m, 1H, CH_2), 1.66-1.42 (m, 3H, H-2 and CH_2 and CH), 1.31-1.16 (m, 1H, CH), 1.17-1.02 (m, 1H, CH_2), 1.07-0.90 (m, 5H, H-7 and CH_2), 0.90 (d, *J* = 6.8, 0.9 Hz, 3H, H-9); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C = 76.5 (C-1), 66.0 (C-10), 40.4 (CH), 40.2 (CH), 39.9 (CH_2), 38.2 (CH), 33.2 (CH_2), 27.9 (CH_2), 18.4 (C-7), 13.5 (C-9). **HRMS** (ESI) *m/z* calculated for $C_{10}H_{20}NaO_2$ [M + Na^+] 195.1361 found 195.1367.

104a''

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 76.5 (C-1'), 66.0 (C-10'), 40.4 (CH), 40.2 (CH), 39.9 (CH_2), 38.0 (CH), 33.3 (CH_2), 30.1 (CH_2), 18.4 (C-7'), 13.3 (C-9').

<u>Synthesis of (1*R*,5*R*,8*R*)-4,8-dimethyl-2-oxabicyclo[3.3.1]nonan-3-one (111a'/a'')</u>



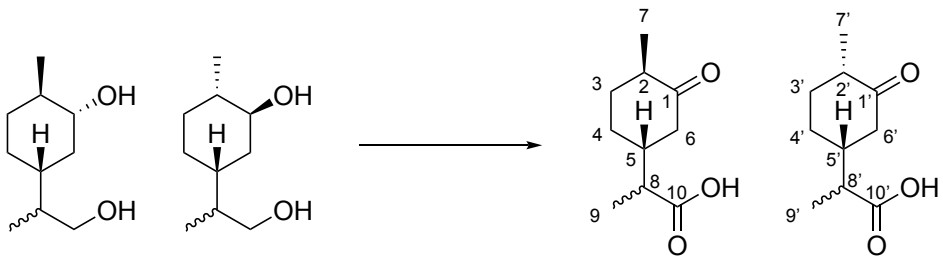
104a **104b** **111a** **113b**

To a solution of **104a** and **104b** (3:1) (17.95 g, 104 mmol) in CH_2Cl_2 (1000 mL) was added a solution of TEMPO (6.5 g, 41.7 mmol) in CH_2Cl_2 (20 mL) dropwise, BAIB (100.4 g, 312 mmol) was subsequently added in portions over 15 min. The reaction was stirred at room temperature (16 h). 5% $Na_2S_2O_{3(aq)}$ (540 mL) then $NaHCO_{3(aq)}$ (1050 mL) was added and the mixture was stirred vigorously (15 min). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 500 mL). The organic

extracts were combined, washed with $NaCl_{(aq)}$ (500 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by silica gel chromatography (5-7% EtOAc in petroleum ether) afforded the epimers **111a' and 111a''** as a pale-yellow oil (5.8 g, 34.50 mmol, 33%). Aldehyde **113b'/b''** was also isolated from the column and discarded. The mixture of epimers **111a'/a''** was cooled to -20 °C to obtain an analytical sample of the major diastereomer **111a'** or **111a''** (reported).

FTIR (ATR) ν_{max} 3248, 2970, 2924, 2865, 2846, 1698; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.50-4.19 (m, 1H, H-1), 2.55-2.46 (m, 1H, H-8), 2.24-2.10 (m, 1H, H-2), 1.93-1.85 (m, 1H, CH_2), 1.85-1.69 (m, 4H, H-5 and CH_2), 1.52-1.43 (m, 1H, CH_2), 1.37-1.31 (m, 1H, CH_2), 1.34 (dd, *J* = 7.6, 1.0 Hz, 3H, H-9), 1.00 (d, *J* = 7.4 Hz, 3H, H-7); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 175.7 (C-10), 80.2 (C-1), 41.0 (C-8), 33.2 (C-5), 32.2 (C-2), 26.3 (CH_2), 21.7 (CH_2), 21.6 (CH_2), 20.1 (C-9), 15.7 (C-7). **HRMS** (ESI) *m/z* calculated for $C_{10}H_{16}NaO_2$ $[M + Na]^+$ 191.1048 found 191.1042.

Synthesis of 2-((1*R*,4*R*)-4-methyl-3-oxocyclohexyl)propanoic acid (112a) and 2-((1*R*,4*S*)-4-methyl-3-oxocyclohexyl)propanoic acid (112b)



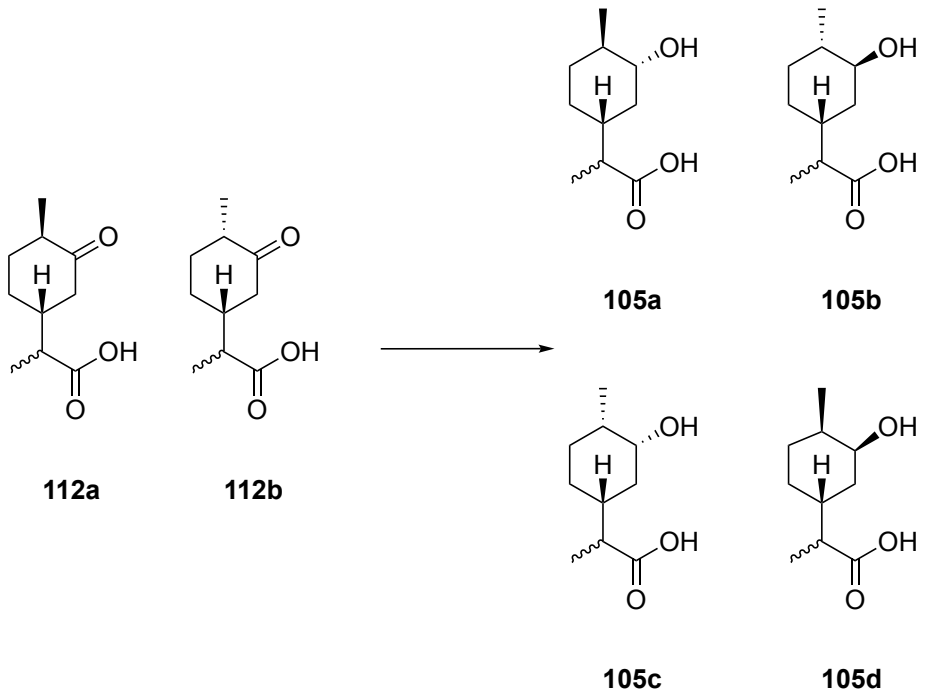
104a **104b** **112a** **112b**

CrO_3 (10 g, 100 mmol) was dissolved in H_2SO_4 (10 mL), the resulting solution was carefully added to H_2O (30 mL) cooled to 0 °C. This solution (3.83 mL, 9.57 mmol) was added dropwise to a solution of **104a** and **104b** (3:1) (500 mg, 2.9 mmol) in acetone (30 mL) at 0 °C and the resulting red solution was stirred (20 min). The reaction mixture was cooled to 0 °C and quenched with 2-propanol until the red colour disappeared and a green colour persisted. The reaction mixture was filtered and the solvent removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (15 mL) and washed with water (3 x 10 mL), $NaCl_{(aq)}$ (10 mL), dried over Na_2SO_4 and

concentrated under reduced pressure to yield the diastereomers **112a** and **112b** as a pale yellow oil (530 mg, 2.9 mmol, quantatative) that was used without further purification. ^{13}C NMR reported for the major diastereomer **112a'** or **112a''** only.

FTIR (ATR) ν_{max} 2972, 2933, 1733, 1701, 1237, 1169; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 10.82 (s, 1H, COOH), 2.54-2.30 (m, 3H, H-2 and H-8 and H-6), 2.27-2.16 (m, 1H, H-6), 2.15-2.01 (m, 2H, H-5 and H-4 or H-3), 1.99-1.86 (m, 1H, H-4 or H-3), 1.60-1.46 (m, 1H, H-4 or H-3), 1.42-1.28 (m, 1H. H-4 or H-3), 1.24-1.15 (d, *J* = 7.0 Hz, 3H, H-9), 1.02 (d, *J* = 6.4 Hz, 3H, H-7); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 212.2 (C-1), 181.0 (C-10), 45.7 (C-6), 44.7 (C-2), 44.6 (C-8), 42.2 (C-5), 34.4 (C-4 or C-3), 28.5 (C-4 or C-3), 14.2 (C-9), 13.7 (C-7); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{16}NaO_3$ $[M + Na]^+$ 207.0997 found 207.0996.

Synthesis of 2-((1*R*)-3-hydroxy-4-methylcyclohexyl)propanoic acid (105a-d)

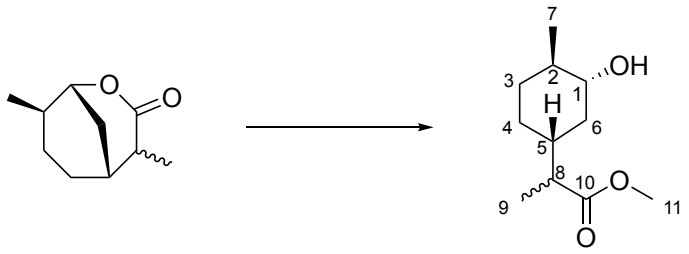


MeOH (30 mL) was cooled to 0 °C and $NaBH_4$ (462 mg, 12.23 mmol) was added in portions. A solution of **112a** and **112b** (3:1) (530 mg, 2.9 mmol) in MeOH (5 mL) was added dropwise and the resulting mixture was stirred (30 min). The reaction was quenched with H_2O (10 mL) and the MeOH removed under reduced pressure. CH_2Cl_2

(20 mL) was added to the residue, then the aqueous was neutralised with $HCl_{(aq)}$ (2M) and extracted into CH_2Cl_2 (2 x 20 mL). The organic extracts were combined and washed with $NaCl_{(aq)}$ (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield the eight diastereomers **105a-d** as a pale yellow oil (202 mg, 1.10 mmol, 38%).

FTIR (ATR) ν_{max} 3350, 2924, 2871, 2603, 1702, 1217; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.00 (br s), 3.94 – 3.85 (m), 3.84 – 3.72 (m), 3.23 – 3.11 (m), 2.51 – 2.19 (m), 2.12-1.82 (m), 1.82–1.58 (m), 1.57 – 1.33 (m), 1.31 – 1.21 (m), 1.20 – 1.11 (m), 1.05-0.99 (m), 0.95 (m); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{18}NaO_3$ [M + Na^+] 209.1154 found 209.1149.

Synthesis of methyl 2-((1*R*,3*R*,4*R*)-3-hydroxy-4-methylcyclohexyl)propanoate (115)

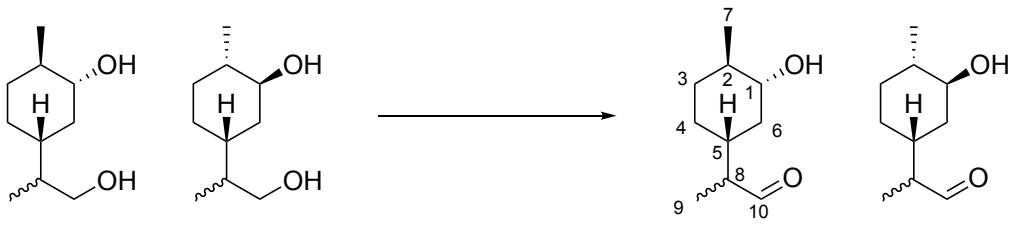


111 **115**

To MeOH (30 mL) cooled to 0 °C was added sodium metal (363 mg, 15.8 mmol) in portions over 20 min. A solution of **111** (1:1) (268 mg, 1.59 mmol) in MeOH (5 mL) was added dropwise over 10 min. The mixture was heated to 75 °C and stirred (15 h). $NH_4Cl_{(aq)}$ (10 mL) was added and MeOH was removed under reduced pressure, the aqueous was extracted into EtOAc (3 x 20 mL). The organic extracts were combined and washed with $NaCl_{(aq)}$ (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield **115** as a colourless oil (286 mg, 1.43 mmol, 84%).

FTIR (ATR) ν_{max} 3399, 2924, 2871, 1725, 1164; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 3.73 -3.63 (m, 3H, H-11), 3.22-3.11 (m, 1H, H-1), 2.37 -2.27 (m, 1H, H-8), 2.04-1.85 (m, 1H, CH_2), 1.81-1.52 (m, 3H, CH and CH_2 and CH_2), 1.30-1.22 (m, 2H, CH and CH_2), 1.15 (d, *J* = 7.1 Hz, 3H, H-9), 1.06-0.97 (m, 5H, H-7 and CH_2 and CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 176.6, 76.1, 76.0, 51.5, 51.4, 44.9, 44.9, 40.0, 39.9, 39.6, 39.6, 38.5, 32.8, 32.8, 30.3, 28.8, 18.2, 14.1, 14.1; **HRMS** (ESI) *m/z* calculated for $C_{11}H_{20}NaO_3$ [M + $Na]^+$ 223.1310 found 223.1308.

Synthesis of 2-((1*R*,3*R*,4*R*)-3-hydroxy-4-methylcyclohexyl)propanal (113a) and 2-((1*R*,3*S*,4*S*)-3-hydroxy-4-methylcyclohexyl)propanal (113b)

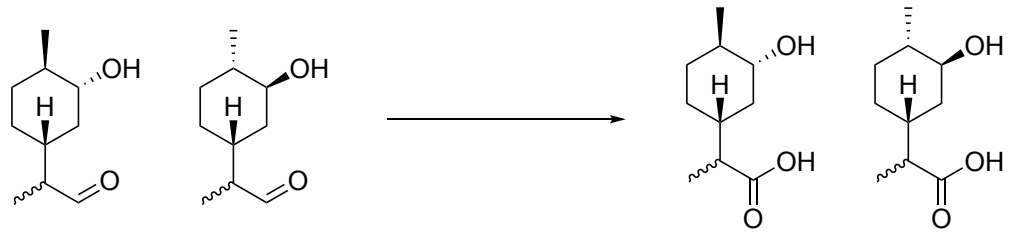


104a **104b** **113a** **113b**

To a solution of **104a** and **104b** (3:1) (5 g, 29.1 mmol) in MeCN (300 mL) was added $[Cu(MeCN)_4]OTf$ (546 mg, 1.4 mmol). A solution of TEMPO (210 mg, 1.4 mmol), 2,2-bipyridyl (210 mg, 1.4 mmol) and 1-methylimidazole (240 mg, 2.91 mmol) in MeCN (9 mL) was added dropwise, and the mixture stirred at room temperature (20 h). The reaction mixture was passed through a plug of silica and the product eluted with Et_2O. The solvent was removed under reduced pressure to give the crude product, purification by silica gel chromatography (15% EtOAc in petroleum ether) afforded the diastereomers **113a** and **113b** (3:1) as a colourless oil (3.83 g, 22.5 mmol, 77%).

FTIR (ATR) ν_{max} 3320, 2953, 2922, 2871, 1714; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 9.69-9.55 (m), 3.70-3.49 (m), 3.23-3.11 (m), 2.34 -2.20 (m), 1.99-1.69 (m), 1.70-1.36 (m), 1.33-1.19 (m), 1.17-1.10 (m), 1.09-1.04 (m), 1.03-0.99 (m), 0.97 (d, *J* = 7.0 Hz); ^{13}C NMR reported for the major diastereomer **113a'** or **113a'' ^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 205.2 (C-10), 76.0 (C-1), 51.2 (C-8), 40.0 (CH), 39.9 (CH_2) , 37.2 (CH), 32.9 (CH_2), 28.3 (CH_2), 18.3 (CH_3), 10.2 (CH_3); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{18}NaO_2$ $[M + Na]^+$ 193.1204 found 193.1201.

Synthesis of 2-((1*R*,3*R*,4*R*)-3-hydroxy-4-methylcyclohexyl)propanoic acid (105a) and 2-((1*R*,3*S*,4*S*)-3-hydroxy-4-methylcyclohexyl)propanoic acid (105b)

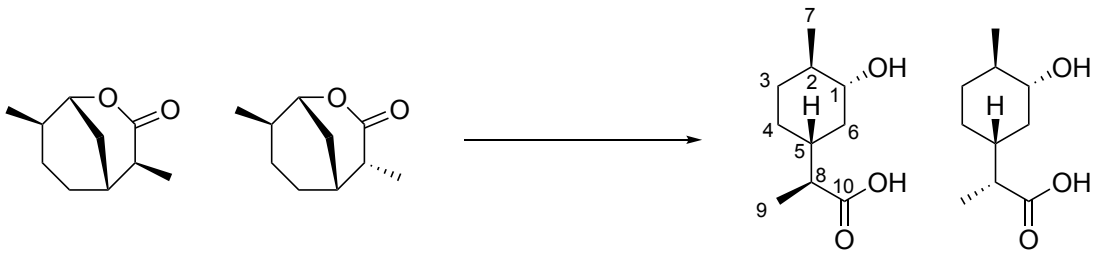


113a **113b** **105a** **105b**

To a solution of **113a** and **113b** (3:1) (3 g, 17.5 mmol) in ^{t}BuOH/H_2O (2:1, 80 mL) was added $NaH_2PO_4{\cdot}2H_2O$ (8.19 g, 52.5 mmol) and the resulting solution was cooled to 0 ^{o}C. H_2O_2 (6.83 mL, 87.5 mmol, 30% w/v in H_2O) was added followed by $NaClO_2$ (11.87 g, 105 mmol, purity assumed to be 80%) in portions over 45 min. The reaction was allowed to stir at 0 ^{o}C (30 min) and then extracted into EtOAc (80 mL). The organic extract was washed with H_2O (5 x 50 mL), $NaCl_{(aq)}$ (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield the the four diastereomers **105a** and **105b** as a white semi-solid. (2.2 g, 11.82 mmol, 68%).

FTIR (ATR) ν_{max} 3437, 2935, 2873, 2567, 1702, 1238; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 6.23 (br s), 3.74-3.45 (m), 3.17 (app td, *J* = 10.4, 4.2 Hz), 2.48 -2.22 (m), 2.03-1.90 (m), 1.80-1.60 (m), 1.32-1.19 (m), 1.20-1.11 (m), 1.06-0.93 (m); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{18}NaO_3$ $[M + Na]^+$ 209.1154 found 209.1146.

Synthesis of (S)-2-((1R,3R,4R)-3-hydroxy-4-methylcyclohexyl)propanoic acid (105a') and (*R*)-2-((1*R*,3*R*,4*R*)-3-hydroxy-4-methylcyclohexyl)propanoic acid (105a'')

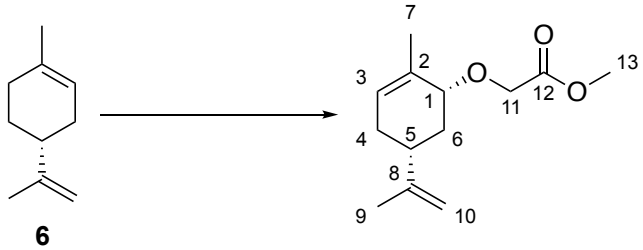


111a' **111a''** **105a'** **105a''**

To a solution of **111a'** and **111a''** (1:1) (927 mg, 5.52 mmol) in THF (80 mL) was added $NaOH_{(aq)}$ (79.8 mL, 79.8 mmol, 1 M), the reaction mixture was heated to reflux and stirred (18 h). The THF was removed under reduced pressure then the aqueous was acidified with $HCl_{(aq)}$ (2 M) and extracted into EtOAc (3 x 30 mL). The organic extracts were combined, washed with $NaCl_{(aq)}$ (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield a mixture of epimers **69a'** and **69a''** as a brown oil (1.01 g, 5.43 mmol, 98%). Recrystallisation from hot EtOAc to yielded a single diastereomer **105a'** or **105a''** as a pale brown solid (525 mg, 2.82 mmol, 51%) (reported).

m.p 125 °C; **FTIR** (ATR) ν_{max} 3239, 2991, 2934, 2538, 1677, 1262 ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 3.21 (app ddd, *J* = 10.9, 9.7, 4.2 Hz, 1H, H-1), 2.32 (app p, *J* = 7.1 Hz, 1H, H-8), 2.03-1.93 (m, 1H, CH_2), 1.84-1.71 (m, 2H, CH_2), 1.71-1.63 (m, 1H, CH), 1.35-1.23 (m, 1H, CH), 1.18 (d, *J* = 7.0 Hz, 3H, H-9), 1.16-1.08 (m, 1H, CH_2), 1.07-0.98 (m, 5H, H-7 and CH_2 and CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 181.0 (C-10), 76.1 (C-1), 45.0 (C-8), 40.0 (CH_2), 39.9 (CH), 39.7 (CH), 32.8 (CH_2), 29.0 (CH_2), 18.4 (C-7), 14.3 (C-9). **HRMS** (ESI) *m/z* calculated for $C_{10}H_{18}NaO_3$ $[M + Na]^+$ 209.1154 found 209.1146.

Synthesis of methyl 2-(((1*R*,5*R*)-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-en-1-yl)oxy)acetate (123)



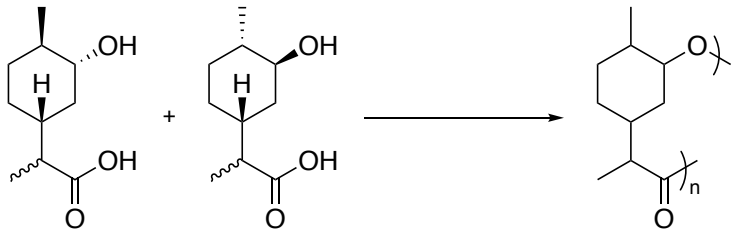
6 **123**

$Pd(OAc)_2$ (19.8 mg, 0.09 mmol), benzoquinone (380 mg, 3.52 mmol), *p*-TsOH (33.5 mg, 0.18 mmol) and methyl glycolate (0.14 mL, 2.20 mmol) were added to toluene (8.8 mL) and the resulting solution was stirred under oxygen (15 min). Limonene (0.36 mL, 2.20 mmol) was added and the solution stirred under an atmosphere of oxygen (18.5 h). The reaction mixture was filtered through celite and concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ (10 mL), washed with $Na_2S_2O_{4(aq)}$ (1 M) (3 x 10 mL), $NaCl_{(aq)}$ (10 mL),dried over $MgSO_4$ and concentrated under reduced pressure to give the crude product. Purification by silica gel chromatography (2% EtOAc in petroleum ether) afforded the title compound **123** (82 mg, 0.37 mmol, 17%) as a yellow oil.

FTIR (ATR) ν_{max} 3507, 3013, 2904, 1756, 1413, 1159; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.69-5.65 (m, 1H, H-3), 4.77 (m, 2H, H-10), 4.21 (d J = 16.25, 1H, H-11), 4.15 (d J = 16.25, 1H, H-11), 3.77 (m, 4H, H-1 and H-13), 2.46-2.36 (m, 1H, H-5), 2.23-2.15 (m, 1H, H-4), 2.08-2.03 (m, 1H, H-6), 1.88-1.82 (m, 4H, H-7 and H-4), 1.76 (brs, 3-H, H-9) 1.45 (app td, J = 13.5, 3.8, 1H, H-6); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 171.2 (C-12), 149.3 (C-2), 132.4 (C-8), 126.7 (C-3), 109.0 (C-10) 77.3 (C-1), 66.7 (C-11), 51.9 (C-13), 35.4 (C-5), 31.8 (C-4), 31.2 (C-6), 21.1 (C-7), 21.0 (C-9); **HRMS** (ESI) *m/z* calculated for $C_{13}H_{20}NaO_3$ [M + Na^+] 247.1305 found 247.1300.

