Heterocyclic functionalised polymers via Ring opening Metathesis Polymerisation (ROMP)

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Declaration

I declare that this thesis was composed by myself and that it describes my own work except where specifically stated in the text. The work was carried out from October 2000 to October 2003 in the Department of Chemistry at the University of Edinburgh under the supervision of Dr. R. M. Paton.

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Lecture Courses and Conferences Attended

The following lecture courses and conferences were attended:

1. Organic research seminars – 3 years attendance.

2. Departmental colloquia, various speakers – 3 years attendance.

3. Molecular machines – 5 lectures, Prof. D. Leigh.

4. Combinatorial Chemistry – 4 lectures, Glaxo-SmithKline, October 2000.

5. *Sigma-Aldrich* Safety workshop Edinburgh, 08/11/00.

6. *RSC* Perkin Divisional Meeting 2000 – Heriott Watt University.

7. *RSC* Perkin Divisional Meeting 2001 – Glasgow University.

8. *RSC* Perkin Divisional Meeting 2002 – University of Dundee (Poster Presented).

9. 12th SCI Graduate Symposium on Novel Organic Chemistry – University of Strathclyde, 2001.

10. Postgradutate NMR Spectroscopy (10 lectures), Drs. G.C. Saunders and P.J. Stevenson, Queens University Belfast (05/02 – 08/02).

11. *Sigma-Aldrich* ½ day Organic symposium, University of Edinburgh, 29/01/03, various speakers.

12. Firbush Postgraduate talks 7th-9th April 2003, 3rd year research seminars.

13. *RSC Macro group* meeting 8th-9th April 2003, University of Durham, Oral presentation given.

14. *Organon* Postgraduate seminar, University of Edinburgh 07/05/03 – Oral presentation given.

Glossary of terms, symbols and abbreviations

atm	atmosphere
AIBN	azoisobutyronitrile
[α]	optical rotation
bp	boiling point
c	cis
cm	centimetre
CM	cross metathesis
Cy	cyclohexyl
CTA	chain transfer agent
δ	chemical shift
d	doublet
DCM	dichloromethane
DEPT	distortionless enhancement by polarisation transfer
DMSO	dimethyl sulfoxide
DP	degree of polymerisation
DTAB	dodecyltrimethylammonium bromide
EI	electron impact
ether	diethyl ether
Et	ethyl
FAB	fast atom bombardment
g	grams
GPC	gel permeation chromatography
h	hours
HOMO	highest occupied molecular orbital
HRMS	high resolution mass spectrometry
IR	infrared
J	coupling constant
lit.	literature
LUMO	lowest unoccupied molecular orbital
m	multiplet
M	moles per litre
M^+	molecular ion
Me	methyl
min	minutes
ml	millilitre

mmHg	pressure in millimetres of mercury
mmol	millimole
Mol	mole
M_n	number average molecular weight
mp	melting point
ms	mass spectrometry
M_w	weight average molecular weight
nd	not determined
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
ppm	parts per million
psi	pounds per square inch
q	quartet
RCM	ring closing metathesis
ROMP	ring opening metathesis polymerisation
s	singlet
t	triplet
TDI	tolylene-2,4-diisocyanate
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	tetramethylsilyl
Tos	*p*-toluenesulfonate

Abstract

Two approaches for the preparation of some novel functionalised polymers were investigated using a combination of nitrile oxide chemistry and Ring opening Metathesis Polymerisation ROMP. In the first case, homopolymers of norbornene (NBE) and norbornadiene (NBD) were synthesised and then modified by 1,3-dipolar cycloaddition of nitrile oxides (RCNO) to the poly(di)enes. These reactions were studied at varying molar ratios of the various nitrile oxides (R = Ph, CO_2Et, CO_2Me), which were generated *in situ* by the thermal dehydrochlorination of the corresponding hydroximoyl chlorides. The second method was via the ROMP of novel isoxazolino norbornenes. Thus, *exo*-3-phenyl-4,7-methano-3a,4,7,7a-tetrahydrobenzisoxazole **81** and *exo*-3-oxa-4-aza-ethyl-tricyclo[5.2.1]dec-4-ene-5-carboxylate **82**, were synthesised via the cycloaddition to NBD of the corresponding nitrile oxide, and were subsequently polymerised using $\{RuCl_2(=CHPh)[P(C_6H_{11})_3]_2\}$ **1** and $\{RuCl_2(=CHPh)[P(C_6H_{11})_3][IH_2Mes]\}$ **2**.