5.3. Experimenal Procedures for Polymer Synthesis

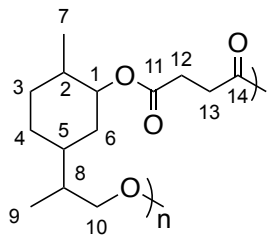
Synthesis of polymer 106



105a **105b** **106**

105a and **105b** (3:1) (500 mg, 2.68 mmol) and $Sn(oct)_2$ (8.5 µL, 1 mol%) were added to a flame dried flask under a flow of N_2, which was heated to either 120 or 180 ^oC and stirred for the required time period. The temperature was then set to 180 ^oC and the system put under vacuum for 24 h. The polymerisation was stopped by cooling to -5 ^oC and the resulting polymer dried under vacuum for 24 h.
FTIR (ATR) ν_{max} 3459, 2932, 1772, 1722, 1457, 1168; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.92-4.32 (m), 3.24-3.08 (m), 2.55-0.75 (m).

Synthesis of polymer 127



127

Solution Polycondensation

Solution polycondensations were carried out under argon with magnetic stirring using a variety of conditions (**Table 10**), an example of a typical procedure is written below.

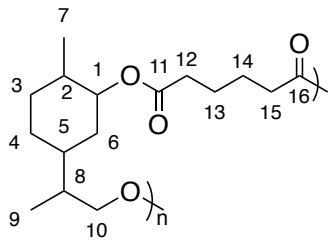
104 (1g, 5.80 mmol) was dissolved in dry dichloromethane (3 mL) and cooled to 0 °C, pyridine (2.29 mL, 29.0 mmol) was added dropwise over 10 minutes. Succinyl chloride (0.90 mL, 6.38 mmol) was dissolved in dry dichloromethane (4.3 mL) and added dropwise over 25 minutes, the resulting solution was then stirred at room temperature (48 h). The polymer was then isolated by precipitation in an excess of MeOH to yield a pale yellow, viscous oil.

Melt Polymerisation

All reagents were dried under vacuum at 25 °C for at least 24 h prior to use. The mixture of **2a** and **2b** (3:1) (1.50 g, 8.70 mmol) was added to a 50 mL round bottomed flask equipped with a condenser and trap cooled to 0 °C. Succinic acid (**9**) (1.13 g, 9.57 mmol) was added, and the reaction heated to 190 °C (6 h). The metal catalyst ($Sn(oct)_2$ or $Ti(OBu)_4$) was added (1 mol%), the temperature increased and the system put under vacuum. After an elapsed time the polymerisation was stopped by cooling to -5 °C and the polymer washed with MeOH.

FTIR (ATR) ν_{max} 3430, 2932, 2878, 1728, 1454, 1187; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.81-4.40 (m, 1H, H-1), 4.16-3.84 (m, 2H, H-10), 2.62 (s, 4H, H-12 and H-13), 1.96-1.26 (m, 8H), 1.20-0.84 (m, 8H).

Syntheisis of Polymer 128



128

104 (1g, 5.80 mmol) was dissolved in dry dichloromethane (3 mL) and cooled to 0 °C, pyridine (2.29 mL, 29.0 mmol) was added dropwise over 10 minutes. Adipoyl chloride (0.925 mL, 6.38 mmol) was dissolved in dry dichloromethane (4.3 mL) and added

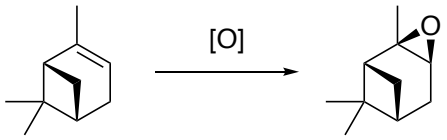
dropwise over 25 minutes, the resulting solution was then stirred at room temperature (48 h). The polymer was then isolated by precipitation in an excess of MeOH to yield a pale yellow, viscous oil.

FTIR (ATR) ν_{max} 3420, 2935, 2876, 1725, 1187; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.85-4.34 (m, 1H, H-1), 4.22-3.78 (m, 2H, H-10), 2.35 (br s, 4H, H-12 and H-15), 1.99-0.86 (m, 19H).

Chapter 2 – Investigations into the Synthesis and Polymerisation of Monomers Derived from α-Pinene

1. Introduction

Society's current model for plastic use is centred around petrochemical feedstocks. Despite significant efforts to introduce polymers from renewable feedstocks for commercial use we still lack sustainable polymers. As previously mentioned terpenes present an attractive feedstock for monomer synthesis as they are currently obtained from waste streams and offer a massive potential for synthetic manipulations. α-Pinene (**11**) is the most abundant turpentine component and therefore research into its use for polymerisation would be very beneficial. This has led to numerous attempts at the polymerisation of this compound.[37,44] However the polymerisation of **11** has not been as successful as β-pinene (**10**), largely due to the absence of a reactive *exo*-cyclic double bond, resulting in a shortage of polymers originating from α-pinene (**11**) in the literature. Turpentine can be composed of up to 97% α-pinene (**11**) and therefore it is prudent that the transformation of α-pinene (**11**) into a monomer should be explored. Although there has been some small success in the cationic homopolymerisation of α-pinene (**11**), there has been few publications concerning the polymerisation of modified or oxygenated **11**. One of the only articles concerning the polymerisation of oxygenated **11** is by Kheira *et al.* and details the ring opening polymerisation of α-pinene oxide (**129**) using a maghnite catalyst to form poly(α-pinene oxide).[139] One of the most common transformations α-pinene (**11**) undergoes is the epoxidation of its endocyclic double bond to form α-pinene oxide (**129**) (**Scheme 41**).



11 **129**

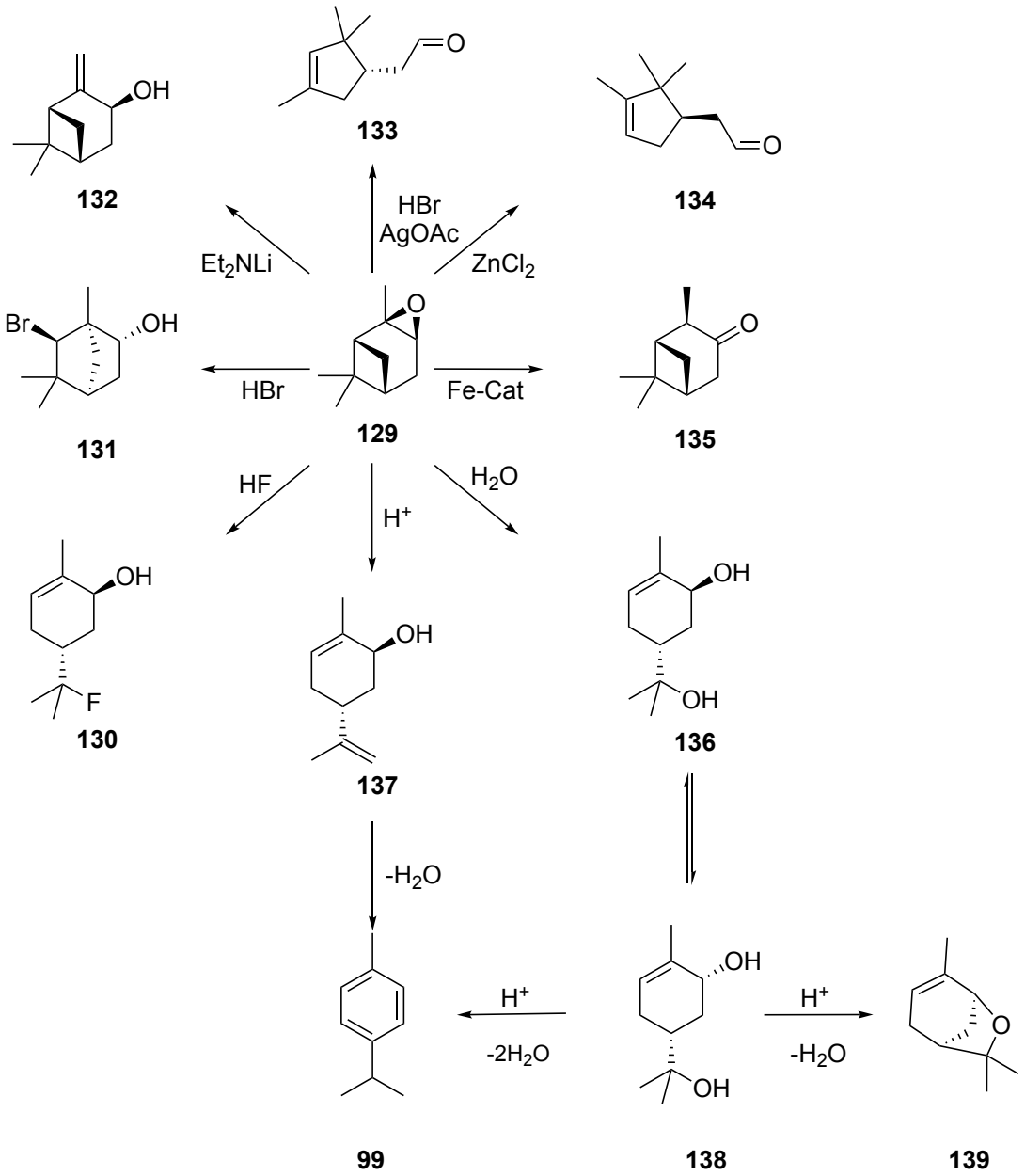
Scheme 41: *Epoxidation of α-pinene (**11**), to form α-pinene oxide (**129**)*

1.1. The chemistry of α-pinene oxide (129)

α-Pinene oxide (**129**) presents a large opportunity with respect to further functionalisation for monomer synthesis, and therefore will be a key intermediate for the synthesis of new monomers in this chapter.

The study of the epoxidation of α-pinene (**11**) is an enormous area in itself and will not be covered in this report, the reader should refer to the comprehensive review on the topic written by Corma *et al.* for more information.[41] As a result of these studies α-pinene oxide (**129**) is synthesised efficiently on an industrial scale for the exploitation of its further transformations and isomerisations to produce chemicals which are of importance to the fragrance industry.[140]

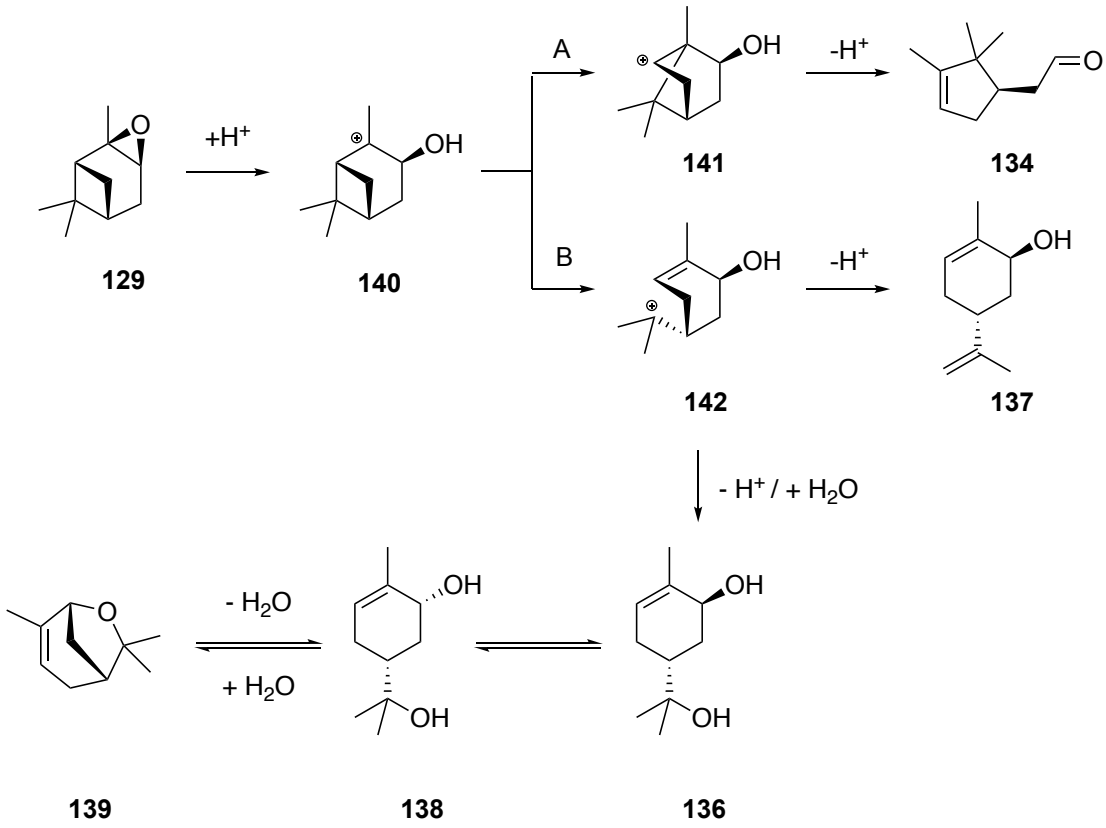
α-Pinene oxide (**129**) is a very reactive species and a variety of catalysts can be used to open the epoxide of **129** to get many products (**Scheme 42**). Among the main terpenoids produced are campholenic aldehyde (**134**)[141], fencholenic aldehyde (**133**)[142], *trans*-sobrerol (**136**)[143], pinol (**139**)[144] and *trans*-carveol (**137**)[145]. Minor products often encountered are *trans*-pinocamphone (**135**), *p*-cymene (**99**), *trans*-pinocarveol (**132**) and other compounds. Lewis acids favour the formation of **134** and **132**, while Bronsted acids favour the formation of **137**, **136**, **135**, and, *p*-cymene (**99**).[146]



Scheme 42: *Products of the ring opening of α-pinene oxide (**129**)*[146]

Campholenic aldehyde (**134**) is an important intermediate used by the fragrance industry in the synthesis of santalol, and is currently prepared by Lewis-acid-catalysed rearrangement of **129**.[145] The isomerisation of α-pinene oxide (**129**) is facile, producing over 100 products under different reaction conditions.[147]

The main products observed from the acid catalysed isomerisation of **129** can be rationalised by the mechanism outlined below (**Scheme 43**) and is characteristic of the structural rearrangements repeatedly encountered in terpenoid chemistry. Once the epoxide **129** has been opened to give carbenium ion **140** one of two competing movements of electrons from the same σ bond can happen: a [1,2] shift (path A) or an E1 elimination (path B) giving carbenium ions **141** and **142** respectively. Subsequent loss of a proton yields *trans*-carveol (**137**) and a rearrangement leads to campholenic aldehyde (**134**).



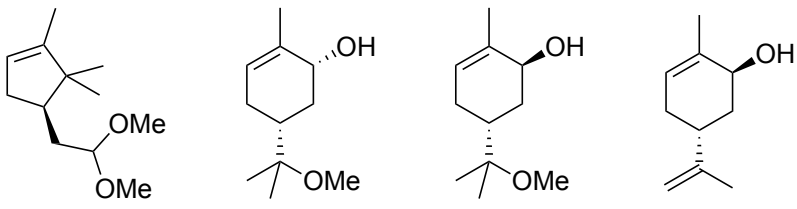
Scheme 43**: Proposed mechanism for the acid catalysed transformations of **129

Traditionally research has focused on the use of homogeneous Lewis acid catalysts for the isomerisation of α-pinene oxide (**129**). The most active and selective homogeneous systems used in this reaction are $ZnCl_2$ and $ZnBr_2$; however, these display low reaction rates and fast, permanent catalyst deactivation, with turnover numbers as low as 20 being reported.[146] Aqueous extraction of these catalysts from

the reaction results in the formation of vast quantities of heavy metal contaminated water which is unattractive from a green and sustainable chemistry perspective. This has resulted in a plethora of research into heterogeneous catalysts for the isomerisation of **129**, including zeolites, heteropoly acids, mesoporous silica and polymer supported catalysts.[140,148–155]

Motherwell *et al.* synthesised molecularly imprinted polymers (MIPs) using *trans*-carvyl amine as an imprint molecule to form the template for the selective isomerisation of **129** to *trans*-carveol (**137**).[153] The amine functionality of the imprint molecule was used to selectively position a sulfonic acid group in the MIP binding pocket utilising 4-styrene sulfonic acid as the functional monomer.

A range of MIPs were synthesised and tested for the synthesis of *trans*-carveol (**137**). The study found that the dominating factor in determining the distribution of the major products was in fact the solvent choice. Using DMF as solvent, up to 70% of the products from acid catalysed isomerisation of α-pinene oxide (**129**) with the polystyrene MIPs were obtained *via* the necessary *para*-menthene tertiary carbocation (**142**), and industrially important *trans*-carveol (**137**) was obtained in a 45% yield. When methanol was used as a solvent the product distribution was different (**Figure 32**). The observed products indicate that solvents with a nucleophilic counter ion can trap the carbenium ion intermediates.

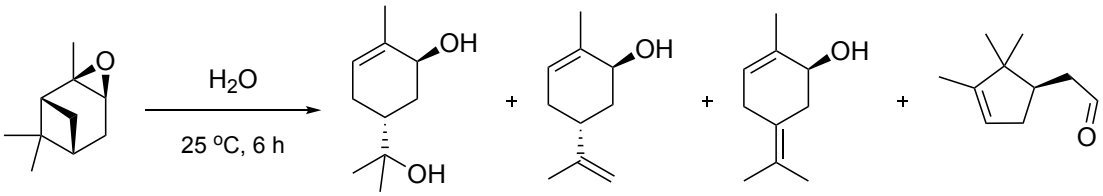


143 **144** **145** **137**

***Figure 32**: Major products synthesised using methanol as a solvent*[153]

Da Silva *et al.* investigated the ability of a tungsten based heteropoly acid $H_3PW_{12}O_{40}$ for the isomerisation of **129** in a variety of solvents. The solvent choice heavily influenced the ratios of observed products: campholenic aldehyde (**134**), trans-carveol (**137**), *trans*-sobrerol (**136**), or pinol (**139**). Each of these useful fragrance compounds were synthesised in good to excellent yields, up to 93% of **137** and up to 70% of **134**, by using an appropriate solvent. It was found that solvent polarity and basicity direct the reaction pathways: nonpolar, nonbasic solvents favoured the formation of **134**; polar, basic solvents promoted the formation of **137**. In weakly basic polar solvents, the major products were compounds **136** and **139**. The heteropoly acid was able to be recovered and was used in very low quanities (0.005-1 mol%), significantly more environmentally friendly than previous homogeneous catalytic methods for the selective synthesis of fragrance compounds in high yields.

In 2013 Xu and Qu reported that α-pinene oxide (**129**) can react with water in a solvolysis-type reaction to give *trans*-sobrerol, (**136**) (**Scheme 44**).[143] When the reaction was performed at 20 °C, enatiomerically pure **136** was obtained, however when the reaction was performed at reflux, a mixture of both *cis* and *trans* soberrol was produced in a ratio of 4:6.



129 **136** 69% **137** 3% **146** 7% **134** 8%

***Scheme 44**: The synthesis of trans-sobrerol (**136**)l by Xu et al.*[143]

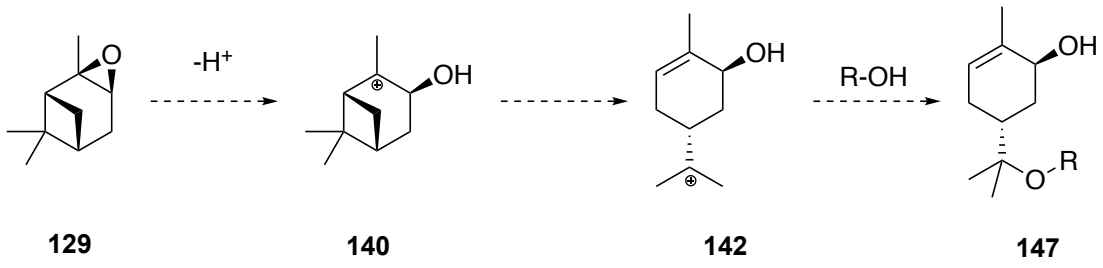
It is proposed that water is able to activate the epoxide, promoting its opening through hydrogen bonding to give the carbenium ion **142**, followed by a rearrangement to relieve the strain of the cyclobutane ring.[156] Water then attacks **140** to give product **136** (**Scheme 44**).

α-Pinene oxide (**129**) is readily produced from α-pinene (**11**), one of the most abundant terpenes, and can readily isomerise into a range of products. The isomerisation can be controlled by nature of the acid catalyst and the solvent choice. The rearrangement of **129** produces products which have the potential to be used as monomers, and the development of sustainable synthetic manipulations of this renewable molecule is an area of great interest.

2. Aims and Objectives

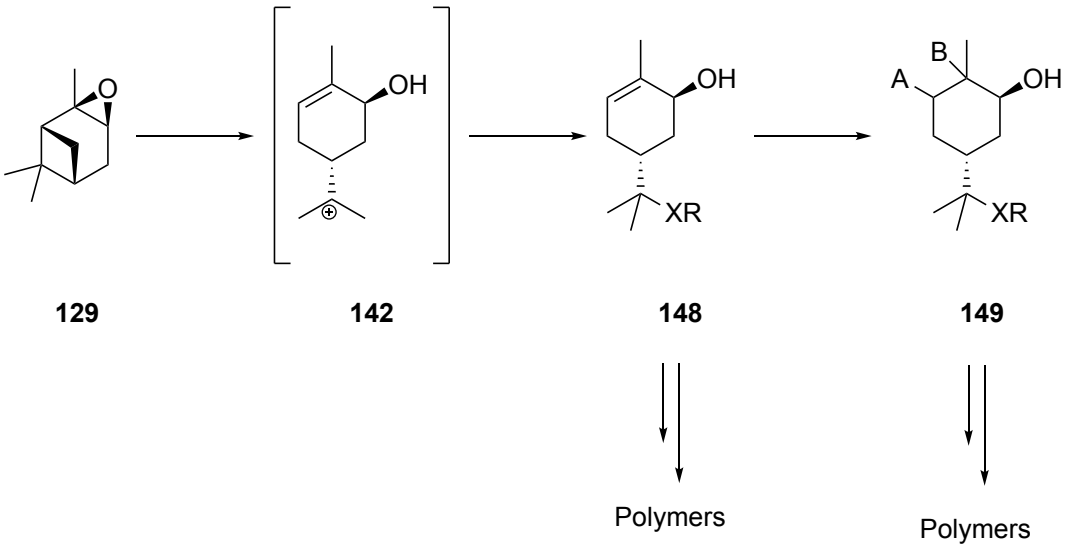
The aim of this research was to utilise the most abundant terpene (α-pinene (**11**)) which has a limited profile in the area of renewable polymers. As previously discussed α-pinene (**11**) can be efficiently transformed into α-pinene oxide (**129**) on an industrial scale. α-Pinene oxide (**129**) is more reactive than α-pinene (**11**) and therefore is a good precursor for monomer synthesis. One aim of this research was to investigate the solvolysis of α-pinene oxide (**129**) using nucleophiles, generating a molecule containing the appropriate functionality to be used as a monomer.

The solvolysis of α-pinene oxide (**129**) goes through a series of carbenium ions (**Scheme 43**). This work it was attempted to trap carbenium ion **142** with an assortment of oxygen based nucleophiles for the synthesis of small molecules which could be used as monomers **147** (**Scheme 45**).



Scheme 45**: Proposed synthesis of monomers via the addition of oxygen based nucleophiles into carbenium ion **142

The literature indicates the solvolysis reaction proceeds with simple oxygen based nucleophiles, such as methanol,[153] the reaction was subsequently attempted with more challenging substrates.



Scheme 46: *Proposed synthesis of monomers from α-pinene oxide (**129**)*

After trapping of the carbenium ion **142** it was proposed that the alkene moiety in **148** could be further functionalised to produce monomers **149** (**Scheme 46**). It was hypothesised that these would yield a polymer with a different backbone and therefore potentially possess different properties.

3. Results and Discussion

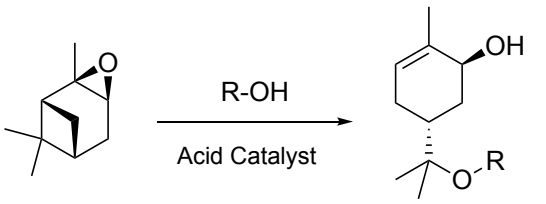
3.1. Towards the Functionalisation of α-Pinene Oxide (129)

3.1.1. Towards the Synthesis of Monomers for Homopolymerisation

Initial studies undertaken in the Stockman group explored the solvolysis reaction using different oxygen based nucleophiles.[157] A range of alcohols were investigated and it was found, an acid catalyst was required to facilitate opening of the epoxide **129** (**Table 13**, **Entry 1**). Previous studies by Stekrova *et al.* have indicated that Lewis acids

usually display high selectivity in favour of campholenic aldehyde (**134**), while in the presence of Brønsted acids, various amounts of *trans*-carveol (**137**) and other *para*-menthenic compounds are also produced.[150] A range of acids were screened, with the focus on Brønsted acids in order to avoid the formation of **134** (**Table 13**). All reactions were monitored by ^{1}H NMR analysis and were worked up when the starting material had been fully consumed or there was no further consumption of starting material observed. In each case the alcohol was used as both the solvent and the reactant.

Table 13: *Acid screen for the synthesis of* ***150*** *and* ***145***



129

150 R = Et
145 R = Me

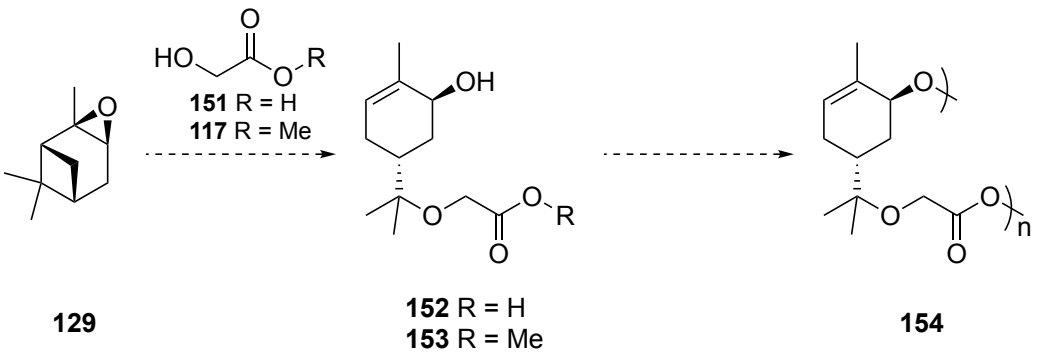
Entry[a]	R	Acid catalyst	Acid (mol%)	Time (h)	Yield (%)
1	Et	No catalyst	N/A	48	0
2	Et	H_2SO_4	0.16	1	4
3	Et	TCNE[158]	12	2	20
4	Et	PTSA	0.16	2	32
5[b]	Me	No catalyst	N/A	6	20
6	Me	H_2SO_4	0.16	2	4
7	Me	TCNE	12	2	11
8	Me	PTSA	0.16	2	35
9	Me	CSA	0.26	2	37

[a]All reactions were carried out by Ms Emma Stoll [b]Reaction carried out in a 50:50 mixture of methanol and water

Initially, the reaction of α-pinene oxide (**129**) and ethanol using sulfuric acid as a catalyst was investigated (**Table 13**, **Entry 2**). Sulfuric acid was chosen because it is a strong Brønsted acid (pKa -3.0).[159] These conditions yielded a high percentage of side products, predominantly **134** and **137**, and a low yield (4%) of the desired product **150**. Tetracyanoethylene (TCNE) is a mild π-acid catalyst and was studied as it has proved to be successful in the ring opening of epoxides, including **129**, in the literature.[158] TCNE gave a substantially improved yield of 20% (**Table 2, Entry 3**). If this reaction was to be applied for the synthesis of a sustainable monomer a higher yield was desirable, from the perspective of green chemistry metrics and for large scale polymerisations.

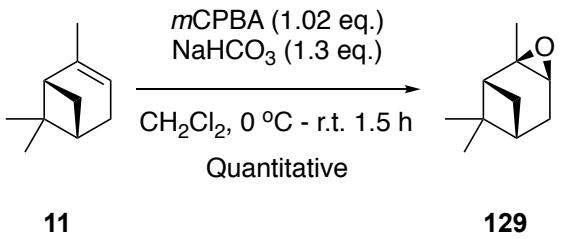
para-Toluenesulfonic acid (*p*-TSA) was chosen as it is a Brønsted acid with a higher pKa than sulfuric acid. Using the weaker acid gave a considerably higher yield than any of the other attempts (**Table 13, Entry 4**). Initial studies used ethanol as the nucleophile, the reaction of α-pinene oxide (**129**) and methanol were subsequently explored to confirm the results were reproducible using a different alcohol (**Table 13**, **Entries 5-9**). The same acids were used to investigate the synthesis of **145** using methanol. Similar trends were observed for the reaction with both ethanol and methanol, sulfuric acid producing the lowest yield of **145** and *p*-TSA giving the highest. Camphor sulfonic acid (CSA) was also investigated for comparison to *p*-TSA (**Table 13**, **Entry 9**) and this gave comparable yields to *p*-TSA. The results show that reasonable yields of *ca.* 35% can be achieved using both methanol and ethanol.

The highest yields were obtained using either *p*-TSA or CSA (**Table 13**, **Entries 4**, **8** and **9**), and therefore subsequent reactions were then carried out using CSA or *p*-TSA as a catalyst. The highest yielding conditions were then used to synthesise molecules which are relevant to polymerisations studies (**Table 14**). One example was proposed to be glycolic acid (**151**); the product would be a terpene derived monomer, **152**, which can undergo polymerisation to form **154** (**Scheme 47**).



Scheme 47: Proposed synthesis of polymers from α-pinene oxide(**129**)

Following the previous optimisation of the synthesis of **145** and **150** it was decided to attempt to trap the carbenium ion **142** with oxygen based nucleophiles which could produce monomers suitable for polymerisation (**Scheme 47**).



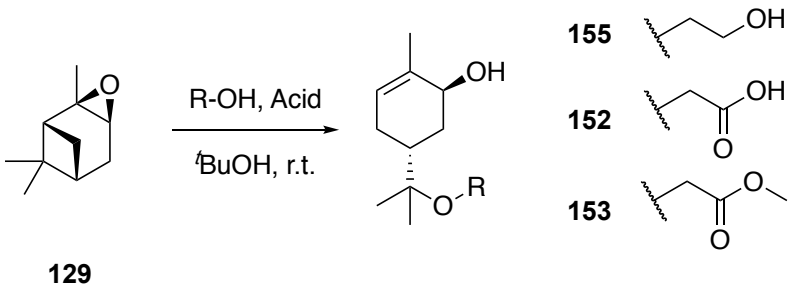
***Scheme 48**: Synthesis of α-pinene oxide (**129**) from α-pinene (**11**)*

α-Pinene oxide (**129**) was accessed through an epoxidation of α-pinene (**11**) using *meta*-chloroperoxybenzoic acid (*m*CPBA), which proceeded smoothly in a quantitative yield.

Ethylene glycol was chosen as a substrate to investigate as it would produce a diol with a primary and a secondary alcohol **108**, which would be able to copolymerise with another bifunctional molecule. Attachment of a carboxylic acid and an ester moiety was also attempted, as this would produce a molecule which is able to homopolymerise. As glycolic acid (**86**) is a solid and methyl glycolate (**87**) is more

expensive than ethylene glycol the reactions were carried out in a solvent, *t*-butanol was chosen as it is a polar, non-nucleophilic solvent.

Table 14: *Reactions of alcohols with α-pinene oxide (**129**) using previously optimised conditions*



129

Entry	Nucleophile	Acid Catalyst	Acid (mol%)	Time (h)	Yield (%)	Product
1[a,b]	Ethylene Glycol	PTSA	0.16	16	36	**155**
2[a,b]	Ethylene Glycol	CSA	0.26	16	38	**155**
3[a]	Glycolic Acid	PTSA	0.16	2	2	**152**
4[a]	Glycolic Acid	CSA	0.26	16	4 (26)[C]	**152**
5	Glycolic acid	CSA	0.26	16	7	**152**
6[a]	Methyl Glycolate	PTSA	0.16	16	6	**153**
7[a]	Methyl Glycolate	CSA	0.26	48	7	**153**
8	Methyl Glycolate	CSA	0.26	5 days	0	**153**

[a]reaction carried out by Ms Emma Stoll. [b]Reaction was carried out neat, in an excess of reagent [C]Quantitative yield (^{1}H NMR spectroscopy)

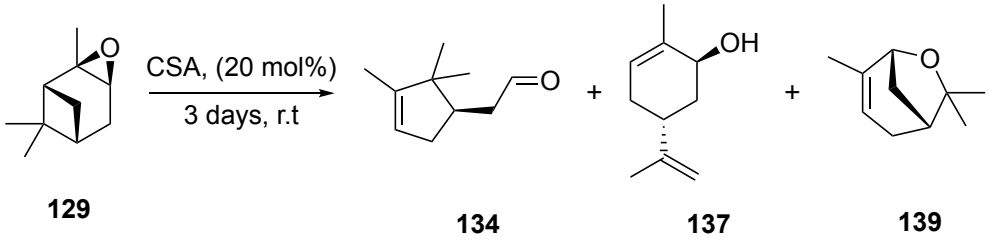
Ethylene glycol was used successfully as a nucleophile under conditions established previously **(Table 14**, **Entries 1** and **2**) to give **155** in a 38% yield. *p*-TSA and CSA gave the best yields previously and these were chosen for the synthesis of **155**, the yields obtained are not significantly different signifying either can be used to catalyse this reaction successfully.

The synthesis of **152** and **153** (**Table 14**, **Entries 3**-**8**) were not as high yielding as previous reactions using the same conditions. It was proposed that reacting with glycolic acid (**151**) (**Table 14**, **Entries 3**-**5**) gave a low isolated yield due to problems with the purification. An ^{1}H NMR yield was calculated using the crude mixture in order to investigate whether the reaction itself was low yielding or the problem was with the purification (**Table 14**, **Entry 4**). ^{1}H NMR analysis with pyrazine as an internal standard indicated that the ^{1}H NMR yield of the reaction was 26%. This is substantially higher than the isolated yield (4%) after silica gel chromatography, indicating purification is not efficient. Throughout this research the purification of the complex mixtures of a range of terpenoid products proved challenging due to the similar R_f values of many of the products. There has been significant separation and isolation difficulties throughout this research and this has resulted in the considerable complications in determining yields and drawing conclusions from many of these reactions.

Reactions with methyl glycolate (**117**) (**Table 14**, **Entries 6**-**8)** especially suffered from low yields, potentially due to the reaction not going to completeion, ^{1}H NMR analysis showed remaining starting material despite running for 5 days (**Table 14**, **Entry 8**). Due to this discrepancy in yields between the different nucleophiles it was necessary to further investigate these reactions.

The effect of solvent on the acid catalysed isomerisation of **129** has previously been established in the literature and was further investigated (**Table 15**).[154] The solvent polarity is essential in influencing whether campholenic aldehyde (**134**) or *trans*-carveol (**137**) is produced. *para*-Menthene type structures are formed in basic, polar solvents such as DMF, however **134** formation occurs in nonpolar solvents, such as cyclohexane.[140,149,151]

Table 15: *Investigation of the effect of solvent on the isomerisation of α-pinene oxide (**129**) under acidic conditions.*



129 **134** **137** **139**

Entry	Solvent	Time	134 (%)[a]	137 (%)[a]	139 (%)[a]	Total (%)[a]	ε^{160}
2	*t*-Butanol	3 days	31	14	11	56	12.5
1	Chloroform	3 days	24	8	16	48	4.81
3	Ethyl acetate	3 days	38	16	22	76	6.02
4	Toluene	3 days	33	16	21	71	2.38
5	Hexane	3 days	23	9	11	43	1.92
6	Chloroform	33 h	31	7	23	56	
7	*t*-Butanol	8 h	25	14	1	45	

[a] Yields were determined by ^{1}H NMR analysis of the unpurified reaction mixture, using pyrazine as an internal standard.

The acid catalysed isomerisation of α-pinene oxide (**129**) in a variety of solvents was investigated. Particular attention was paid to the quantity of acid catalyst needed for **129** to be completely consumed (**Table 15**, **Entries 1**-**5**).

0.26 mol% of CSA was added to **129** in a variety of solvents, chosen for their varying polarities. After 3 hours ^{1}H NMR analysis showed starting material was still present and the reactions were allowed to stir for a further 3 hours. ^{1}H NMR analysis was repeated to investigate whether the ratio of starting material to products had changed, it had not in each case and therefore another portion of acid was added (1.3 mol%). The reactions were again monitored by ^{1}H NMR analysis, a reduction in the amount of starting material, **129**, was observed. Continuous monitoring by ^{1}H NMR analysis was necessary to identify when there was no further change in the ratios of starting materials to product. At this point additional CSA was added (8.5 mol%) and again monitored by ^{1}H NMR analysis. The amount of acid continued to be

increased gradually and the reaction was monitored using ^{1}H NMR spectroscopy, until there was no starting material remaining. The total amount of acid added to observe complete conversion was 20 mol%. The solvent was then removed and the crude residue analysed by ^{1}H NMR using pyrazine as an internal standard to calculate the yields of **134**, **137** and **139**.

The reactions carried out in chloroform and *t*-butanol were repeated for shorter time periods to see if this would increase the amount of **137** produced with respect to the by-products (**Table 15**, **Entries 6** and **7)**. However no significant improvement was observed.

The yields of *trans*-carveol (**137**), pinol (**137**) and campholenic aldehyde (**134**) were quantified using the peaks in the ^{1}H NMR spectra (**Figure 33**). **137** was quantified using its two terminal vinylic protons at 4.74 ppm and the vinylic proton at 5.63 ppm. Campholenic aldehyde (**134**) was quantified *via* its vinylic proton at 5.25 ppm. Pinol (**139**) was quantified *via* the vinylic proton at 5.13 ppm, the proton geminal to the ether ring at 3.62 ppm and the proton at 3.03 ppm.

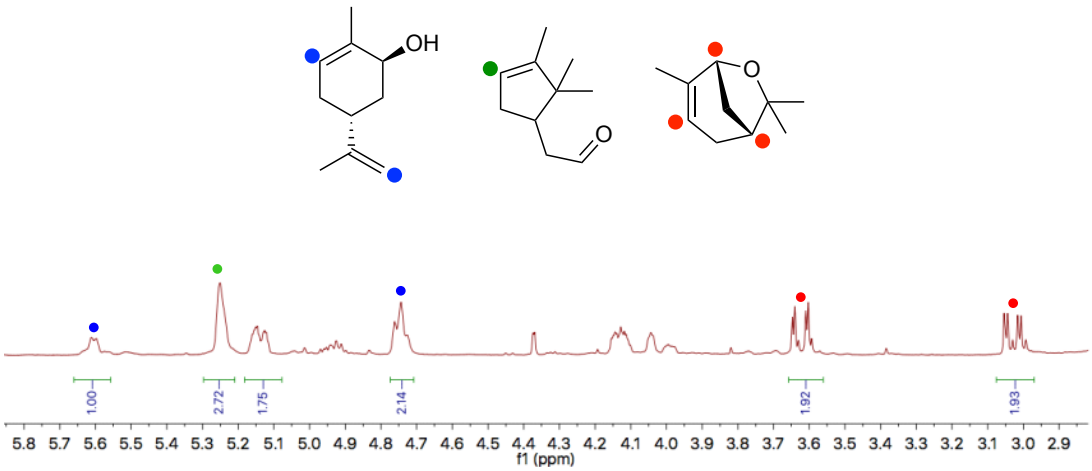


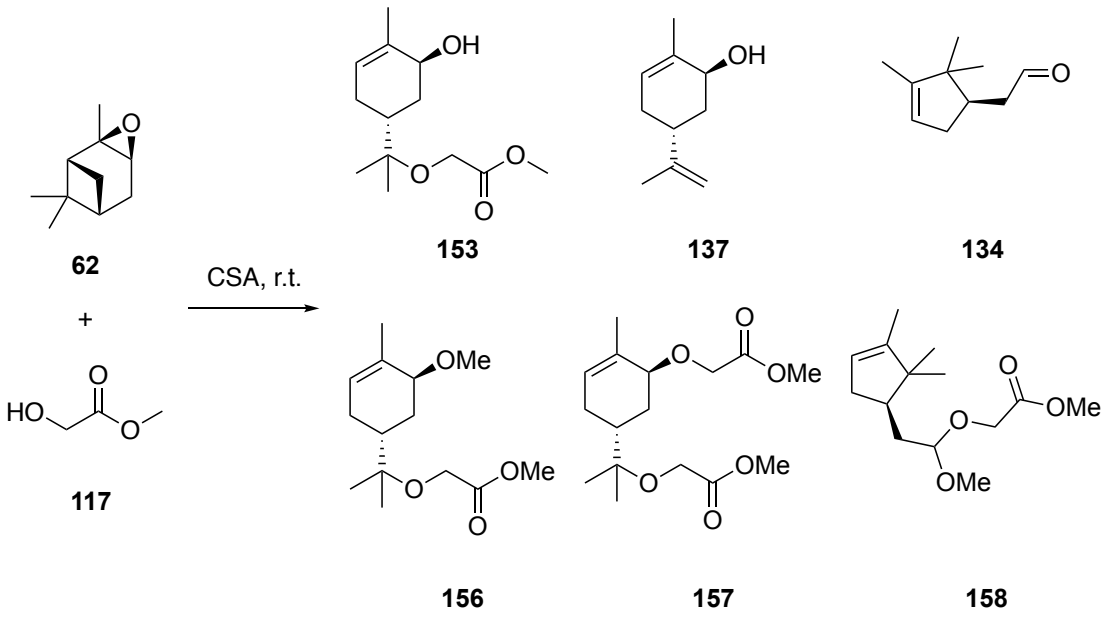
Figure 33: *An example ^{1}H NMR spectra showing the peaks used to determine the yields of **137**, **134** and **139***

The solvent choice seemed to influence the product distribution and also the total crude mass, however there was not an obvious trend between the product distributions and the dielectric constants of the solvents. Focusing on the crude yield of the major products, ethyl acetate and toluene gave the highest values, 76% and 71% respectively (**Table 15, Entries 3** and **4**).

It is hypothesised in the literature that the differing Lewis basicites of the solvents leads to varying abilities to stabilise the carbenium ions formed in the transition states.[154,152] It is proposed that **139** is formed from the dehydration of *cis*-carveol (**138**).[156] Epimerisation of **136** to **138** is slow (*vide supra)*, and therefore **139** is only formed when the reaction was left for a long time in certain solvents.

After investigation of the acid catalysed isomerisation of α-pinene oxide (**129**) in a variety of solvents with no nucleophilic species. It was decided to repeat the synthesis of **153** in an assortment of solvents (**Table 16**). Due to the highest yield of **153** obtained when the reaction was carried out in toluene, the synthesis of **153** was attempted again using toluene as the solvent (**Table 16**, **Entry 1**). Products **134** and **137** were detected by ^{1}H NMR analysis of the reaction mixture and the mass of the desired product **153** was detected by HRMS analysis (m/z = 265.1419), however none of **153** was isolated.

Table 16**: Investigation into acid concentration and solvent effects on the formation of **153



Entry	Time	Products	Solvent	Acid (mol%)	Alcohol (eq.)
1	8 h	**137** + **134**	Toluene	30	1
2	24 h	**137** + **134**	DMF	30	1
3	1 h	N/A	Acetone	20	1
4[a]	1.5 h	**134** + **156** + **157** + **158**	Methyl Glycolate	0.2	20
5[a]	1 h	**134** + **156** + **157** + **158**	Methyl Glycolate	0.2	20

[a]reaction was performed neat.

In 2004, Motherwell *et al.* reported that DMF was able to stabilise the formation of the *para*-menthene tertiary carbenium ion **142**. It was therefore hypothesised that this might be advantageous for the formation of the desired product **153**, thus the reaction was carried out in DMF (**Table 16**, **Entry 2**). ^{1}H NMR analysis of the reaction mixture proved challenging due to the high boiling point of DMF and the starting material's sensitivity to water. The reaction was therefore worked up after 24 hours, to give a crude mixture of products in a 32% yield. The crude residue was purified by column chromatography on silica gel, to yield **134** and **137** however the desired product **153** was not isolated. The reaction was attempted in acetone (**Table**

16, **Entry 3**), analysis using TLC indicated a complicated mixture of products and attempts at purification was not attempted.

The highest yields of previous reactions have been achieved when the reagent was used as the solvent. These conditions were applied to the synthesis of **153** (**Table 16, Entries 4** and **5**). The reaction was monitored by ^{1}H NMR analysis and was complete within one hour. Due to the high boiling point of methyl glycolate (**117**) the reaction mixture was loaded directly onto silica for purification using silica gel chromatography. The purification of the crude mixture yielded fractions which were made up of a number of products, however clean samples of **157**, **158** and **134** were collected. ^{1}H NMR analysis of the purified compounds resulted in the conclusion that **156**, **157**, **158** and, **134** were formed. HRMS analysis of the crude mixture prior to purification indicated that the product had been formed (m/z = 265.1418) despite this **153** was not isolated.

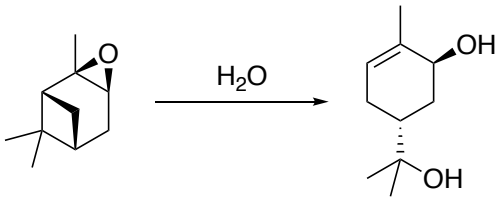
In conclusion, the solvolysis of α-pinene oxide (**129**) produces a complicated mixture of products suggesting the involvement of several reactive carbenium intermediates, making the reaction itself extremely challenging to study. The solvolysis reaction has been optimised for a range of alcohol based nucleophiles and the resulting product distribution extensively studied. Two potential novel terpene based monomers **152** and **155** have been synthesised in reasonable yields (11% and 38% respectively) and after scale up could be used for synthesis of novel, renewable polyesters. The mass recovery from reactions is often lower than 60% and there are discrepancies between ^{1}H NMR yields and isolated yields obtained after purification, therefore it was decided not to take these monomers forward for polymerisation studies.