Extensive use has been made of monomeric alkenes as model compounds, both to test the synthetic pathways and to assist in establishing the structure of products from the equivalent polymer reactions; for this purpose *trans*-5-decene and cyclopentene were used.

Isoxazolino norbornenes can be polymerised with control of molecular weight (M_w and M_n) by reacting *exo*-3-oxa-4-aza-ethyl-tricyclo[5.2.1]dec-4-ene-5-carboxylate **82** with varying ratios of a suitable chain transfer agent (CTA), hex-1-ene. Thus, [CTA]/[**82**] of 0.00, 0.05, 0.10, 0.15 and 0.25 yielded oligomers with an average degree of polymerisation av DP, of 554, 157, 16, 8 and 4 (determined by GPC and NMR end group analysis). A sample of isoxazolino functionalised oligomer (n = 16) was converted into its hydrogenated analogue (83%) by treatment with *p*-toluenesulfonyl hydrazide.

Having established that isoxazolino-norbornenes were suitable monomers for ROMP, the feasibility of using the analogous isoxazolidino compounds was examined. *exo*-4-Methyl-5^{exo}-phenyl-3-oxa-4-aza-tricyclo[5.2.1.0^{2,6exo}]dec-8-ene **114** (70%), was prepared by the cycloaddition of *N*-methyl-*C*-phenyl nitrone to NBD. The analogous *exo, endo* cycloadduct **111** from the cycloaddition of *C,N*-diphenylnitrone to NBD was also synthesised and the isoxazolidines polymerised using the initiators **1** and **2**. The polymerisation of **111** and **114** with **1** yielded polymers with an av DP of 251 and 234, whereas with **2** the values increased to n = 490 and 683 respectively. An increase in polydispersity index (PDI) of 1.84 to 2.37 and 1.54 to 2.09 for was observed on going from **1** to **2**; attributed to the greater difference between K_i (initiation rate) and K_p (propagation rate) of **2**.

Glycosyl isoxazolino functionalised polymers were synthesised via ROMP as possible targets for uses such as cell agglutination inhibitors, for cell aggregation and for leukocyte trafficking in anti-inflammatory agents. Thus, *exo*-3-(2',3',4',-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **168** and *exo*-3-(2',3',4',5'-tetra-*O*-acetyl-β-D-glucopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **169** prepared by the cycloaddition to norbornadiene of glycosyl nitrile oxides, generated *in situ* by the isocyanate-mediated dehydration of the corresponding pyranosylnitromethane compound, were polymerised using the ruthenium complexes **1** and **2**. The oligomerisation of *exo*-3-(2',3',4',-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **168** was effected using the ruthenium carbene (**1**), with increasing monomer/initiator ratios [M]:[I] employed to produce polymers of increasing length. With homogeneous conditions, a linear relationship between [**168**]:[**1**] (3/1, 10/1, 30/1, 50/1, 70/1, 85/1) and the av DP (3, 14, 40, 62, 76, 100) was observed. This relationship and the low PDI values (1.15-1.67) obtained are characteristic of a controlled polymerisation.

Reduction of the carbohydrate functionalised oligomer **178** with tosyl hydrazide proved successful (69%) yielding the hydrogenated analogue **185**. Random and block copolymers were prepared using initiators **1** and **2**. When complex **2** was adopted for the homo- / co-polymerisations, an increase in PDI and av DP was observed.

Deacetylation of *exo*-3-(2',3',4',-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **168** using a triethylamine/methanol mixture yielded *exo*-3-(2',3',4',-tri-*O*-hydroxy-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **176** (93%). Attempts at aqueous polymerisation of **176** with various reaction conditions and catalyst systems show promising results.

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Chapter 1 – Functionalised polymers and copolymers

1.0 Introduction

1.1 Foreword

This thesis is concerned with the synthesis of functionalised polymers using a combination of ring opening metathesis polymerisation (ROMP) and 1,3-dipolar cycloaddition chemistry.
1,3-Dipolar cycloaddition reactions have been studied extensively for the construction of 5-membered heterocycles but, in contrast, there has been limited application in polymer chemistry.

The preparation of polymers bearing isoxazoline functionality is investigated using two approaches. The first is via the synthesis of a polymer using ROMP and modifying the polymeric alkene units via 1,3-dipolar cycloaddition. The second route entails the synthesis of norbornene-type monomers incorporating isoxazoline substituents, and their subsequent ROMP.