3.1.2. Optimisation of the Synthesis of *trans*-Sobrerol (136) for Copolymerisation

One of the common products from the hydrolysis of α-pinene oxide (**129**) is *trans*-sobrerol (**136**). This diol was hypothesised to act as a co-monomer for the synthesis of polyesters. *trans*-Sobrerol (**136**) has been previously synthesised in the literature by Xu *et al.* and these conditions were selected as a starting point for future

investigations (**Table 17**, **Entry 1**). The reaction is carried out by simply mixing α-pinene oxide (**129**) in water. The water acts as the nucleophile, catalyst, and the solvent. Using these conditions, **136** was synthesised in a 47% yield.

Table 17: *Investigations into the synthesis of trans-sobrerol (**136**)*



129 **136**

Entry	Concentration (M)	Scale (mmol)	Time (h)	Yield (%)
1[a]	0.083	10	4.5	47
2[b]	0.083	66	4	55
3[c]	0.083	98	4	27
4	0.083	10	18	32
5	0.083	10	28	35
6	0.083	10	55	49
7	0.25	253	18	51

[a]purified through column chromatography [b]passed through plug of silica [c]recrystalisation

The literature quoted a 69% yield for the synthesis of **136**, however the yield could not be replicated using the literature conditions. Optimisation reactions were conducted in an attempt to improve the yield. The reaction was repeated on a larger scale and due to the large scale the purification was attempted using a recrystallisation in ethyl acetate, as opposed to a column chromatography (**Table 17**, **Entry 3**). This gave a lower yield than using column chromatography (27% *vs* 47%). The reaction was attempted again for a longer period of time (18 h) (**Table 17**, **Entry 4**) and the work up was changed from an organic extraction to the removal of the aqueous solvent under reduced pressure to leave the solid *trans*-sobrerol (**136**) (32%) and some side products. This residue was then washed using cold dichloromethane to yield pure **136**. This work up uses less organic solvent and also less lab time, consequently it was decided to use this procedure for all future reactions. The duration of the reaction was then investigated. The time was increased in an attempt

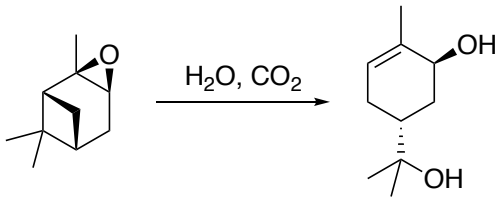
to increase the yield (**Table 17**, **Entries 4**-**6**). The yields steadily increased with the length of the reaction (32% - 49%). However a long reaction time (55 h) was required to achieve the highest yield (**Table 17**, **Entry 6**). The reaction was then performed at a higher concentration in order to reduce the amount of water used (**Table 17, Entry 7**), the reaction was worked up after 18 h and **136** was isolated in a 51% yield.

Although it was desirable to synthesise **136** without the need to add a catalyst, the yields achieved were not as high as those in the literature. It was therefore decided to use conditions detailed in a patent, which describes the synthesis of **136** using CO_2 as an acid catalyst.[161] The CO_2 was bubbled through the water and the pH was monitored until it reached 3.7, the solution was then heated to 35 ^oC. At this point α-pinene oxide (**129**) was added and the reaction heated to 100 ^oC (**Table 18**, **Entry 1**). *trans*-Sobrerol (**136**) crashed out of the solution as a white solid which could then be isolated simply through a filtration, before purification by washing with cold dichloromethane. The yield for this reaction was low (28%) despite the patent quoting a yield of >95%; it was therefore decided to investigate the reaction further to attempt to increase the yield.

It was hypothesised that conducting the reaction at 100 ^oC could be causing the product to decompose and therefore the time was reduced to 1 h (**Table 18, Entry 2**). Again, white solid crashed out of the reaction and this was isolated and washed, yielding **136** in a 52% yield, a significant increase on the previous 28%. As mentioned previously, the reaction of α-pinene oxide (**129**) produces by-products, including campholenic aldehyde (**134**), and it was suggested in the literature that temperatures above 35 ^oC encourages the formation of this by-product.[162] The literature also indicated that the CO_2 could be added as a solid to lower the pH, and this method was used for all subsequent reactions. The reaction was therefore repeated at 35 ^oC in an attempt to supress the formation of **134** (**Table 18**, **Entry 3**). The α-pinene oxide (**129**) was added at room temperature (22 ^oC) and the temperature was then increased to 35 ^oC. The product was isolated in a lower yield than previous reactions (26%) and it was hypothesised that this was due to the addition of the α-pinene oxide (**129**) at a lower temperature. The reactions were repeated at 35 ^oC for 4 h and 16 h (**Table 18**, **Entries 4** and **5**) to give yields of 44% for both time periods. The reaction was

repeated and the temperature was increased to 50 °C for the duration of the reaction which gave a slightly lower yield of 40% (**Table 18, Entry 6**).

Table 18: *Synthesis of trans-sobrerol (**136**) using CO_2 as a catalyst*



129 **136**

Entry	Concentration (M)	Scale (mmol)	Time (h)	Temp Added (°C)	Temp (°C)	Yield (%) (^{1}H NMR Yield)
1[a]	3.85	77	3	35	100	28
2[a]	3.85	77	1	35	100	52
3	1.3	77	22	22	35	26
4	0.5	6.6	4	35	35	44
5	0.5	6.6	16	35	35	44
6	0.5	6.6	1	35	50	40
7	3.85	77		35	100	44 (51)
8	3.85	77	24	35	35	49 (55)
9	3.85	77	24	35	100	No solid crashed out
10	3.85	77	24	r.t.	r.t.	50 (56)
11	3.85	77	24	0	r.t.	38 (43)
12	3.85	77	24	5	5	26 (31)
13[b]	3.85	77	24	r.t.	r.t.	68

[a]CO_2 was bubbled through reaction prior to addition. [b]CO_2 was continuously bubbled through the reaction.

The reaction cannot be monitored using standard techniques (mass spectrometry, TLC or ^{1}H NMR spectroscopy). This is due to the inability for mass spectrometry to detect **129**, reactivity of **129** with silica, and the non-homogeneity of the reaction mixture. Subsequently it was decided to monitor the reaction using *in situ* fourier transform infrared (FTIR) spectroscopy in order to investigate the consumption of **129** and the formation of the desired product **136** and the by-product **134**.

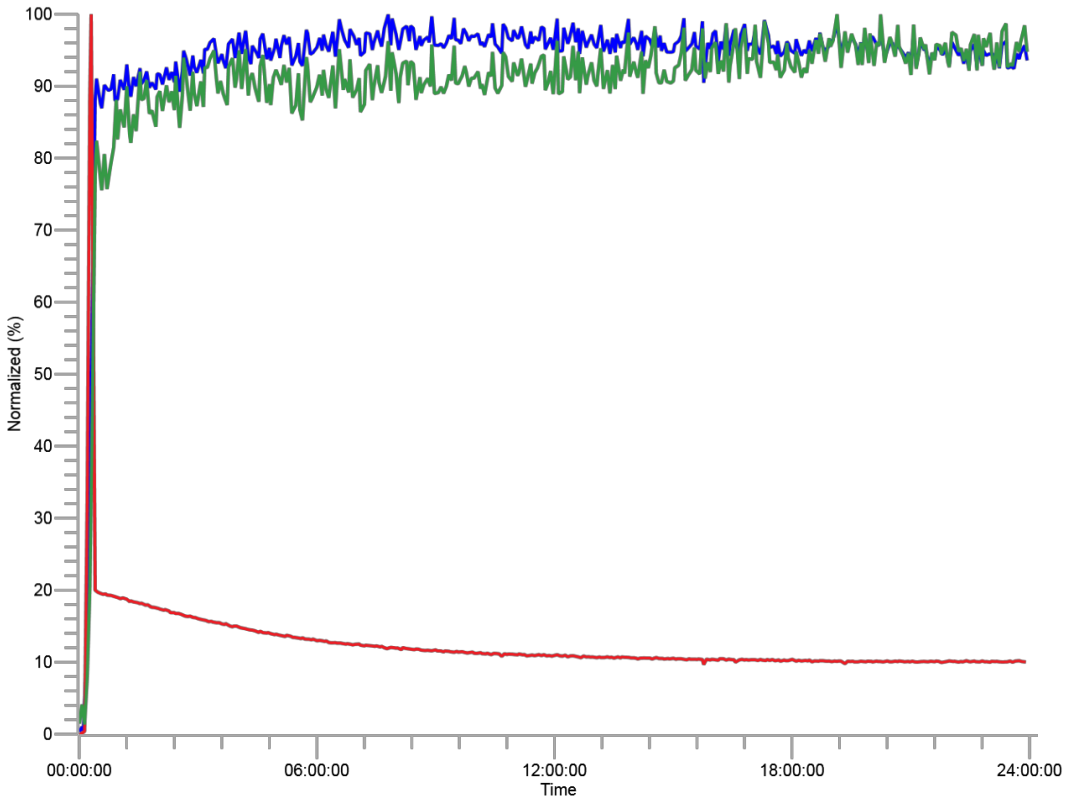


***Figure 34**: Reaction profile of the synthesis of **136** at 100 °C (**Table 18, Entry 7**). The red, green and blue lines represent the concentrations of α-pinene oxide (**129**), campholenic aldehyde (**134**), and trans-sobrerol (**136**) respectively.*

The reactions carried out at temperatures of 100 °C and 35 °C were repeated using time resolved IR (**Table 6**, **Entries 7** and **8**). Peaks arising from **129**, **136** and **134** were tracked using the software to show the consumption of the starting material alongside the formation of the desired product **136** and the by-product **134**. At 100 °C the reaction appeared to be finished after approximately 30 min and after that point the quantities of reagents didn't vary significantly (**Figure 34**). There was some concern that the purification method of washing the crude material with cold dichloromethane was resulting in loss of some of the product in the washings. It was therefore decided to include an internal standard in the ^{1}H NMR analysis of the product. The ^{1}H NMR analysis indicated that the product was synthesised in a 51% yield, and after washing the product was isolated in a 44% yield.

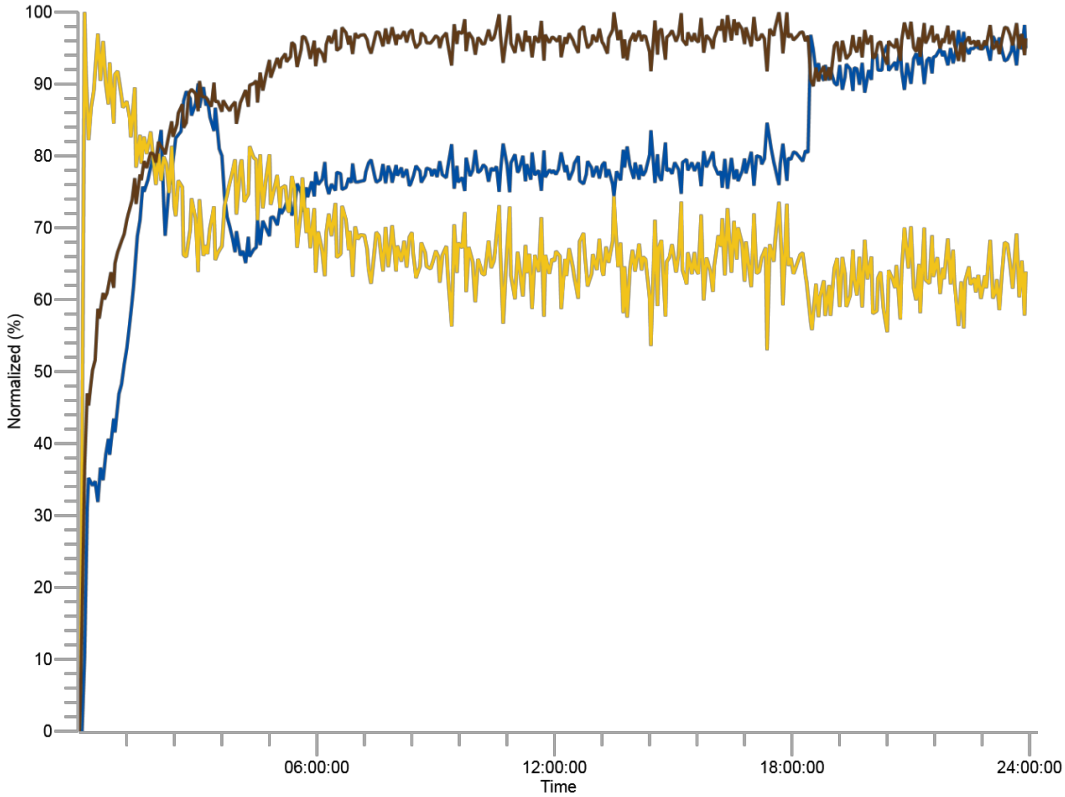


***Figure 35**: reaction profile of the reaction at 35 °C. (**Table 18, Entry 8**). The yellow, blue and brown lines represent the concentrations of α-pinene oxide (**129**), campholenic aldehyde (**134**), and trans-sobrerol (**136**) respectively.*

The reaction was repeated at 35 °C to try and inhibit the formation of the aldehyde **134**. The reaction profile indicated that the starting material was completely consumed after approximately 8 hours, a significantly longer period of time than the reaction that was performed at 100 °C. The reactions carried out at the lower temperatures gave higher yields, both the quantitative ^{1}H NMR and isolated yields were higher (55 and 49% respectively). From the ^{1}H NMR analysis it was suggested that the wash with cold dichloromethane results in an approximate 5% loss of yield; this is still preferable over a labour and resource intensive column. It was hypothesised that at lower temperatures the formation of **134** was supressed leading to the higher yield of **136**. Therefore the temperature was lowered further and the reaction was repeated at room temperature (**Table 18**, **Entry 10**). This reaction produced **136** in the highest yield of 56% (50% isolated). The reaction temperature was then decreased to 5 °C, however the isolated yield dropped significantly to 26%.

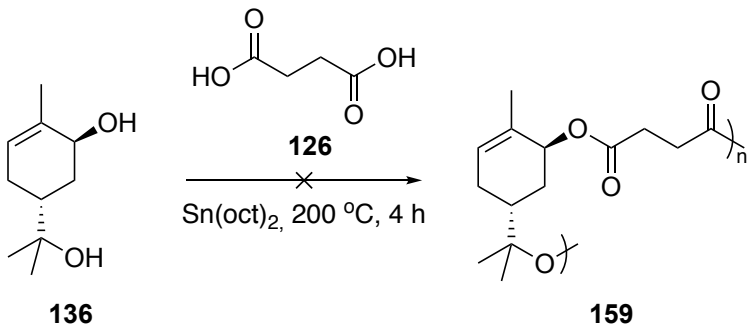
It was concluded that the temperature needed to be high enough to achieve a reasonable yield, however there is a point where the temperature gets too high, and the formation of by-products lowers the yield.

The reaction that gave the highest yield was carried out at room temperature, it was therefore decided to repeat this reaction with the CO_2 being bubbled through for the duration of the reaction (**Table 18, Entry 13**). It was hypothesised that this would ensure that the reaction was at the optimum pH throughout the reaction for the synthesis of **136**. **136** was isolated in a 68% yield and analysis using quantitative ^{1}H NMR spectroscopy indicated that the product was pure. This represents a significant increase in the yield and has the benefit of not needing purification steps.

The synthesis of *trans*-sobrerol (**136**) was investigated and the procedure optimised. **136** was synthesised in a 68% yield using a simple and easily scalable procedure with little to no purification needed. A large scale synthesis of **136** was then carried out in order to take forward a large amount of material for polymerisation studies.

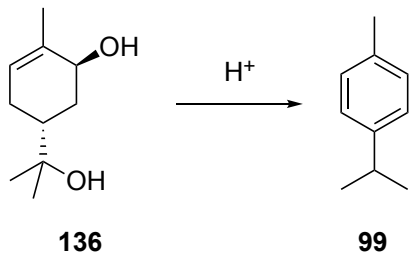
3.1.3. Attempted Polymerisation of trans-Sobrerol (136) with a Comonomer

The polymerisation of **136** with succinic acid (**126**) was next investigated. The catalyst chosen was $Sn(oct)_2$ as it is known to be an effective catalyst for the polycondensation reaction between carboxylic acids and alcohols.[135] The polycondensation between **126** and **136** was performed at 200 ^{o}C and was monitored every 15 minutes, using ^{1}H NMR spectroscopy, for 4 hours.



Scheme 49**: Attempted polymerisation of **136** and **126

The polymerisation reaction was unsuccessful and ^{1}H NMR analysis showed that *p*-cymene (**99**) was being formed with no detection of polymer **159** (**Figure 36**). Peaks at 7.08 and 2.84 ppm in the ^{1}H NMR spectrum confirms the presence of *p*-cymene, and these increase in intensity as the reaction progresses and the peak at 4.00 ppm corresponding to the diol decreases. This is proposed to happen due to the dehydration of *trans*-sorberol (**136**) in the presence of succinic acid (**126**), and is driven by the stabilisation effect of the formation of the aromatic ring (**Scheme 50**).[156]



Scheme 50**: Acid catalysed dehydration of **136** to form **99

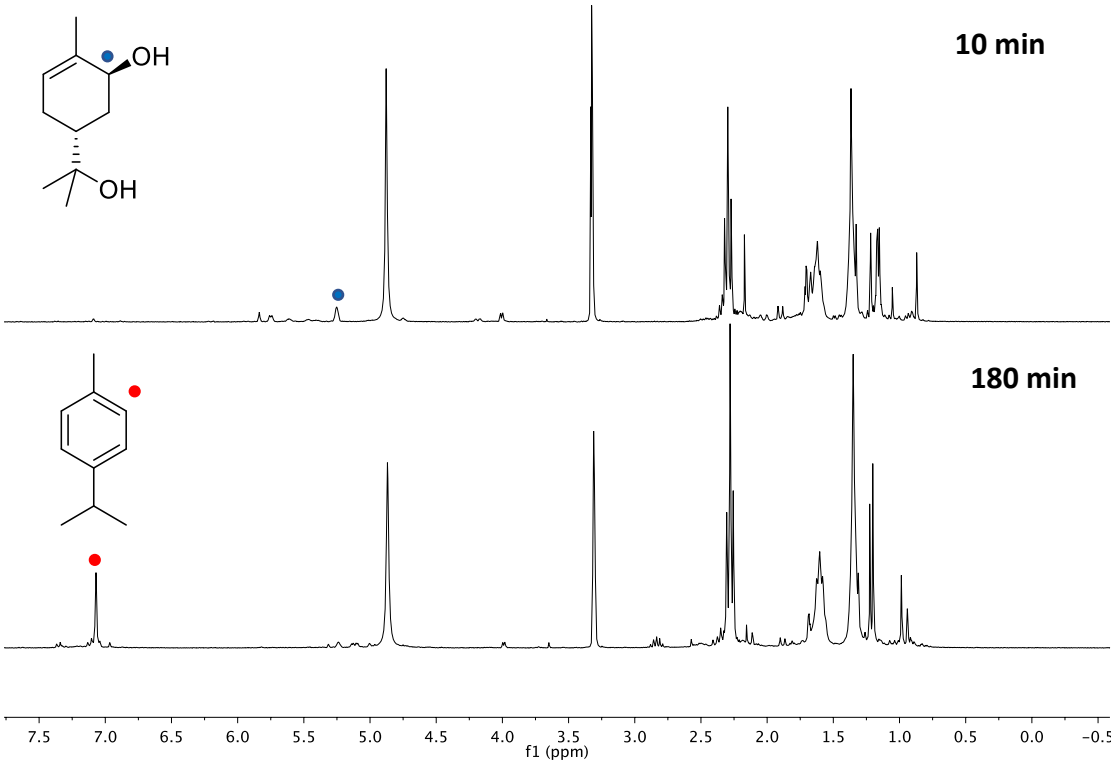
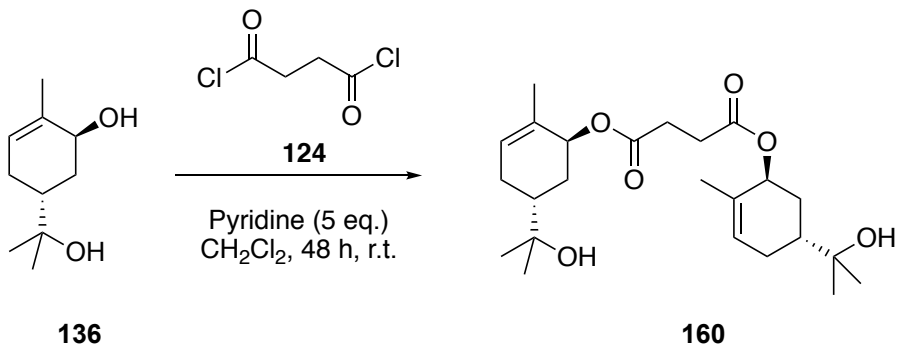


Figure 36: *^{1}H NMR analysis of the polymerisation of **126** and **136**. Spectrum at 10 min shows the monomer and the spectrum after 180 min shows the formation of p-cymene (**99**)*

To overcome the sensitivity of **136** to acidic conditions, it was decided to use succinyl chloride (**124**) as the co-monomer. Acyl chlorides are common comonomers for the synthesis of polyesters and allowed the use of a solution polycondensation technique.[163] The method involves the use of a 1:1 stoichiometric ratio of diol to diacid chloride in a suitable solvent with an excess of pyridine to neutralise the HCl condensate, ensuring **136** isn't exposed to acidic conditions (**Scheme 51**).[164,131]



Scheme 51: *Synthesis of tertiary alcohol capped diester **160***

The reaction was analysed using ^{1}H NMR spectroscopy which indicated that *trans*-sobrerol (**136**) had been consumed. Shifts in the ^{1}H NMR were observed, the resonance at 4.04 ppm was shifted to 5.29 ppm indicating the esterification was successful. Integrations indicated the diester **160** was synthesised, and this was also observed using mass spectrometry analysis (m/z = 446.2596).

It was hypothesised that **160** was synthesised due to the sterically hindered tertiary alcohol not reacting with the acyl chloride **124**. As the other site for esterification is a quaternary carbon, the ^{13}C NMR spectrum was analysed looking for a chemical shift at 72.5 ppm. The ^{13}C NMR showed no substantial shift for that carbon, and this absence of significant shift implied that the tertiary alcohol group did not react with the acyl chloride **124**.

GPC analysis suggested that the polymerisation reaction did not form high molecular weight polymers (>1 kDa). MALDI-TOF was also used to analyse the polymers formed and this agreed with the highest molecular weight species being <1 kDa.