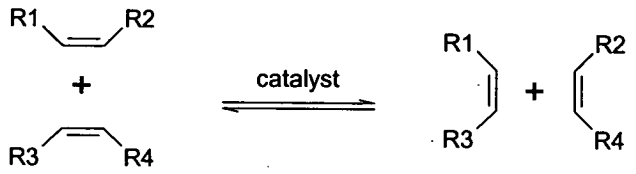
Polymers functionalised with carbohydrate residues (glycopolymers) are important as they offer multivalent displays of saccharides which play important roles in specific recognition events with cell surface proteins. Strained systems based on functionalised norbornenes are well established monomers for ROMP, and thus provide an attractive method for the preparation of polymeric isoxazolines bearing carbohydrate substituents.

In the Introduction four topics are therefore discussed. The first section provides a background to olefin metathesis, and ROMP in particular. The second gives a brief account of nitrile oxide – isoxazoline chemistry. In the third part current applications of functionalised homopolymers are surveyed and finally aspects of copolymerisation are discussed.

1.2. Olefin metathesis

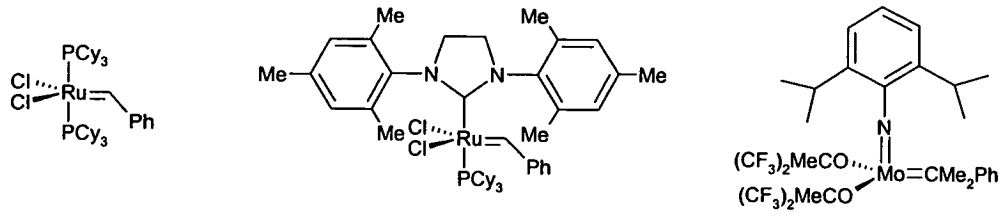
1.2.1 Introduction

The term metathesis comes from the Greek words *meta* and *tithemi* meaning to change and place respectively and olefin metathesis thus involves the exchange of alkylidene substituents between substituted alkenes (Scheme 1.1).



Scheme 1.1

The development of stable metal alkylidene complexes has resulted in a significant broadening of the potential applications of this reaction for the synthesis of natural and non-natural products.[1] The most versatile and popular catalysts are the ruthenium complexes **1** and **2** of the general formula $\{RuX_2(=CHPh)[L]_2\}$ which were introduced by Grubbs and co-workers,[2] and the molybdenum complexes **3** of the type, $[(NAr)(OR')_2M=CHR]$ developed by Shrock and co-workers (Figure 1.1).[3] This carbon-carbon bond forming reaction has come to the forefront of organic synthesis under the guise of its three main applications, Cross Metathesis (CM), Ring Opening Metathesis Polymerisation (ROMP) and Ring Closing Metathesis (RCM)

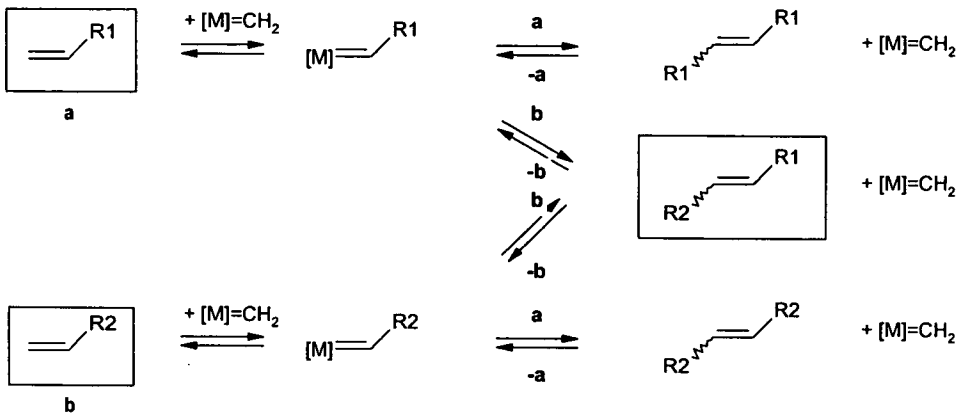


1 **2** **3**

Figure 1.1

Cross metathesis (CM)