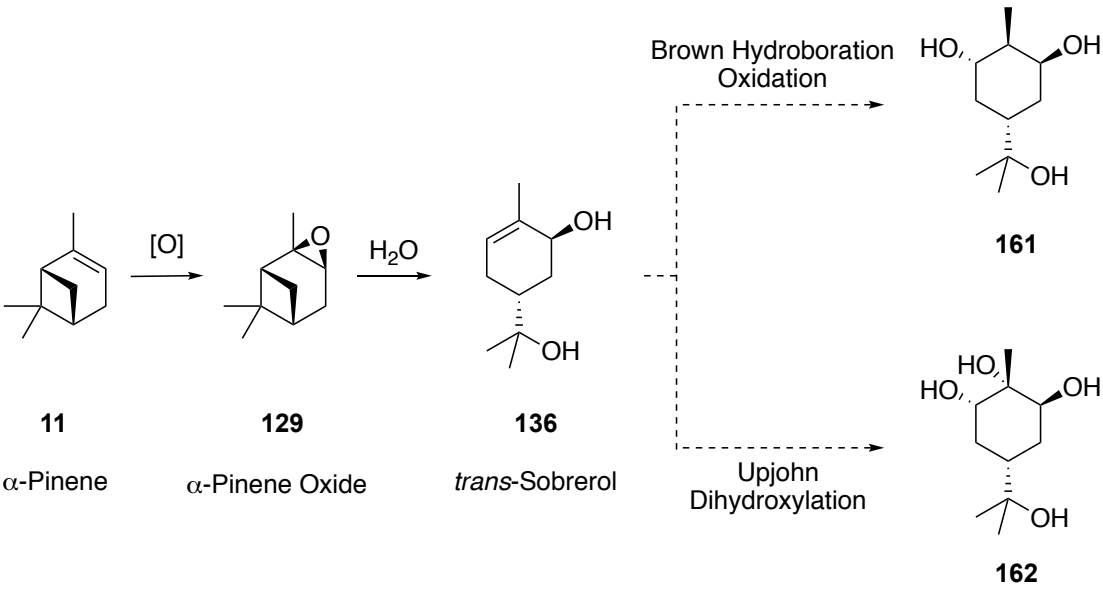
trans-Sobrerol (**136**) was seemingly not useful in the synthesis of polymers, as it didn't possess two reactive centres needed for step growth polymerisation. Despite this; it was hypothesised that the alkene functionality could be further functionalised to synthesise a molecule which could be used for step growth polymerisation.

3.2. Synthesis of *trans*-Sobrerol derived diols for copolymerisation

3.2.1. Synthesis of Monomers

As previous investigations show *trans*-Sobrerol **(136)** only possesses one reactive centre towards step-growth polymerisation (secondary hydroxyl group), consequently it could not be used in the synthesis of polymers. It was hypothesised that a convergent strategy could be employed, resulting in the synthesis of two new α-pinene (**11**) derived monomers (**161** and **162**). Utilising the alkene functionality of *trans*-sobrerol (**136**), it was hypothesised that Brown hydroboration and Upjohn

dihydroxylation could be used to access the 'triol' **161** and the 'tetraol' **162** respectively (**Scheme 52**).



Scheme 52: *Proposed synthesis of triol **161** and tetraol **162***

The triol **161** and tetraol **162** both contain the same core structure, possessing a *p*-menthane core with a tertiary alcohol group at C8, and two hydroxyl groups on C2 and C6 (**Figure 37**). For **162** C1 is functionalised with a fourth hydroxyl group and in the case of **161** C1 is bonded to a hydrogen. It was theorised that the polymerisation would proceed through the two hydroxyl groups in the C2 and C6 positions and the tertiary alcohol groups in the C1 and C8 positions would not take part in the polymerisation (**Figure 37**). The resulting polymer would contain free hydroxyl groups and it was theorised that this would increase the hydrophilicity adding the potential for water solubility of the polymer.

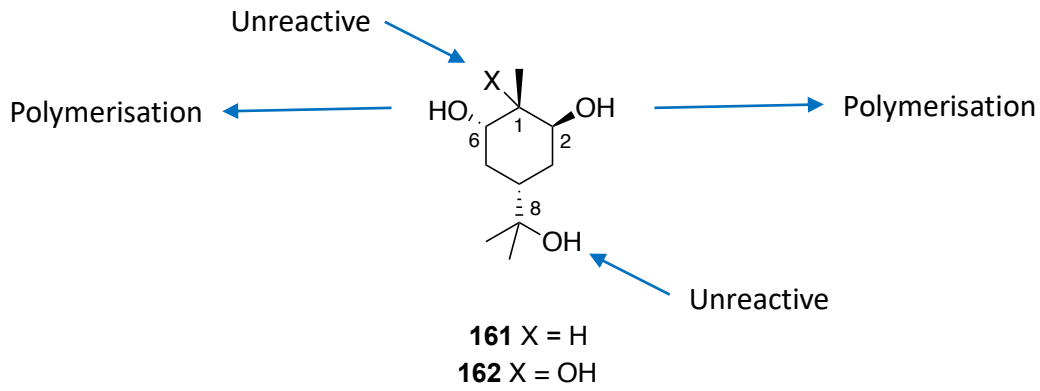
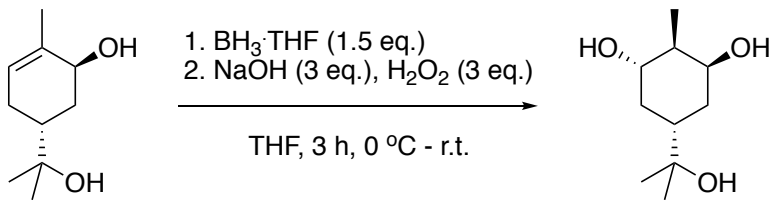


Figure 37: *Predicted polymerisation of* ***161*** *and* ***162*** *through their two secondary alcohols*

It was decided to first investigate the synthesis of triol **161** using a Brown hydroboration / oxidation sequence employed previously in this research.

It was hypothesised that monomer **161** would not be sensitive to acidic conditions due to the absence of a double bond, meaning the driving force of the formation of an aromatic compound (*p*-cymene (**99**)) will no longer be problematic. **161** could be used in melt and solution polycondensations to form a polymer with a free tertiary alcohol functionalisation. Hydroxyl functionalised polymers have generated a lot of interest in polymer chemistry due to their potential for many applications such as drug delivery systems.[165]

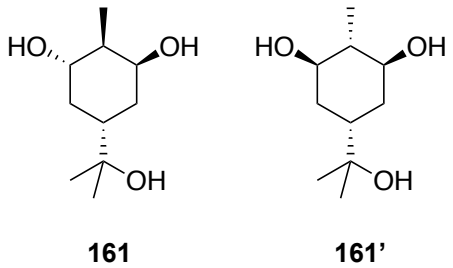


136 **161**

Scheme 53: *Synthesis of triol* ***161*** *using a Brown hydroboration oxidation*

The monomer **161** was synthesised using the Brown hydroboration / oxidation conditions previously established for the synthesis of monomer **104** (**Scheme 53**). Compound **161** was successfully synthesised and purified *via* a recrystallisation in acetonitrile.

The hydroboration / oxidation reaction proceeded stereoselectively to incorporate an alcohol group generating **161** and **161'** with a d.r. of (85:15) (**Figure 37**). The major diastereomer being **161**, where the newly added hydroxyl functionality is in a *trans* configuration to the original OH group, subsequent recrystallisation from hot acetonitrile yielded the major diastereomer **161** in a 55% yield. The minor diastereomer was isolated *via* silica gel column chromatography and identified using ^{1}H NMR spectroscopic analysis.



161 **161'**

Figure 37: *The two diastereomers resulting from the Brown hydroboration / oxidation of* ***136*** *(d.r.85:15)*

Single crystals of the major diastereomer suitable for X-ray diffraction studies were grown by slow evaporation in deuterated chloroform, which allowed for the assignment of absolute stereochemistry (**Figure 38**).

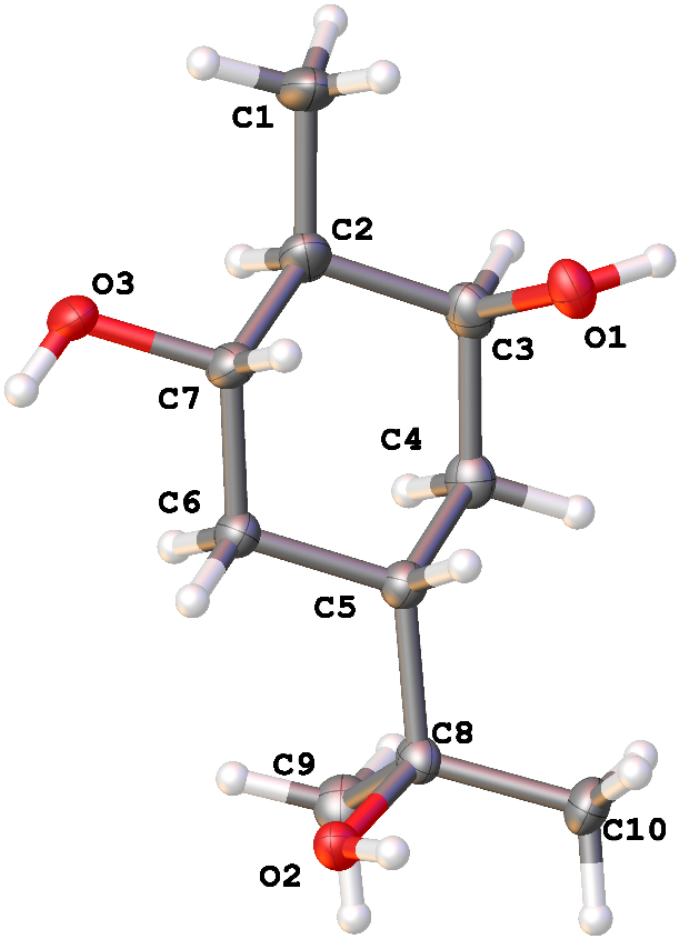
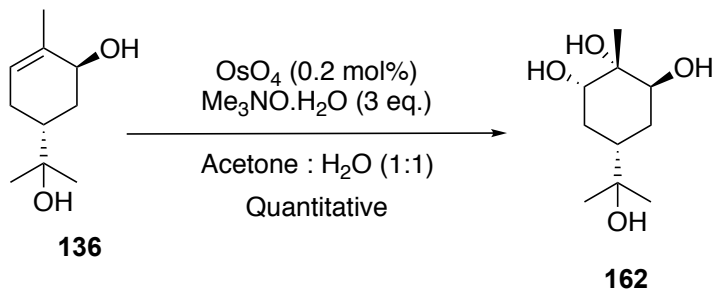


***Figure 38**: Molecular structure of **161** determined by X-ray crystallography.*

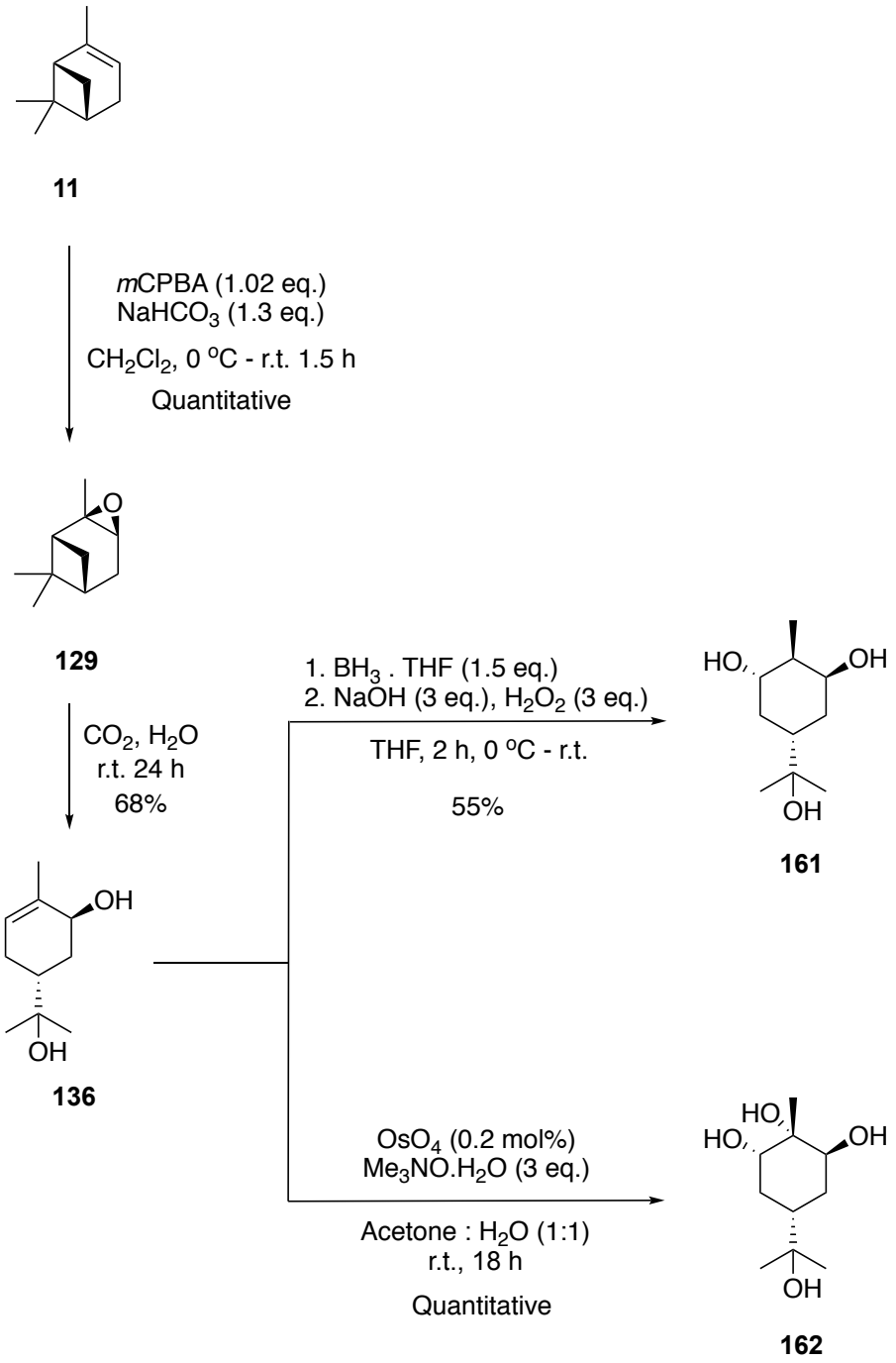
The second novel monomer was accessed from *trans*-sobrerol (**136**) using an Upjohn dihydroxylation (**Scheme 54**). The reaction proceeded smoothly to give **162** after 18 h in a quantitative yield after purification *via* column chromatography.



***Scheme 54:** Synthesis of tetraol **162** from trans-sobrerol (**136**). (Performed by Dr Jonathan Moore)*

The Upjohn dihydroxylation proceeds *syn*-selectively however in this case the reaction also proceeded diastereoselectively to give **162** as a single diastereomer. It is hypothesised that the osmium tetroxide adds to the bottom face of the *trans*-sobrerol due to the steric constraints of the allylic alcohol. The stereochemistry was confirmed using single crystal X-ray diffraction spectroscopy.

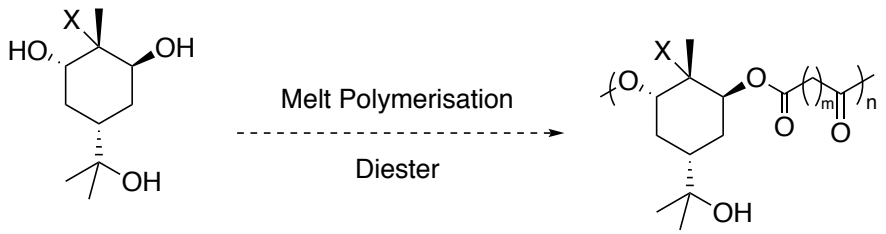
Two new molecules which are hypothesised to possess the correct functionality to polymerise were synthesised from *trans*-sobreol (**Scheme 55**). This represents the first synthesis of monomers for step-growth polymerisation from α-pinene (**11**). The Brown hydroboration / hydroboration and the Upjohn dihydroxylation proceed in a stereoselective manner to give the monomers **161** and **162** respectively as single diastereomers, in three steps from **11**. The triol **161** synthesised in an overall yield of 37% over three steps and the tetraol **162** in an impressive 68% yield over three steps. Both reactions were performed on the multigram scale and the material taken forward for polymerisation studies.



Scheme 55**: Synthesis of triol **161** and tetraol **162** from **11

3.2.2. Polymerisations of triol 161 and tetraol 162

The synthesis of both the triol **161** and tetraol **162** were scaled up to the multigram scale in order to perform polymerisation studies. It was hypothesised that both monomers would polymerise through their secondary alcohols and that the tertiary hydroxyls would remain unreacted as seen previously using **136** (**Scheme 56**).

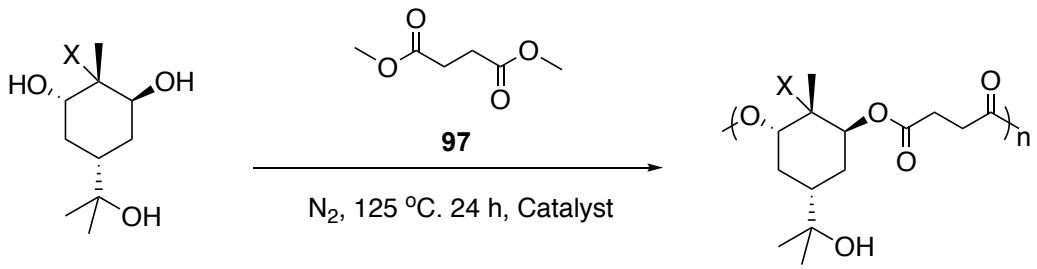


161 X = H
162 X = OH

163 X = H
164 X = OH

Scheme 56: *Proposed polymerisation of **161** and **162** with a diester*

Table 19: *Attempted polymerisation of **161** and **162** using dimethyl succinate (**97**)*



161 X = H
162 X = OH

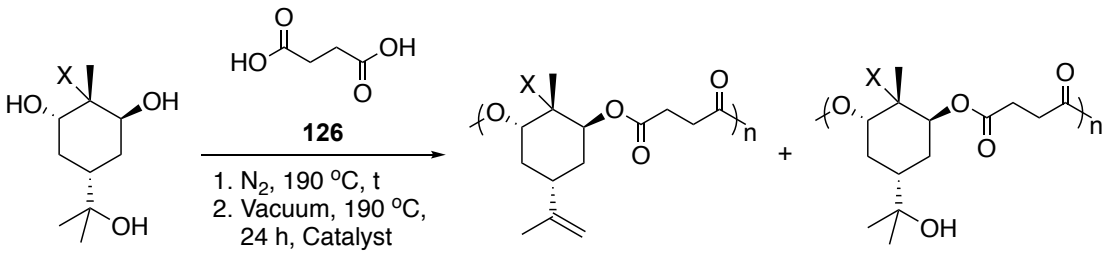
163 X = H
164 X = OH

Entry	Monomer	Catalyst	Catalyst (mol%)	Polymerisation
1	Triol	TBD	5	No
2	Triol	TBD	10	No
3	Triol	$Ti(OBu)_4$	1	No
4	Tetraol	TBD	5	No
5	Tetraol	TBD	10	No
6	Tetraol	$Ti(OBu)_4$	1	No

Polymerisations were attempted using dimethyl succinate (**97**) as the comonomer under melt conditions. TBD and $Ti(OBu)_4$ have both been shown to be active catalysts in the polymerisation of a diol and diester,[166] and therefore these were selected to catalyse the reaction. The monomers were heated to 125 ^oC for 24 h at which point ^1H NMR analysis was used to probe the reactions. For each reaction, the analysis revealed that the monomers remained intact and no transesterification had occurred (**Table 19**).

The use of a diester as a comonomer was unsuccessful, however it is common for both diesters and dicarboxylic acids to be used for the synthesis of polyesters using melt polymerisation techniques.[163] Therefore it was proposed to use a diacid to act as the comonomer. The polymerisations were performed using standard melt conditions described previously in this project. Both tin and titanium catalysts were investigated at 190 ^oC (**Table 20**). The diacid used as the comonomer was again chosen to be succinic acid as it can be obtained from renewable resources.[133] **161** was submitted to the polymerisation conditions (**Table 20**, **Entry 2**).

Table 20: *Polymerisation studies of **161** and **162** with succinic acid (**126**)*



161 X = H
162 X = OH

165 X = H
166 X = OH

163 X = H
164 X = OH

Entry	Monomer	Catalyst	T (°C)	Product	M_n (Da)	T_g (°C)
1	**161**	$Sn(oct)_2$	3	**165**	8100	66
2	**161**	$Sn(oct)_2$	24	**165**	8700	68
3	**161**	$Ti(OBu)_4$	24	**165**	8000	65
4	**162**	$Sn(oct)_2$	3	**166**	5800	80
5	**162**	$Sn(oct)_2$	24	**166**	6900	77
6	**162**	$Ti(OBu)_4$	24	**166**	5700	78

The ^{1}H NMR analysis of the polymer indicated that the esterification was successful. Suggested by the shift of the resonances of the protons *alpha* to the oxygen from ~3.5 and 3.9 ppm to ~5 ppm. To further investigate the polymerisation ^{13}C NMR analysis was performed. The analysis showed that the peaks at ~27 ppm corresponding to the two methyl groups in the C8 position had shifted significantly up-field, indicating the tertiary alcohol may not have remained intact during the polymerisation. There was also a carbon shift at a ppm at 109 ppm which was not present in the monomer, and using DEPT-135 analysis alongside HSQC NMR analysis this was found to be a CH_2 carbon (**Figure 40**). The shift and multiplicity is indicative of alkenic protons. This analysis suggests that under the acidic conditions of the polymerisation the tertiary alcohol may have eliminated to yield a terminal alkene producing the polymer **165**.

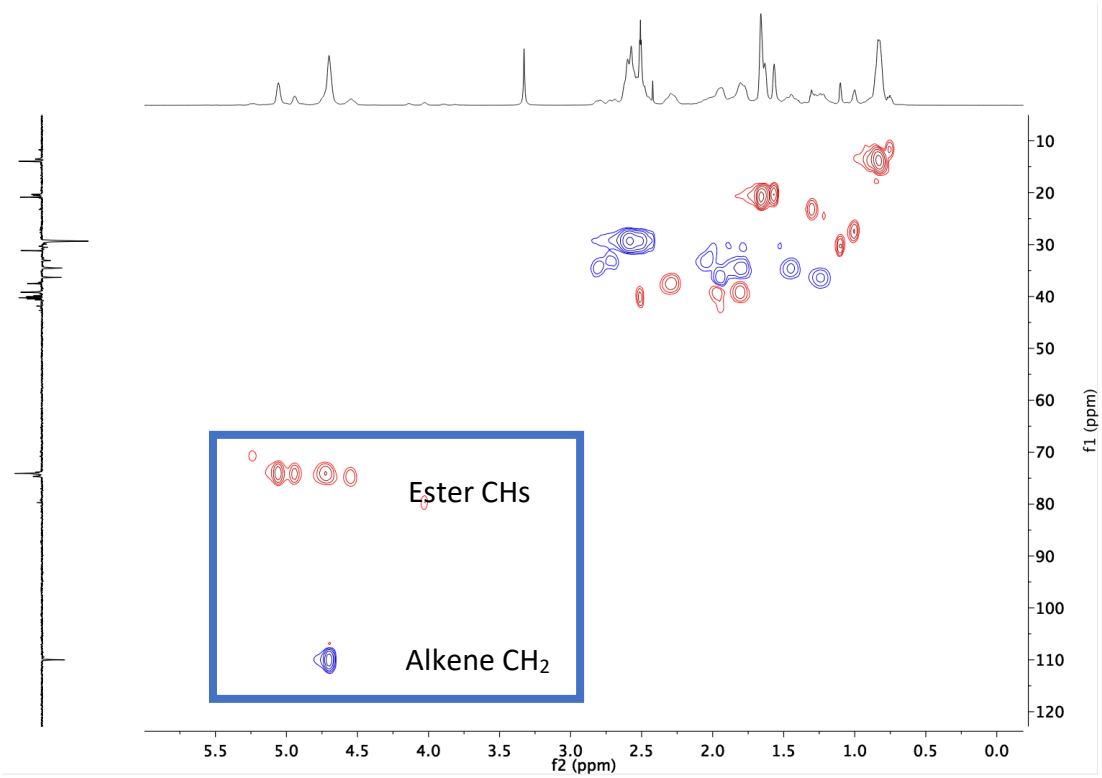


Figure 39: *Multiplicity edited HSQC NMR spectra of the polymer* ***165***

The polymerisation was repeated with the tetraol **162** using the same conditions (**Table 20**, **Entry 5**) and the ^{1}H NMR analysis indicated that the hydroxyl group had again been eliminated under the acidic conditions to give the polymer **166**. The HSQC NMR analysis indicated the presence of one alkenic CH_2 and from this is was assumed that the alcohol at the C6 position had not undergone elimination.

The polymerisations were attempted with stannous and titanate catalysts for different lengths of time (**Table 20**). The resulting polymers were analysed using GPC and DMA to probe their molecular weights and T_gs. The triol **161** was able to reach molecular weights of up to 8.7 kDa (**Table 20**, **Entries 1-3**) and the tetraol **162** slightly lower M_ns of 6.9 kDa (**Table 20**, Entries 4-6). In general, the tetraol-based polymers had a lower molecular weights than their comparative triol-based polymers. It was hypothesised that this may be due to the increased rigidity of the tertiary alcohol at

the C6 position on the tetraol **162** resulting in a higher amount of steric hindrance in the polymerisation of the tetraol **162**.

Varying the reaction time and the catalyst didn't result in a large difference in the polymer properties (M_ns and T_gs). Arguably the optimum conditions are those using the titanium catalyst due to its green chemistry credentials such as low toxicity and high natural abundancy.[163]

Analysis of the polymers using DMA showed T_gs of between 65 and 80 °C. The triol polymers had T_gs in the range of 65-68 °C, and the tetraol based polymers exhibited T_gs in the range of 77-80 °C (**Table 20**). The triol-based polymers have lower glass transition temperatures than the tetraol-based polymers despite the fact that they have higher molecular weights. This may be be due to the fact that they are less rigid than the tetraol polymers due to the absence of the alcohol in the C6 position. Both polymers have relatively high T_gs for aliphatic polyesters derived from renewable resources. In fact, to the best of our knowledge, the highest T_g of a terpene derived polyester is 70 °C.[102] Polyesters **165** and **166** also have the benefit of being derived from the most abundant terpene, showing an example of an α-pinene based polymer which displays a unique backbone and high T_gs. It is hypothesised that because the backbone incorporates the cyclohexane ring, this imparts the structural rigidity to give the polymer the high T_gs observed, despite the low molecular weights (< 10 kDa).[167–169] The polymers have a terminal double bond in the pendant chain and it is hypothesised that this could be beneficial for post polymerisation functionalisation or cross-linking in the future.

3.3. Investigations into the Stereocomplexation of Polymer 165

The monomer **161** is a single enantiomer containing four defined stereocentres and therefore have the potential to form stereoregular polymers. It was hypothesised that as the two alcohol functionalities on the ring are axial and equatorial there would be a preference in the reactivity of them with the diacid. The hydoxyl group which is equatorial on the ring could be more reactive towards nucleophilic attack on the

diacid and therefore react preferentially. This would potentially induce regularity in the polymer. It was hypothesised that there are two methods of bonding of two molecules of the triol (**161**) and acid (**126**) labelled **A** and **B** (**Figure 40**). The ^{1}H NMR analysis of **165** indicates that the polymer could have a stereoregular structure (**Figure 39**), the resonances in the spectrum corresponding to the protons *alpha* to the ester are four defined peaks indicative of regularity in the polymer backbone. It was predicted that if the polymerisation proceeded through the bonding displayed in **A** it would display two distinct peaks in ^{1}H NMR however through **B** it would result in four distinct peaks and if the polymer was completely random the resonances in the ^{1}H NMR spectrum would be broad. Therefore it was tentatively concluded that the polymer was syndiotactic and displayed some regularity *via* bonding in structures **A** and **B**. It was decided to attempt to take advantage of the stereoregularity of the polymer, by forming stereocomplexes with its enantiomer.

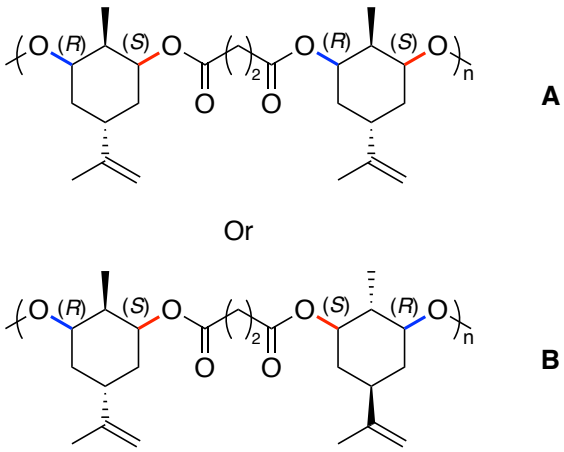
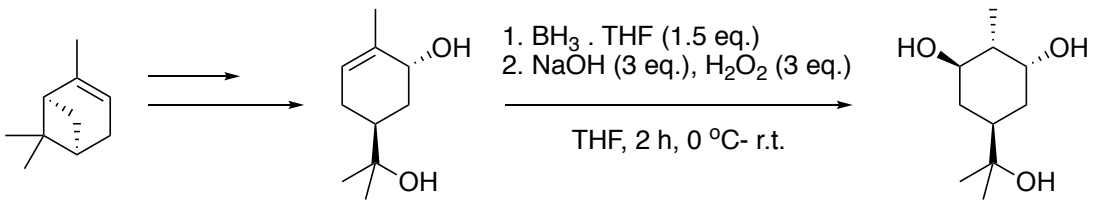


Figure 40: *The proposed bonding between the triol **161** and the succinic acid (**126**)*

One characteristic of stereoregular polymers is the formation of a stereocomplex, a polymer stereocomplex is defined as an interaction between two complementing stereoregular polymers.[170] The first example of stereocomplexation (stereoselective association) for enantiomeric polymers, i.e. between (*R*)- and (*S*)-configured (or L- and D-configured) polymer chains, was reported by Pauling and Corey for a polypeptide in 1953.[170] The main interactions, resulting in the complexation, are suggested to rely on

stereoselective van der Waals forces. The polymers can undergo non-covalent interactions forming a new composite, which can exhibit altered physical properties when compared to the parent polymers. The complementing polymer molecules can be a pair of isotactic and syndiotactic polymers or two optically active polymers of opposite enantiomers with identical chemical compositions. A third group consists of hetero-stereocomplexes formed by polymers from differing polymer families (like polyesters and polyamides) having opposite stereoregular configuration. Isotactic polymer chains of opposite chirality are also found to interact and form homo-stereocomplexes, a common example is poly(D and L-lactic acid).[171] Homo-stereocomplexes are found among those polyesters, which consist of monomers with at least one chiral centre in the polymer backbone. The obtained isotacticity is a function of the enantiomeric excess of the used monomers. Stereocomplexes of this group of polymers are obtained between D- and L-isotactic polymers.

In order to investigate the potential of the polymer **165** to form a stereocomplex it was necessary to first synthesise the enantiomer of the monomer **161**. (+)-α-pinene ((+)-**11**) was used as the starting material and identical reaction conditions were used to synthesise the opposite enantiomer of **161**, dubbed (-)-**161** (**Scheme 57**).



(+)-**11** (+)-**136** (-)-**161**

Scheme 57: *Synthesis of (-)-**161** from (+)-α-pinene (**11**)*

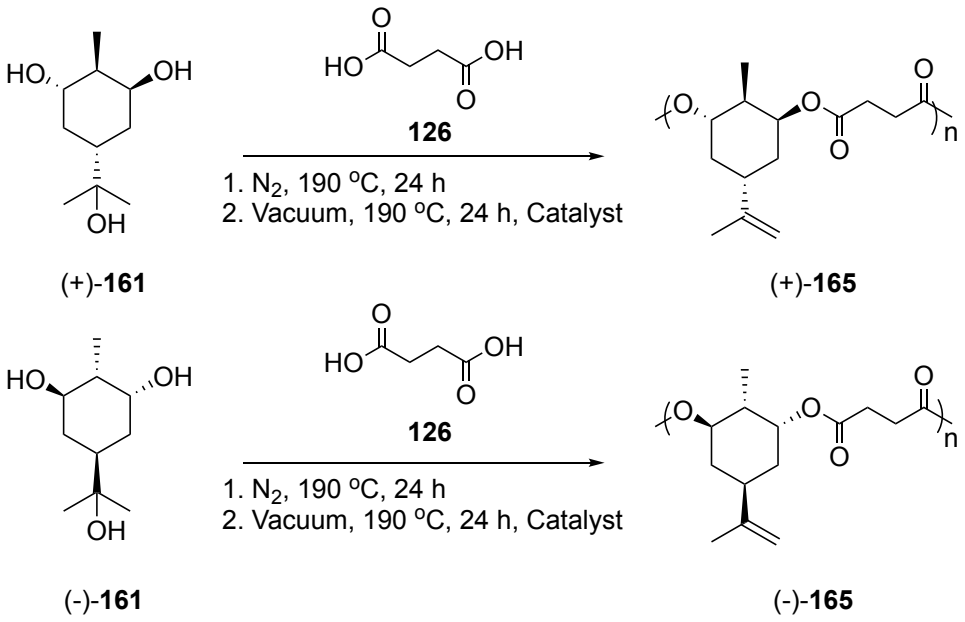
(-)-**161** was synthesied *via* epoxidation of (+)-α-pinene ((+)-**11**) to form (+)-α-pinene oxide ((+)-**129**) which, upon reaction with water and carbon dioxide was transformed to (+)-*trans*-sobrerol ((+)-**136**). A Brown hydroboration / oxidation was then used to access (-)-**161**, and a recrystallisation in hot acetonitrile generated as a single diastereomer (-)-**161** in a comparable yield to the synthesis of (-)-**161**.

In order to confirm the synthesis of the (-) and (+) enantiomers of **161**, the specific rotations of the relevant molecules were measured. It was found that the molecules all displayed a change in sign upon measurement of the refractive index indicating that they are enantiomers of the original compound synthesised (**Table 21**). This was also repeated for the polymer and again a change of sign was observed which is good indication that the polymers synthesised are enantiomerically enriched samples of (-) and (+) respectively.

Table 21: *Refractive index measurements of the +/- compounds used in the synthesis of* ***165***

Entry	Compound	$[\alpha]_D$ (From (+)-α-pinene)	$[\alpha]_D$ (From (-)-α-pinene)
1	**11**	1.46	-1.32
2	**129**	38.27	-40.48
3	**136**	118.57	-132.63
4	**161**	-33.58	58.34
5	**165**	-63.03	61.93

In order to increase the probability of synthesising a stereocomplex, the (+) and (-) polymers should be of a similar molecular weight. Therefore, two identical polymerisations were set up, using conditions previously established (**Scheme 58**).



Scheme 58: *Polymerisation of (-)-****161*** *and (+)-****161*** *to yield the polymers (-)-****165*** *and (+)-****165*** *respectively*

The polymers (+)-**165** and (-)-**165** were synthesised and the structures confirmed using ^{1}H NMR spectroscopic analysis. The polymers were also analysed using GPC to ensure that they had comparable molecular weights. The GPC analysis indicated that the polymes were synthesised to almost identical molecular weights (6.5 kDa). In order to induce stereocomplexation the polymers were blended. This was carried out by dissolution in dichloromethane to give a homogenous solution of equal concentration. These solutions were then combined and the dichloromethane removed under reduced pressure to give the stereocomplex (**Figure 41**).

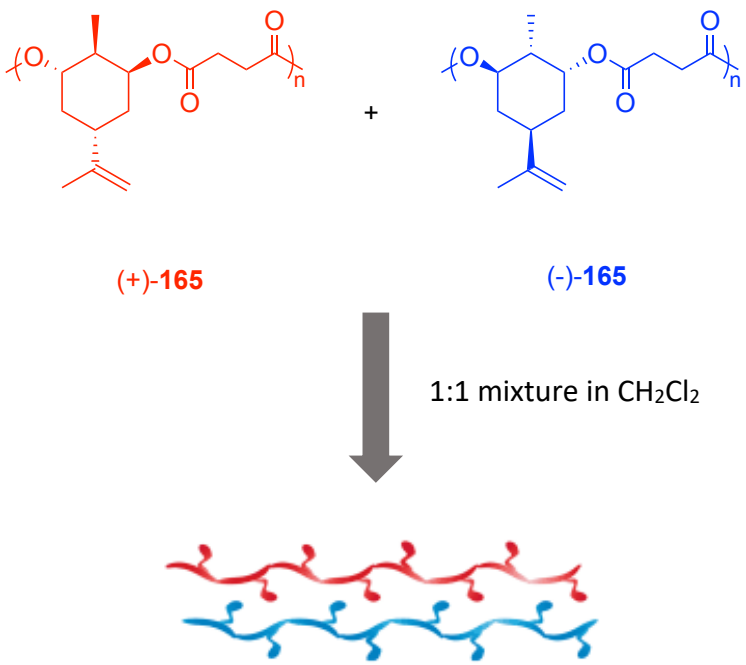


Figure 41: *Stereocomplexation of (+)-**165** and (-)-**165***

Stereocomplexes are known to display improved thermal properties to their constituent polymers and it was therefore decided to probe the formation of a stereocomplex using DMA analysis. One of the most well-known polyesters to form a stereocomplex is poly(lactic acid) (PLA). There has been a significant amount of research into the sterecomplexation of PLA as the two enantiomers can be accessed through the ROP of D- or L-lactide. The sterecomplex of D- and L-PLA shows improved properties from the individual polymers, for example the T_g of the D- and L-PLA is

50-65 °C *vs* 65-72 °C for the stereocomplex.[171] The T_gs of (+)-(**165**), (-)-**165** and the blend of the two polymers were investigated using DMA (**Figure 42**).

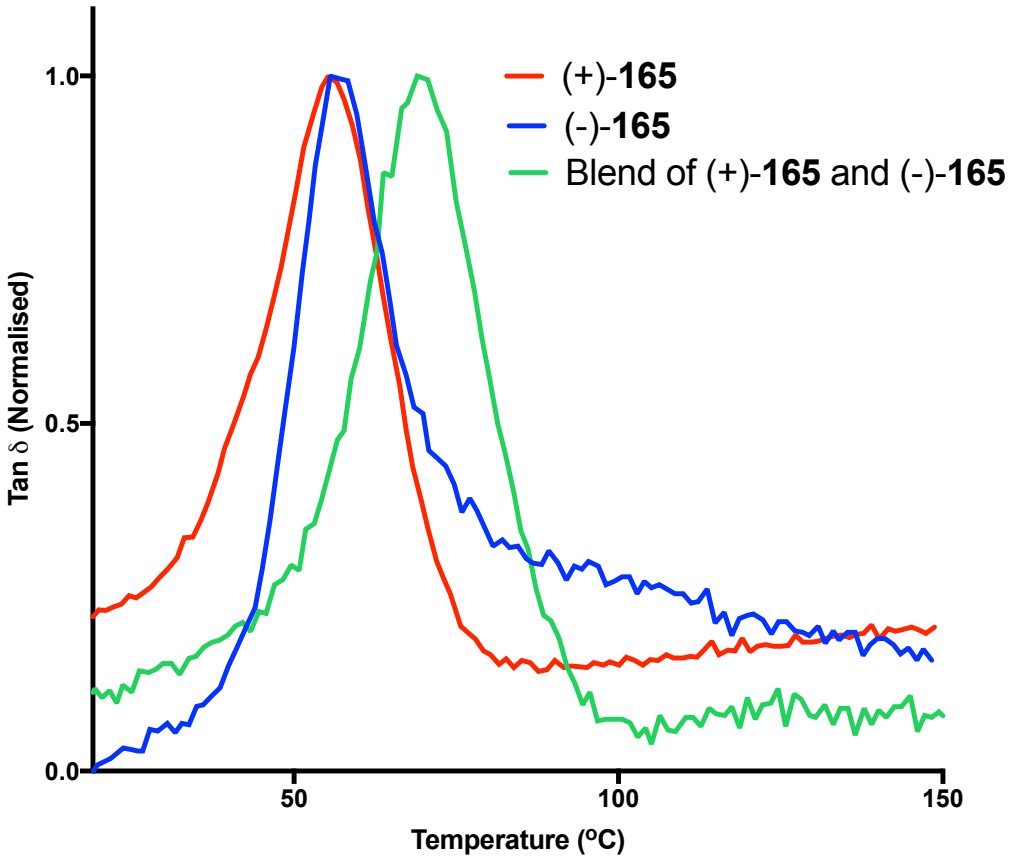


Figure 42: *DMA analysis of polymers*

The DMA analysis indicated T_gs of 55 °C for the individual polymers, these are slightly lower than those obtained before, however this is to be expected due to the lower M_ns in comparison to previously synthesised **165**. In contrast the stereocomplex displayed a T_g of 69 °C, representing an increase in the T_g of 14 °C. This rise in the glass transition temperature indicates that the stereocomplex was successfully synthesised, showing potential for further investigation of the properties and applications of a novel stereocomplexed polymer synthesised from renewable resources.

4. Conclusions and Future Work

In conclusion, α-pinene (**11**) has been successfully transformed into monomers for step growth polymerisation. The monomer synthesis was centralised around the hydrolysis of α-pinene oxide (**129**) to form trans-sobrerol (**136**). The solvolysis of α-pinene oxide (**129**) for the incorporation of oxygen based nucleophiles was also investigated, however this did not lead to the synthesis of molecules which could be used as monomers in polymerisation studies due to side reactions leading to low yields.

The most promising polymers were synthesised from the triol **161** and tetraol **162** which are able to co-polymersise with succinic acid (**126**) to give a polymer containing a cyclohexane ring in the backbone. The polymers reached molecular weights of ~ 8 kDa and high glass transition temperatures (~75 ^{o}C) in comparison to other aliphatic polymers obtained from renewable resources. It was hypothesised that the polymer **165** was stereoregular and therefore had the potential to form stereocompelxes. The opposite enantiomer of **165** was synthesied from (+)-α-pinene ((+)-**11**), the enantiomers were blended and the resultant polymer was found to possess a higher T_g than the constituent polymers. This provides a strong indication of formation of a stereocomplex.

The polymers **165** and **166** each contain a terminal alkene moiety in their pendant chains, future work could involve utilising these reactive functional groups to produce terpene-derived polymers with interesting properties. For example the double bond could be used to induce cross linking between the chains, opening up the opportunity for the polymer to be used in coatings. Another strategy could be to perform post polymerisation modifications through the functionalisation of the double bond. These strategies present promising future investigations towards tuning these polymers for potential applications.

The synthesis of a stereoregular polyester through polycondensation without the use of a chiral catalyst has not before been reported, and is hypothesised to originate from

the inherent chirality of the monomer itself. This could be explored further in order to ascertain exactly the mechanism of the polymerisation and therefore rationalise how the polymer is bonded. This study could be achieved through the controlled synthesis of dimers, trimers and tetramers and subsequent ^{1}H NMR analysis to deduce the stereochemical outcomes of these reactions. This could potentially lead to the optimisation of the polymerisation towards stereoregularity and further investigations into the structure of the stereocomplex formed from the blend of the polymers (+)-**165** and (-)-**165**.

CONCLUSIONS

The substitution of petrochemical derived feedstocks for plastic production is an essential area of research and this report has demonstrated the potential for terpenes to be a significant and useful waste stream for polymer applications. Utilising the reactive alkene moieties and latent chirality of limonene and α-pinene has allowed the synthesis of four novel monomers which can polymerise under step-growth polymerisation conditions. The synthesis of oxygenated terpene-derived monomers has allowed the synthesis of renewable polyesters, which due to their ester linkages also show high potential for end of life solutions, which are imperative in the design of renewable polymers.

Two terpene derived monomers (**105** and **104**) have been synthesised from limonene (**6**) and their polymerisation potentials investigated. The first being a hydroxy-acid which was shown to homo-polymerise allowing access to a polyester with 100% of its carbon content coming from the terpene molecule. The hydroxy-acid was polymerised to yield low molecular weight polymers with (M_ns *ca*. 2.6 kDa) and T_gs of *ca.* 44 ^oC. The limonene diol intermediate was used as a co-monomer with the renewable diacid, succinic acid, to produce a polyester with impressive molecular weights (up to 30 kDa) and low T_gs (ca. 20^oC). Perhaps the most promising property of this polymer is the ability to degrade under basic conditions allowing full reclamation of its substituent terpene derived diol, which works towards the production of a circular polymer, currently one of the biggest challenges for plastic waste in society.

α-Pinene was also derivatised into monomers for step growth polymerisation. The monomer synthesis was centralised around the hydrolysis of α-pinene oxide under mild conditions to form *trans*-sobrerol, which was further functionalised to produce two polyols. These polyols were able to successful act as a co monomer for the synthesis of polyesters. These polymers possessed notably high T_gs for renewable aliphatic polyesters, due in part to the cyclohexane ring in their backbones. The polymers reached molecular weights of ~ 8 kDa and high glass transition temperatures (~75 ^oC). These materials also contain a free alkene in their pendant group, opening

up opportunities for cross-linking and post polymerisation functionalisation applications. Possibly the most interesting property of the polymer was its ability to undergo sterocomplexation with its corresponding enantiomer. This resulted in a stereocomplexed polymer with improved thermal properties than its constituent polymers.

In conclusion this project has allowed the synthesis of four novel polyesters which are derived from two different terpene sources. Furthermore the polyesters synthesised display a range of molecular weights and T_gs demonstrating the diversity of terpenes as a renewable feedstock. The four polymers synthesised have an assortment of properties, including: degradability, post-polymerisation functionalisation and the potential for the tuning of the thermal properties through stereocomplexation. This project clearly demonstrated that in the future terpene waste streams present a significant opportunity in the field of sustainable polymers.

5. Experimental

5.1. General Experimental

THF was freshly distilled from sodium metal and benzophenone; water was deionised before use. All other reagents were purchased from a chemical supplier and used without further purification. TLCs were performed on silica gel on aluminium and were visualised using a potassium permanganate or phosphomolybdic acid or vanillin dip. Experiments carried out under inert atmosphere used argon or nitrogen, and glassware was flame dried prior to use. All solutions are saturated unless stated otherwise.