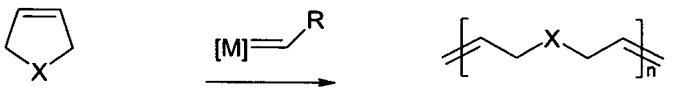
Cross-metathesis between two acyclic olefins offers various possibilities for converting readily available terminal alkenes into higher–substituted olefins as outline in Scheme 1.2. The use of highly substituted asymmetric olefins is not practical because of the expected complex spectrum of products. On the other hand the use of terminal olefins results in the formation of volatile ethene as the by-product, which provides a driving force for the reaction. Therefore, almost all applications of cross-metathesis as a synthetic method employ reactions between terminal olefins. The reaction is not very stereoselective, however, and often affords a mixture of *cis* and *trans* alkenes.



Scheme 1.2

Ring opening metathesis polymerisation (ROMP)

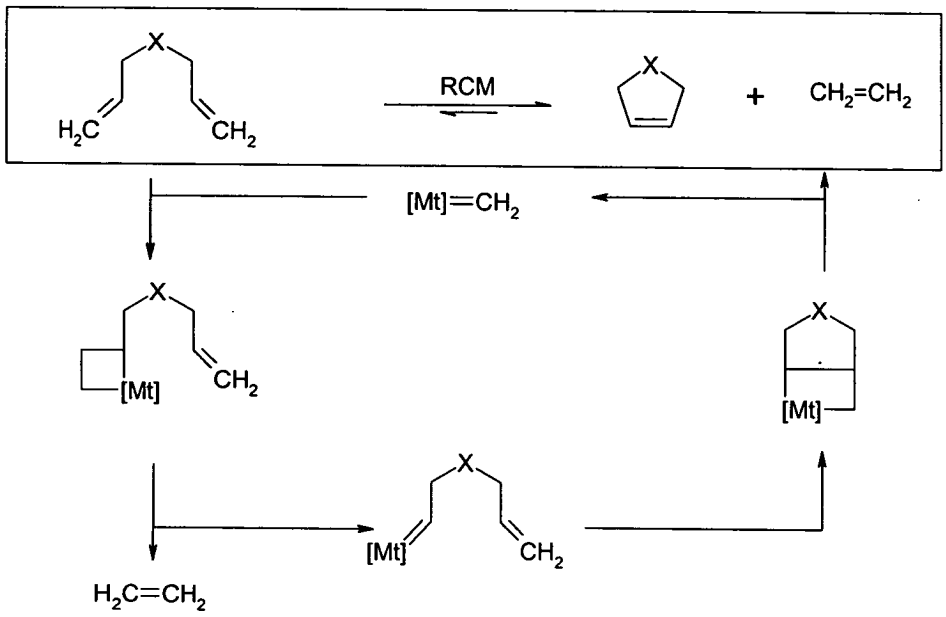
ROMP involves the polymerisation of a strained cyclic monomer to generate a thermodynamically more stable polymer (Scheme 1.3). The driving force of the process is the relief of this ring strain. This application is discussed in detail in Section 1.3.



Scheme 1.3

Ring closing metathesis (RCM)

Ring closing metathesis is the intramolecular olefin metathesis between an α,ω-diene to form unstrained rings. The reaction is driven both entropically and by the expulsion of an alkene such as ethene (Scheme 1.4). An important factor for productive RCM is the sensitivity of the metathesis initiator to the substituent pattern of the olefin, as this constitutes a kinetic obstacle for the retro reaction. This application of olefin metathesis has been extended to the synthesis of a wide range of natural and non-natural products.[4]