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, $(CD_3)_2SO$ or CD_3OD at ambient temperature using Bruker DPX400 (400 MHz), AV400 (400 MHz), AV3400HD (400 MHz), AV3400 (400 MHz) and AV3500 (500 MHz) spectrometers. Data are expressed as chemical shifts in parts per million (ppm) relative to residual solvent signals ($CHCl_3$, ^{1}H NMR 7.27), ($CDCl_3$, ^{13}C NMR 77.0), ($(CH_3)_2SO$ ^{1}H NMR 2.50), ($(CD_3)_2SO$ ^{13}C NMR 39.5), (CH_3OH ^{1}H NMR 3.31) or (CD_3OD ^{13}C NMR 49.0) as the internal standard on the δ scale. The following abbreviations are used to designate the multiplicity of each signal; s, singlet; d, doublet; dd, doublet of doublets; dddd, doublet of doublet of doublet of doublets; t, triplet; dt, doublet of triplets; ddt, doublet of doublet of triplets; q, quartet; m, multiplet; apt, apparent; br, broad. Coupling constants *J* are given in hertz (Hz).

Size exclusion chromatography (SEC) was performed using an Agilent 1260 Infinity Series HPLC (Agilent Technologies, USA) in Chloroform (HPLC grade, Fisher Scientific) at room temperature using two Agilent PL-gel 5 µm mixed-C columns (300 x 7.5 mm) in series with a PL-gel 10 µm Guard Column (50 x 7.5 mm). A flow rate of 0.5 mL min^{-1} was used. A PMMA column calibration was used alongside a differential refractometer (DRI, Wyatt) for sample detection and analysis.

Dynamic mechanical analysis (DMA) was used to determine the T_g of the polymers. Measurements were performed on a Triton Technologies DMA (now Mettler Toledo DMA1) using the powder pocket accessory. The sample (40 mg ± 5 mg) was weighed into a powder pocket. Samples were measured at 1 and 10 Hz in single cantilever bending geometry between -100–100 °C. The value of the T_g was taken as the peak of the tan delta (tan δ) curve.

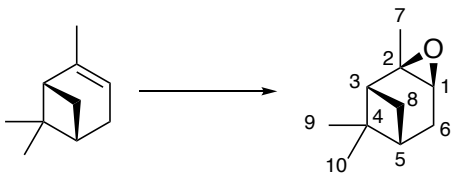
Infra-red spectra were recorded using a Bruker Tensor 27 FT-IR spectrophotometer using either an ATR attachment or a solution cell using $CHCl_3$ as the solvent and their peaks are quoted as υ_{max} in cm^{-1}. High-resolution mass spectra were obtained using a Bruker MicroTOF mass spectrometer operating in electrospray ionisation (ESI) mode.

Experiments monitored using React IR were done using a Metler Toledo ReactiR 15 equipped with a diamond probe and a LN2 NCT; SE MCT detector.

Optical rotation data was recorded 23 ^oC using a ADP440 polarimeter, with either neat sample or an appropriate solvent.

5.2. Synthesis of Compounds

Synthesis of α-pinene oxide (129)



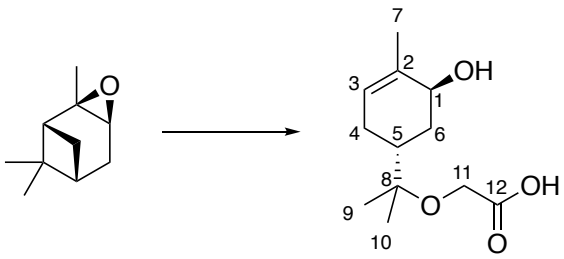
11 **129**

To a solution of *m*CPBA (25.8 g, 149.7 mmol) and $NaHCO_3$ (16 g, 190 mmol) in CH_2Cl_2 (350 mL) cooled to 0 ^oC was added α-pinene (23.3. mL, 147 mmol) in CH_2Cl_2 (30 mL) ensuring that the temperature is kept between 5 and 10 ^oC. The reaction was stirred (1 h) and Na_2SO_3 (7.35 g in 73.5 mL of H_2O) was added and the reaction was allowed

to warm to r.t. and stirred (30 min). The reaction mixture was diluted with H_2O (100 mL) and the organic phase separated and washed with $Na_2CO_{3(aq)}$ (5%, 100 mL). The aqueous washings were extracted with CH_2Cl_2 (2 x 50 mL), the organic extracts were combined, washed with $NaCl_{(aq)}$, (100 mL) dried over $MgSO_4$ and concentrated under reduced pressure to yield the title compound in a quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 3.02 (d, *J* = 4.15 Hz, 1H, H-1), 1.99-1.82 (m, 4H, H-8 and H-6), 1.71-1.65 (m, 1H, H-3 or H-5), 1.58 (d, *J* = 9.47 Hz, 1H, H-3 or H-5), 1.30 (s, 3H, H-9 or H-10), 1.25 (s, 3H, H-9 or H-10), 0.90 (s, 3H, H-7); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 60.5, 57.0, 45.2, 40.7, 39.9, 27.8, 26.8, 26.0, 22.5, 20.3. (in agreement with Saladino *et al.*[172]).

Synthesis of 2-((2-((1*R*,5*S*)-5-hydroxy-4-methylcyclohex-3-en-1-yl)propan-2-yl)oxy)acetic acid (152)

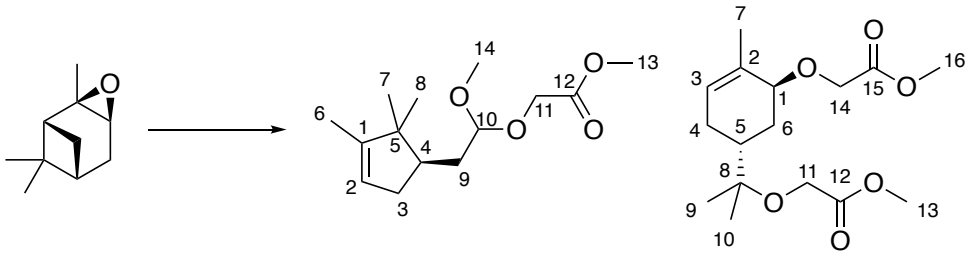


129 **152**

To a solution of glycolic acid (2.45 g, 32.5 mmol) in ^{t}BuOH (100 mL) was added α-pinene oxide (5.2 mL, 32.5 mmol) dropwise followed by the addition of CSA (20 mg, 0.09 mmol) and the reaction was stirred vigorously at room temperature (16 h). ^{t}BuOH was removed under reduced pressure, the residue dissolved in EtOAc (20 mL) and separated between $NaOH_{(aq)}$ (3 M, 20 mL). The organic extract was discarded, the aqueous was acidified with $H_2SO_{4(aq)}$ (2 M) and the product was extracted with EtOAc (3 x 20 mL). The organic extracts were combined, washed with $NaCl_{(aq)}$ (40 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified using silica gel chromatography (50% EtOAc and 1% AcOH in petroleum ether) to afford the title compound as a colourless oil (522 mg, 2.29 mmol, 7%).

FTIR (ATR) ν_{max} 3570, 2947, 1763, 1395, 1227, 1159; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.58-5.52 (m, 1H, H-3), 4.08-4.03 (m, 3H, H-1 and H-11), 2.03-1.87 (m, 3H, CH_2), 1.79 (s, 3H, H-7), 1.47-1.33 (m, 1H, CH_2), 1.17 (s, 3H, H-9 or H-10), 1.16 (s, 3H, H-9 or H-10), 1.07 (s, 1H, H-5); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_c 177.2 (C-12), 134.4 (C-2), 125.5 (C-3), 78.91 (C-8), 68.7 (C-1), 59.7 (C-11), 36.2 (C-5), 32.6 (C-4 or C-6), 27.3 (C-4 or C-6), 23.0 (C--9 or C-10), 22.3 (C-9 or C-10), 20.9 (C-7); **HRMS** (ESI) *m/z* calculated for $[C_{12}H_{20}NaO_4]^+$ 251.1259 found 251.1283 ($M + Na^+$).

Synthesis of methyl 2-(1-methoxy-2-((*R*)-2,2,3-trimethylcyclopent-3-en-1-yl)ethoxy)acetate (158) and of methyl 2-((2-((1*R*,5*S*)-5-(2-methoxy-2-oxoethoxy)-4-methylcyclohex-3-en-1-yl)propan-2-yl)oxy)acetate (157)



129 **158** **157**

To a stirred solution of α-pinene oxide (0.52 mL, 3.25 mmol) in methyl glycolate (5.07 mL, 65.7 mmol) camphor-sulfonic acid (2 mg, $8.6x10^{-3}$ mmol) was added, the reaction was stirred at room temperature (15 min). The reaction mixture was adsorbed onto silica gel and purified by column chromatography (EtOAc 1-10% in petroleum ether) to afford **157** (73 mg, 0.23 mmol, 1%) and **158** (21 mg, 0.06 mmol) as a colourless oils.

158

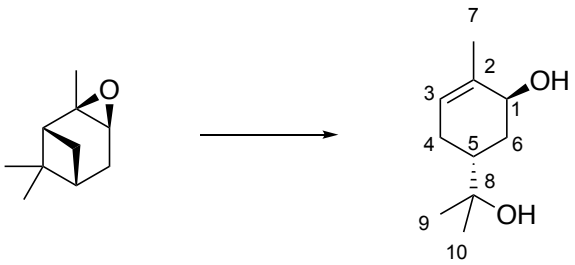
FTIR (Sol/$CHCl_3$) ν_{max} 3509, 3080, 2937, 1754, 1473, 1263; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.25-5.21 (m, 1H, H-2), 4.67-4.61 (m, 1H, H-10), 4.19-4.11 (m, 2H, H-11), 3.77-3.75 (m, 3H, H-13), 3.34 (d J = 10.1, 3H, H-14), 2.40-2.27 (m, 1H, H-3a or H-3b), 1.91-1.81 (m, 2H, H-4 and H-3a or H-3b), 1.61 (s, 3H, H-6), 1.55-1.51 (m, 2H, H-9), 0.98 (s, 3H, H-7 or H-8), 0.74 (s, 3H, H-7 or H-8); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 170.8 (C-12), 148.2 (C-1), 121.9 (C-2), 103.4 (C-10), 62.3 (C-11), 53.1 (C-14), 51.86 (C-13), 46.8 (C-5), 45.1 (C-

9), 35.8 (C-4), 35.5 (C-3), 25.4 (C-7 or C-18), 19.9 (C-7 or C-8), 12.7 (C-6); **HRMS** (ESI) *m/z* calculated for $[C_{14}H_{24}NaO_4]^+$ 279.1572 found 279.1561 (M + Na^+).

157

FTIR (Sol/$CHCl_3$) ν_{max} 3508, 3105, 3098, 2905, 2507, 1759; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.62-5.58 (m, 1H, H-3), 4.15 (d *J* = 16.2, 1H, H-14), 4.09 (d *J* = 16.2, 1H, H-14), 4.03 (d *J* = 16.2, 1H, H-11), 3.98 (d *J* = 16.2, 1H, H-11), 3.72 (s, 3H, H-13 or H-16), 3.70 (s, 3H, H-13 or H-16), 3.74-3.71 (m, 1H, H-1), 2.17-2.10 (m, 1H, H-6), 2.06-1.90 (m, 2H, H-5 and H-4), 1.80 (s, 3H, H-7), 1.82-1.75 (m, 1H, H-4), 1.27-1.17 (m, 1H, H-6), 1.14 (s, 3H, H-9 or H-10), 1.13 (s, 3H, H-9 or H-10); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 171.6 (C-12), 171.1 (C-15), 132.5 (C-2), 126.5 (C-3), 76.9 (C-1), 66.5 (C-14), 60.0 (C-11), 51.8 (C-13 or C-16), 51.7 (C-13 or C-16), 35.6 (C-5), 27.1 (C-4), 23.2 (C-9 or C-10), 22.6 (C-9 or C-10), 21.0 (C-7); **HRMS** (ESI) *m/z* calculated for $[C_{16}H_{26}NaO_6]^+$ 337.1627 found 337.1628 (M + Na^+).

Synthesis of *trans*-sobrerol (136)



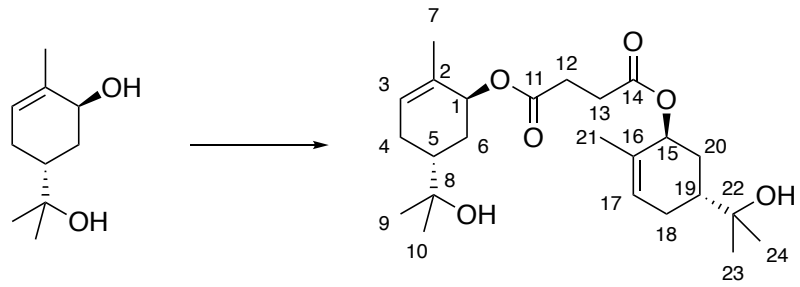
129 **136**

CO_2 was continuously bubbled through water (20 mL) until saturation was reached (approx. pH 4.5), α-pinene oxide (11.8 g, 77.51 mmol) was added and the mixture stirred at room temperature for 24 h. A white solid crashed out, the mixture cooled and the solid isolated through filtration. The crude solid was washed with cold CH_2Cl_2 (2 x 10 mL) to give the title compound as a white crystalline solid (8.91 g, 52.4 mmol, 68%).

T_m = 131 °C; **FTIR** (ATR) ν_{max} 3323, 2974, 2887, 1376, 1052, 918; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.57 (m, 1H, H-3), 4.04 (dd, *J* = 3.9, 2.3, 1H, H-1), 2.17-2.08 (m, 1H, H-4), 2.04-

1.99 (m, 1H, H-6), 1.84-1.67 (m, 5H), 1.41 (app td, *J* = 13.2, 3.9, 1H, H-6), 1.21 (s, 3H, H-9 or H-10), 1.18 (s, 3H, H-9 or H-10); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 134.5 (C-2), 125.3 (C-3), 72.5 (C-8), 68.9 (C-1), 39.0 (C-5), 32.9 (C-4), 27.8 (C-9 or C-10), 27.3 (C-6), 26.5 (C-9 or C-10), 21.0 (C-7); **HRMS** (ESI) m/z calculated for $[C_{10}H_{18}NaO_2]^+$ 193.1204 found 193.1207 ($M + Na^+$).

Synthesis of 160



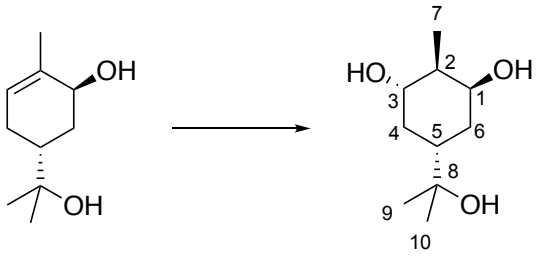
136 **160**

trans-Sobrerol (1g, 5.87 mmol) was dissolved in dry dichloromethane (3 mL) and cooled to 0 ^oC, pyridine (2.34 mL, 29 mmol) was added dropwise over 10 minutes. Succinyl chloride (0.71 mL, 6.46 mmol) was dissolved in dry dichloromethane (4.3 mL) and added dropwise over 25 minutes, the resulting solution was then stirred at room temperature (48 h). An excess of cold MeOH was then added carefully, the CH_2Cl_2 was then separated and removed under reduced pressure to yield **160** as a brown oil (351 mg, 0.83 mmol, 28%).

FTIR (ATR) ν_{max} 3414, 2970, 1723, 1566, 1187; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 5.73 (d, *J*=1.6, 1H, H-3 or H-17), 5.71 (q, *J*=1.8, 1H, H-3 or H-17), 5.28-5.24 (m, 2H, H-1 and H-15), 2.67-2.61 (m, 4H, H-12 and H-13), 2.21-2.16 (m, 1H, H-4 or H-18), 2.16-2.12 (m, 1H, H-4 or H-18), 2.08 (p, *J*=2.4, 1H, H-6 or H-20), 2.04 (p, *J*=2.2, 1H, H-6 or H-20), 1.85-1.78 (m, 2H, H-4 and H-18), 1.76-1.72 (m, 2H, H-5 and H-19), 1.69-1.66 (m, 6H, H-7 and H-21), 1.43 (app ddd, *J*=14.2, 12.8, 3.9, 2H, H-6 and H-20), 1.20 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.14 (d, *J*=1.0, 6H, 2 x CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C 172.3 (C-11 or C-13), 172.2 (C-11 or C-13), 130.9 (C-2 or C-16), 130.8 (C-2 or C-16), 128.1 (C-3 or C-17), 128.0 (C-3 or C-17), 72.0 (C-8 or C-22), 72.0 (C-8 or C-22), 71.5 (C-1 or C-15), 71.3 (C-1 or C-15), 39.6 (C-5 and C-19), 29.9 (C-12 or C-13), 29.8 (C-12 or C-13),

29.7 (C-6 or C-20), 29.6 (C-6 or C-20), 27.9 (CH_3), 27.8 (CH_3), 27.1 (C-4 or C-18), 27.1 (C-4 or C-18), 25.9 (CH_3), 25.8 (CH_3), 20.6 (C-7 and C-21); **HRMS** (ESI) m/z calculated for $[C_{24}H_{38}NaO_6]^+$ 445.2566 found 445.2572 (M + Na^+).

Synthesis of (1*S*,2*S*)-5*t*-(2-hydroxypropan-2-yl)-2*c*-methylcyclohexane-1*r*,3*t*-diol (161)



136 **161**

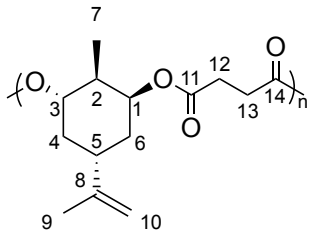
To a solution of *trans*-sobrerol (6.53 g, 38.3 mmol) in THF (35 mL) cooled to 0 °C was added BH_3·THF (1 M in THF) (57.5 mL, 57.5 mmol) dropwise over 30 min and the resulting solution stirred (30 min). The reaction mixture was allowed to warm to room temperature and stirred (2 h). The reaction was cooled to 0 °C and $NaOH_{(aq)}$ (2 M, 57.5 mL) was added dropwise followed by dropwise addition of $H_2O_{2(aq)}$ (30%, 13.2 mL) and the reaction was allowed to warm to room temperature and stirred (16 h). Na_2SO_3 (7.5 g) was added in portions and stirred (15 min). The solvent was removed under reduced pressure the residue dissolved in MeOH and the solid removed *via* filtration. The filtrate was concentrated under reduced pressure, the resulting solid was dissolved in hot MeCN (82 °C) and the solid was filtered off while the solution was hot. The filtrate was then concentrated under reduced pressure and recrystallised from MeCN to yield the title compound (4.00 g, 21.3 mmol, 55%)

T_m = 109-128 °C; **FTIR** (ATR) ν_{max} /cm^{-1}: 3330, 2975, 2928, 1424, 1033, 917, **^{1}H NMR** (400 MHz, CD_3OD) δ_H 3.94-3.90 (m, 1H, H-1), 3.50 (app td, *J*=10.74, 4.39, 1H, H-3), 2.11-2.04 (m, 1H, H-4), 1.93-1.86, (m, 1H, H-6), 1.87-1.79 (m, 1H, H-2), 1.35-1.26 (m, 1H, H-5), 1.25 (d, J 2.5, 1H, H-6), 1.17 (s, 3H, H-9 or H-10), 1.18 (s, 3H, H-9 or H-10), 1.09 (m, 3H, H-7), 1.07 (m, 1H, H-4) **^{13}C NMR** (101 MHz, CD_3OD) δ_C 71.3 (C-8), 71.3 (C-1), 70.8 (C-3), 45.1 (C-5), 42.4 (C-2), 37.7 (C-4), 35.5 (C-6), 27.3 (C-9 or C10), 26.3 (C9

or C10), 14.8 (C-7); **HRMS** (ESI) m/z calculated for $[C_{10}H_{20}NaO_3]^+$ 211.1310 found 211.1305 ($M + Na^+$).

5.3. Synthesis of Polymers

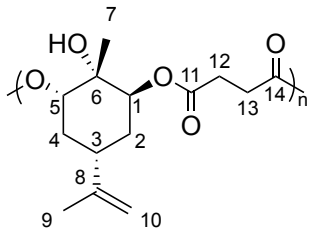
Synthesis of polymer 165



165

All reagents were dried under vacuum at 25 °C for at least 24 hrs prior to use. A dry round bottom flask was charged with **161** (500 mg, 2.63 mmol) and succinic acid (341 mg, 2.89 mmol). The reaction was heated to 190 °C and stirred for 24 h under nitrogen. $Sn(oct)_2$ (8.52 μL, 0.026 mmol) was added and the reaction was put under vacuum for a further 24 h. After this time the reaction was allowed to cool and the polymer was isolated as a pale yellow solid. **FTIR** (ATR) ν_{max} 2967, 2936, 1725, 1645, 1375, 1154, 1066 **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ_H 5.08-4.47 (m, 2H, H-1 and H-3), 4.72-4.65 (s, 2H, H-10), 2.57 (br s, 4H, H-12 and H-13), 2.36-2.30 (m, 1H, H-5 or H-2), 1.98-1.90 (m, 1H, CH_2), 1.84-1.73 (m, 2H, H-5 or H-2 and CH_2), 1.65 (s, 3H, H-9), 1.49-1.38 (m, 1H, CH_2), 1,32-1.18 (m, 1H, CH_2), 0.82 (s, 3H, H-7); **^{13}C NMR** (101 MHz, $(CD_3)_2SO$) δ_C 171.4 (C-11 or C-14), 171.2 (C-11 or C14), 147.5 (C-8), 109.4 (C-10), 74.2 (C-1 or C-3), 73.6 (C-1 or C-3), 38.7 (C-5 or C-2), 37.0 (C-5 or C-2), 35.9 (C-6 or C-4), 34.1 (C-6 or C-4), 28.9 (C-12 and C-13), 20.4 (C-9), 13.5 (C-7).

Synthesis of polymer 165



166

All reagents were dried under vacuum at 25 °C for at least 24 hrs prior to use. A dry round bottom flask was charged with **162** (500 mg, 2.63 mmol) and succinic acid (342 mg, 2.89 mmol). The reaction was heated to 190 °C and stirred for 24 h under nitrogen. $Sn(oct)_2$ (8.52 μL, 0.026 mmol) was added and the reaction was put under vacuum for a further 24 h. After this time the reaction was allowed to cool and the polymer was isolated as a pale yellow solid. **FTIR** (ATR) ν_{max} /cm^{-1} 3458, 2963, 2932, 1731, 1591, 1152, 1016; **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ_H = 5.16-4.50 (m, 2H, H-1 and H-5), 4.72-4.69 (m, 2H, H-10), 2.58 (br s, 4H, H-12 and H-13), 2.29-1.88 (m, 3H), 1.35-0.71 (m, 8H).

Crystallography

Single crystals were grown through slow evaporation in deuterated chloroform. A suitable crystal was selected for each and were examined in fomblin film on a micromount on a GV1000, TitanS2 diffractometer. The crystals were kept at 120(2) K during data collection. Using Olex2, the structures were solved with the olex2.solve structure solution program using Charge Flipping and refined with the ShelXL refinement package using Least Squares minimisation.[61–63]

REFERENCES

1 C. Williams and M. Hillmyer, *Polym. Rev.*, 2008, **48**, 1–10.

2 M. Okada, *Prog. Polym. Sci.*, 2002, **27**, 87–133.

3 Ellen MacArthur Foundation, *The New Plastics Economy: Rethinking the future of plastics*, 2016.

4 A. L. Holmberg, K. H. Reno, R. P. Wool and T. H. Epps, *Soft Matter*, 2014, **10**, 7405–24.

5 B. P. Mooney, *Biochem. J.*, 2009, **418**, 219–32.

6 P. Anastas and N. Eghbali, *Chem. Soc. Rev.*, 2010, **39**, 301–12.

7 K. Yao and C. Tang, *Macromolecules*, 2013, **46**, 1689–1712.

8 C. Vilela, A. F. Sousa, A. C. Fonseca, A. C. Serra, J. F. J. Coelho, C. S. R. Freire and A. J. D. Silvestre, *Polym. Chem.*, 2014, **5**, 3119–3141.

9 D. R. Dodds and R. A. Gross, *Science.*, 2007, **318**, 1250–1251.

10 A. J. Ragauskas, *Science.*, 2006, **311**, 484–489.

11 P. Anastas, *Green Chem.*, 2008, **10**, 607.

12 A. K. Mohanty, M. Misra and L. T. Drzal, *J. Polym. Environ.*, 2002, **10**, 19–26.

13 H. Ringsdorf, *Angew. Chem. Int. Ed.*, 2004, **43**, 1064–1076.

14 M. Winnacker and B. Rieger, *ChemSusChem*, 2015, **8**, 2455–2471.

15 A. Gandini and T. M. Lacerda, *Prog. Polym. Sci.*, 2015, **48**, 1–39.

16 R. T. Mathers, *J. Polym. Sci. Part A Polym. Chem.*, 2012, **50**, 1–15.

17 A. Gandini, *Macromolecules*, 2008, **41**, 9491–9504.

18 M. A. Hillmyer and W. B. Tolman, *Acc. Chem. Res.*, 2014, **47**, 2390–2396.

19 G. W. Huber, S. Iborra and A. Corma, *Chem. Rev.*, 2006, **106**, 4044–98.

20 H. Sugimoto and S. Inoue, *J. Polym. Sci. Part A Polym. Chem.*, 2004, **42**, 5561–5573.

21 S. Curia and S. M. Howdle, *Polym. Chem.*, 2016, **7**, 2130–2142.

22 R. E. Drumright, P. R. Gruber and D. E. Henton, *Adv. Mater.*, 2000, **12**, 1841–1846.

23 M. R. Yates and C. Y. Barlow, *Resour. Conserv. Recycl.*, 2013, **78**, 54–66.

24 S. Mecking, *Angew. Chem. Int. Ed. Engl.*, 2004, **43**, 1078–85.

25 B. J. O'Keefe, M. A. Hillmyer and W. B. Tolman, *J. Chem. Soc. Dalton Trans.*,

2001, 2215–2224.

26 D. Bourissou, S. Moebs-Sanchez and B. Martín-Vaca, *Comptes Rendus Chim.*, 2007, **10**, 775–794.

27 C. R. Álvarez-Chávez, S. Edwards, R. Moure-Eraso and K. Geiser, *J. Clean. Prod.*, 2012, **23**, 47–56.

28 M. Mascal and E. B. Nikitin, *Angew. Chem. Int. Ed.*, 2008, **47**, 7924–7926.

29 A. Gandini, *Prog. Polym. Sci.*, 1997, **22**, 1203–1379.

30 A. Gandini and M. N. Belgacem, in *Materials, Chemicals, and Energy from Forest Biomass*, 2007, pp. 280–295.

31 J. Ma, Y. Pang, M. Wang, J. Xu, H. Ma and X. Nie, *J. Mater. Chem.*, 2012, **22**, 3457–3461.

32 A. Gandini, D. Coelho, M. Gomes, B. Reis and A. Silvestre, *J. Mater. Chem.*, 2009, **19**, 8656–8664.

33 J. N. Chheda, Y. Roman-Leshkov and J. a. Dumesic, *Green Chem.*, 2007, **9**, 342–350.

34 M. D. Refvik and R. C. Larock, *J. Am. Oil Chem. Soc.*, 1999, **76**, 99–102.

35 L. Montero de Espinosa and M. A. R. Meier, *Eur. Polym. J.*, 2011, **47**, 837–852.

36 P. A. Wilbon, F. Chu and C. Tang, *Macromol. Rapid Commun.*, 2013, 34, 8–37.

37 W. J. Roberts and A. R. Day, *J. Am. Chem. Soc.*, 1950, **72**, 1226–1230.

38 A. J. D. Silvestre and A. Gandini, in *Monomers, Polymers and Composites from Renewable Resources*, eds. M. N. Belgacem and A. Gandini, Elsevier, 2008, pp. 17–38.

39 W. F. Erman, *Chemistry of Monoterpenes,* 1985.

40 J. Derfer and S. Traynor, *Chemistry of Turpentine*, 1989.

41 A. Corma, S. Iborra and A. Velty, *Chem. Rev.*, 2007, **107**, 2411–2502.

42 H. Pietila, A. Sivola and H. Sheffer, *J. Polym. Sci. Part A Polym. Chem.*, 1970, **8**, 727–737.

43 M. O. Carmody and W. H. Carmody, *J. Am. Chem. Soc.*, 1937, **59**, 1312–1312.

44 J. Lu, M. Kamigaito, M. Sawamoto, T. Higashimura and Y.-X. Deng, *J. Appl. Polym. Sci.*, 1996, **61**, 1011–1016.

45 J. Lu, M. Kamigaito, M. Sawamoto, T. Higashimura and Y.-X. Deng, *Macromolecules*, 1997, **30**, 27–31.

46 J. Lu, M. Kamigaito, M. Sawamoto, T. Higashimura and Y.-X. Deng, *Macromolecules*, 1997, **30**, 22–26.

47 J. Lu, M. Kamigaito, M. Sawamoto, T. Higashimura and Y. Deng, *J. Polym. Sci. Part A Polym. Chem.*, 1997, **35**, 1423–1430.

48 P. Yu, A.-L. Li, H. Liang and J. Lu, *J. Polym. Sci. Part A Polym. Chem.*, 2007, **45**, 3739–3746.

49 J. Emsley, *The Elements*, 1995.

50 K. Satoh, H. Sugiyama and M. Kamigaito, *Green Chem.*, 2006, **8**, 878.

51 K. Satoh, A. Nakahara, K. Mukunoki, H. Sugiyama, H. Saito and M. Kamigaito, *Polym. Chem.*, 2014, **5**, 3222–3230.

52 N. A. Kukhta, I. V. Vasilenko and S. V. Kostjuk, *Green Chem.*, 2011, **13**, 2362.

53 H. Sheffer, G. Greco and G. Paik, *J. Appl. Polym. Sci.*, 1983, **28**, 1701–1705.

54 C. Snyder, W. McIver and H. Sheffer, *J. Appl. Polym. Sci.*, 1977, **21**, 131–139.

55 A.-L. Li, W. Zhang, H. Liang and J. Lu, *Polymer (Guildf).*, 2004, **45**, 6533–6537.

56

57 T. Higashimura, J. Lu, M. Kamigaito, M. Sawamoto and Y.-X. Deng, *Die Makromol. Chem*, 1993, **194**, 3441–3453.

58 A. B. Radbil', T. A. Zhurinova, E. B. Starostina and B. A. Radbil', *Russ. J. Appl. Chem.*, 2005, **78**, 1126–1130.

59 T. Higashimura and Y. Deng, *Makromol, Chem.*, 1992, **2321**, 2311–2321.

60 L. Li, S. Yu, F. Liu, J. Yang and S. Zhaug, *Catal. Letters*, 2005, **100**, 227–233.

61 M. Firdaus, L. Montero de Espinosa and M. A. R. Meier, *Macromolecules*, 2011, **44**, 7253–7262.

62 M. Bahr, A. Bitto and R. Mulhaupt, *Green Chem.*, 2012, **14**, 1447–1454.

63 F. J. B. Brum, F. N. Laux and M. M. C. Forte, *Des. Monomers Polym.*, 2013, **16**, 291–301.

64 K. Satoh, M. Matsuda, K. Nagai and M. Kamigaito, *J. Am. Chem. Soc.*, 2010, **132**, 10003–10005.

65 M. Matsuda, K. Satoh and M. Kamigaito, *Macromolecules*, 2013, **46**, 5473–5482.

66 A. Singh and M. Kamal, *J. Appl. Polym. Sci.*, 2012, **125**, 1456–1459.

67 R. T. Mathers, K. C. McMahon, K. Damodaran, C. J. Retarides and D. J. Kelley,

Macromolecules, 2006, **39**, 8982–8986.

68 S. Ren, L. Zhang and M. A. Dubé, *J. Appl. Polym. Sci.*, 2015, **132**, 42821.

69 R. Mülhaupt, *Macromol. Chem. Phys.*, 2013, **214**, 159–174.

70 V. Negro, G. Mancini, B. Ruggeri and D. Fino, *Bioresour. Technol.*, 2016, **214**, 806–815.

71 S. Kobayashi, C. Lu, T. R. Hoye and M. A. Hillmyer, *J. Am. Chem. Soc.*, 2009, **131**, 7960–7961.

72 P. Sarkar and A. K. Bhowmick, *RSC Adv.*, 2014, **4**, 61343–61354.

73 J. Hilschmann and G. Kali, *Eur. Polym. J.*, 2015, **73**, 363–373.

74 C. M. Byrne, S. D. Allen, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2004, **126**, 11404–5.

75 O. Hauenstein, M. Reiter, S. Agarwal, B. Rieger and A. Greiner, *Green Chem.*, 2016, **18**, 760–770.

76 F. Auriemma, C. De Rosa, M. R. Di Caprio, R. Di Girolamo, W. C. Ellis and G. W. Coates, *Angew. Chemie Int. Ed.*, 2015, **54**, 1215–1218.

77 C. C. C. R. De Carvalho and M. M. R. Da Fonseca, *Food Chem.*, 2006, **95**, 413–422.

78 J. R. Lowe, M. T. Martello, W. B. Tolman and M. A. Hillmyer, *Polym. Chem.*, 2011, **2**, 702–708.

79 D. Zhang, M. A. Hillmyer and W. B. Tolman, *Biomacromolecules*, 2005, **6**, 2091–2095.

80 M. Winnacker, S. Vagin, V. Auer and B. Rieger, *Macromol. Chem. Phys.*, 2014, **215**, 1654–1660.

81 M. Winnacker, A. Tischner, M. Neumeier and B. Rieger, *RSC Adv.*, 2015, **5**, 77699–77705.

82 M. Winnacker, M. Neumeier, X. Zhang, C. M. Papadakis and B. Rieger, *Macromol. Rapid Commun.*, 2016, **37**, 851–857.

83 H. Miyaji, K. Satoh and M. Kamigaito, *Angew. Chemie - Int. Ed.*, 2016, **55**, 1372–1376.

84 H. C. Quilter, M. Hutchby, M. G. Davidson and M. D. Jones, *Polym. Chem.*, 2017, **8**, 833–837.

85 M. Winnacker and J. Sag, *Chem. Commun.*, 2018, **54**, 841–844.

86 M. F. Sainz, J. A. Souto, D. Regentova, M. K. G. Johansson, S. T. Timhagen, D. J. Irvine, P. Buijsen, C. E. Koning, R. A. Stockman and S. M. Howdle, *Polym. Chem.*, 2016, **7**, 2882–2887.

87 M. S. Lima, C. S. M. F. Costa, J. F. J. Coelho, A. C. Fonseca and A. C. Serra, *Green Chem.*, 2018, **20**, 4880-4890.

88 S. Maiti, S. S. Ray and A. K. Kundu, *Prog. Polym. Sci.*, 1989, **14**, 297–338.

89 P. W. J. Wang, K. YAo, P. Wilbon, *Rosin-based chemicals and polymers*, 2012.

90 X. Liu, W. Xin and J. Zhang, *Green Chem.*, 2009, **11**, 1018.

91 Y. Zheng, K. Yao, J. Lee, D. Chandler, J. Wang, C. Wang, F. Chu and C. Tang, *Macromolecules*, 2010, **43**, 5922–5924.

92 J. K. Stille, *J. Chem. Educ.*, 1981, **58**, 862.

93 W. H. Carothers and J. A. Arvin, *J. Am. Chem. Soc.*, 1929, **51**, 2560–2570.

94 W. H. Carothers, *J. Am. Chem. Soc.*, 1929, **51**, 2548–2559.

95 A. Duda and A. Kowalski, in *Handbook of Ring-Opening Polymerization*, eds. P. Dubois, O. Coulembier and J. Raquez, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2009, pp. 1–51.

96 P. J. Flory, *Chem. Rev.*, 1946, **39**, 137–197.

97 R. Rouseff and P. R. Perez-Cacho, in *Flavours and Fragrances*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2007, pp. 117–134.

98 A. F. Thomas and Y. Bessière, *Nat. Prod. Rep.*, 1989, **6**, 291–309.

99 R. Ciriminna, M. Lomeli-Rodriguez, P. Demma Carà, J. a Lopez-Sanchez and M. Pagliaro, *Chem. Commun.*, 2014, **50**, 15288–96.

100 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2001, **40**, 2004–2021.

101 M. Firdaus and M. A. R. Meier, *Green Chem.*, 2013, **15**, 370–380.

102 S. Roth, I. Funk, M. Hofer and V. Sieber, *ChemSusChem*, 2017, **10**, 3574–3580.

103 M. Colonna, C. Berti, M. Fiorini, E. Binassi, M. Mazzacurati, M. Vannini and S. Karanam, *Green Chem.*, 2011, **13**, 2543.

104 H. C. Brown and C. D. Pfaffenberger, *Tetrahedron*, 1975, **31**, 925–928.

105 L. M. Jackman, S. Sternhell, D. H. R. Barton and W. Doering, *Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Elsevier, 1969.

106 J. B. Lambert and J. E. Goldstein, J. *Am. Chem. Soc.,* 1977, **17**, 5689-5693.

107 D. C. Harrowven, D. D. Pascoe, D. Demurtas and H. O. Bourne, *Angew. Chemie Int. Ed.*, 2005, **44**, 1221–1222.

108 T. M. Hansen, G. J. Florence, P. Lugo-Mas, J. Chen, J. N. Abrams and C. J. Forsyth, *Tetrahedron Lett.*, 2003, **44**, 57–59.

109 M. . Togo. G, Fernandez, *TEMPO-Mediated Oxidations 6.1.*, 1975.

110 I. Paterson and M. Tudge, *Angew. Chem. Int. Ed.*, 2003, **42**, 343–347.

111 G. Tojo and M. Fernández, *Oxidation of primary alcohols to carboxylic acids: a guide to current common practice*, Springer, 2007.

112 R. Bloch and C. Brillet, *Synlett*, 1991, **11**, 829–830.

113 J. Einhorn, C. Einhorn, F. Ratajczak and J.-L. Pierre, *J. Org. Chem.*, 1996, **61**, 7452–7454.

114 J. M. Hoover and S. S. Stahl, *J. Am. Chem. Soc.*, 2011, **133**, 16901–16910.

115 J. M. Hoover, J. E. Steves and S. S. Stahl, *Nat. Protoc.*, 2012, **7**, 1161–1166.

116 N. J. Hill, J. M. Hoover and S. S. Stahl, *J. Chem. Educ.*, 2013, **90**, 102–105.

117 R. A. Sheldon, *Green Chem.*, 2017, **19**, 18–43.

118 K. C. Nicolaou, A. Li and D. J. Edmonds, *Angew. Chem. Int. Ed.*, 2006, **45**, 7086–7090.

119 B. S. Bal, W. E. Childers and H. W. Pinnick, *Tetrahedron*, 1981, **37**, 2091–2096.

120 T. V. T. Phan, C. Gallardo and J. Mane, *Green Chem.*, 2015, **17**, 2846–2852.

121 H. Zhang and M. W. Grinstaff, *Macromol. Rapid Commun.*, 2014, **35**, 1906–1924.

122 C. Alemán, O. Betran, J. Casanovas, K. N. Houk and H. K. Hall, *J. Org. Chem.*, 2009, **74**, 6237–6244.

123 P. Olsén, K. Odelius and A.-C. Albertsson, *Biomacromolecules*, 2016, **17**, 699–709.

124 E. N. Stepurko and G. N. Roganov, *Fibre Chem.*, 2014, **46**, 80–89.

125 M. T. Martello, A. Burns and M. Hillmyer, *ACS Macro Lett.*, 2012, **1**, 131–135.

126 X. Lou, C. Detrembleur and R. Jérôme, *Macromolecules*, 2002, **35**, 1190–1195.

127 B. M. Cooper, D. Chan-Seng, D. Samanta, X. Zhang, S. Parelkar and T. Emrick, *Chem. Commun.*, 2009, 815–817.

128 L. Simón and J. M. Goodman, *J. Org. Chem.*, 2007, **72**, 9656–9662.

129 M. Xiong, D. K. Schneiderman, F. S. Bates, M. A. Hillmyer and K. Zhang, *Proc. Natl. Acad. Sci.*, 2014, **111**, 8357–8362.

130 J. A. Gonçalves, A. C. Bueno and E. V. Gusevskaya, *J. Mol. Catal. A Chem.*, 2006, **252**, 5–11.

131 S. Gharbi, J. P. Andreolety and A. Gandini, *Eur. Polym. J.*, 2000, **36**, 463–472.

132 T. Fox and P. Flory, *J. Polym. Sci.*, 1954, **14**, 315–319.

133 M. Jiang, J. Ma, M. Wu, R. Liu, L. Liang, F. Xin, W. Zhang, H. Jia and W. Dong, *Bioresour. Technol.*, 2017, **245**, 1710–1717.

134 K. Loos, *Biocatalysis in Polymer Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany.

135 E. Gubbels, L. Jasinska-Walc and C. E. Koning, *J. Polym. Sci. Part A Polym. Chem.*, 2013, **51**, 890–898.

136 V. P. Ananikov, *Sustainable Catalysis*, Royal Society of Chemistry, Cambridge, 2015, vol. 55.

137 M. Hong and E. Y.-X. Chen, *Green Chem.*, 2017, **19**, 3692–3706.

138 M. R. Thomsett, J. C. Moore, A. Buchard, S. M. Howdle and R. A. Stockman, *Green Chem*., 2019, **21**, 149-156.

139 B. Kheira, H. Aicha and Y. Ahmed, *Available online www.jocpr.com J. Chem. Pharm. Res.*, 2015, **7**, 988–993.

140 W. F. Hölderich, J. Röseler, G. Heitmann and A. T. Liebens, *Catal. Today*, 1997, **37**, 353–366.

141 B. Arbusow, *Berichte der Dtsch. Chem. Gesellschaft (A B Ser.*, 1935, **68**, 1430–1435.

142 P. H. Boyle, W. Cocker, D. H. Grayson and P. V. R. Shannon, *J. Chem. Soc. D*, 1971, **6**, 395–396.

143 Z. B. Xu and J. Qu, *Chem. - A Eur. J.*, 2013, **19**, 314–323.

144 W. Cocker, K. J. Crowley and K. Srinivasan, *J. Chem. Soc. Perkin Trans. 1*, 1972, 1971.

145 E. E. Royals and J. C. Leffingwell, *J. Org. Chem.*, 1964, **29**, 2098–2099.

146 J. Kaminska, M. A. Schwegler, A. J. Hoefnagel and H. van Bekkum, *Recl. des Trav. Chim. des Pays-Bas*, 2010, **111**, 432–437.

147 K. Wilson, A. Rénson and J. H. Clark, *Catal. Letters*, 1999, **61**, 51–55.

148 N. Ravasio, F. Zaccheria, M. Guidotti and R. Psaro, *Top. Catal.*, 2004, **27**, 157–168.

149 M. Stekrova, N. Kumar, P. M-Arvela, O. V. Ardashov, K. P. Volcho, N. F. Salakhutdinov and D. Y. Murzin, *Materials (Basel).*, 2013, **6**, 2103–2118.

150 M. Stekrova, N. Kumar, A. Aho, I. Sinev, W. Grünert, J. Dahl, J. Roine, S. S. Arzumanov, P. Mäki-Arvela and D. Y. Murzin, *Appl. Catal. A Gen.*, 2014, **470**, 162–176.

151 S. M. Bruno, C. A. Gamelas, A. C. Gomes, A. A. Valente, M. Pillinger, C. C. Romão and I. S. Gonçalves, *Catal. Commun.*, 2012, **23**, 58–61.

152 M. Golets, S. Ajaikumar and J. P. Mikkola, *Chem. Rev.*, 2015, **115**, 3141–3169.

153 W. B. Motherwell, M. J. Bingham, J. Pothier and Y. Six, *Tetrahedron*, 2004, **60**, 3231–3241.

154 K. A. Da Silva Rocha, J. L. Hoehne and E. V. Gusevskaya, *Chem. - A Eur. J.*, 2008, **14**, 6166–6172.

155 K. Wilson, A. Renson and J. H. Clark, *Catal. Letters*, 1999, **61**, 51–55.

156 D. B. Bleier and M. J. Elrod, *J. Phys. Chem. A*, 2013, **117**, 4223–4232.

157 S. Emma, Masters Report, University of Nottingham, 2016.

158 C. Uyanik, J. R. Hanson, P. B. Hitchcock and M. A. Lazar, *Tetrahedron*, 2005, **61**, 4323–4327.

159 I. M. Kolthoff and P. J. Eleing, *New York, Intersci. Encycl. Inc*, 1959, 1, 4655.

160 J. Comyn, *Int. J. Adhes. Adhes.*, 1997, **17**, 177.

161 C. Corvi-Mora, US Pat., 4 639 469, 1987.

162 A. J. Durbetaki and S. M. Linder, US Pat., 2 949 489, 1960.

163 E. Le Roux, in *Sustainable Catalysis: With Non-endangered Metals, Part 1*, ed. M. North, Royal Society of Chemistry, 2015, pp. 116–139.

164 H. Ben Abderrazak, A. Fildier, S. Marque, D. Prim, H. Ben Romdhane, H. R. Kricheldorf and S. Chatti, *Eur. Polym. J.*, 2011, **47**, 2097–2110.

165 D. J. Valenti and K. B. Wagener, *Macromolecules*, 1998, **31**, 2764–2773.

166 A. Díaz, R. Katsarava and J. Puiggalí, *Int. J. Mol. Sci.*, 2014, **15**, 7064–7123.

167 L. Mascia, *Polymers in industry from A-Z : a concise encyclopedia*, Wiley-VCH, 2012.

168 M. Zhang, G. I. Ozturk and T. E. Long, presented in part at the PSTC TECH 34

Technical seminar, Orlando, 2011.

169 X. Yu, J. Jia, S. Xu, K. U. Lao, M. J. Sanford, R. K. Ramakrishnan, S. I. Nazarenko, T. R. Hoye, G. W. Coates and R. A. DiStasio, *Nat. Commun.*, 2018, **9**, 2880.

170 L. Pauling and R. B. Corey, *Proc. Natl. Acad. Sci. U. S. A.*, 1953, **39**, 253–6.

171 H. Tsuji, *Macromol. Biosci.*, 2005, **5**, 569–597.

172 R. Saladino, A. Andreoni, V. Neri and C. Crestini, *Tetrahedron*, 2005, **61**, 1069–1075.