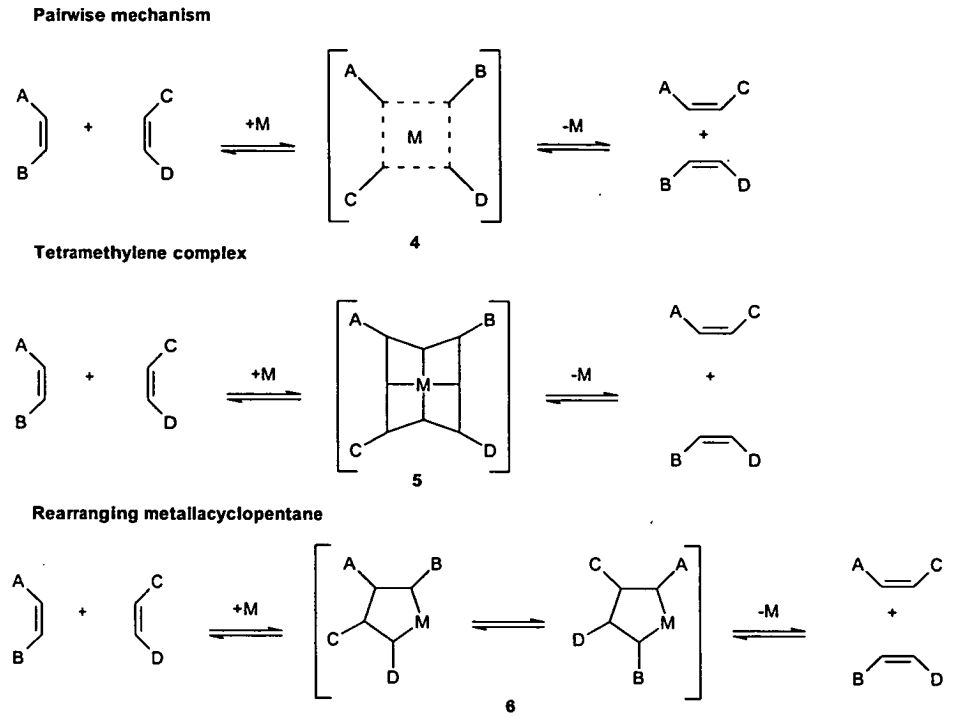


X = e.g. $(CH_2)_n$, O, NR

Scheme 1.4

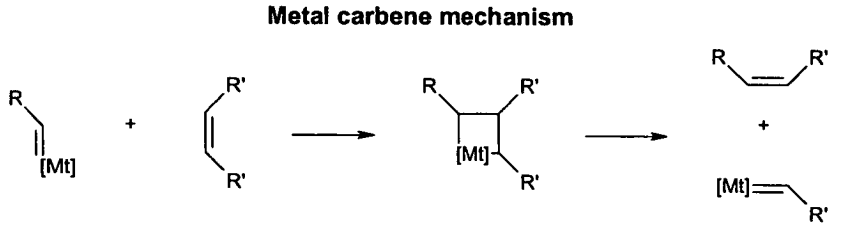
1.2.2 Mechanism of olefin metathesis

The first postulated mechanism by Calderon *et al.*[5] in 1968 described olefin metathesis as proceeding by a pairwise mechanism where the *p*-orbitals on the olefins overlapped with the metal *d*-orbitals to form a type of metal-cyclobutane **4**. In 1971, Petit *et al.*[6] proposed that the reaction involved a tetramethylene complex **5**, in which four methylene units are bonded to a central metal atom. In an attempt to explain metathesis Grubbs *et al.*[7] stated in 1972 that the redistribution of groups around the double bonds was due to a rearranging metallacyclopentane intermediate **6** (Scheme 1.5). Had people been aware of work by the French chemists Herrison and Chauvin[8] published in the early 1970s, these incorrect proposals may not have arisen.



Scheme 1.5

The now commonly accepted mechanism for the olefin metathesis reaction, which was first proposed in 1971 by Herrison and Chauvin,[8] involves a [2+2] cycloaddition reaction between a transition metal alkylidene and an olefin to form an intermediate metallacyclobutane (Scheme 1.6). This metallacycle then undergoes alternative [2+2] cycloreversion to afford a new alkylidene and a new olefin. The process eventually leads to an equilibrium mixture of olefins. This mechanism was finally proven by Shrock in 1980 for the metathesis of *cis*-pent-2-ene catalysed with complexes of the type [P(CH$_3$)$_3$](O-tert-C$_4$H$_9$)2(Cl)M5C(H)(tert-C$_4$H$_9$) [M = Nb or Ta].[9]



Scheme 1.6

[2+2] Cycloaddition reactions between two alkenes to give cyclobutanes are symmetry forbidden and normally occur only photochemically. However, when the reaction is between a metal carbene and an olefin, the symmetry restriction is lifted and the reaction proceeds. Fischer carbenes usually

contain an electron rich metal (e.g. Cr^0, Mo^0, Re^{+1}) and a carbocation like carbon, whereas Schrock carbenes possess an electron deficient metal (e.g. Ta^{+3}, Nb^{+3}) and a carbanion like carbon (Figure 1.2).

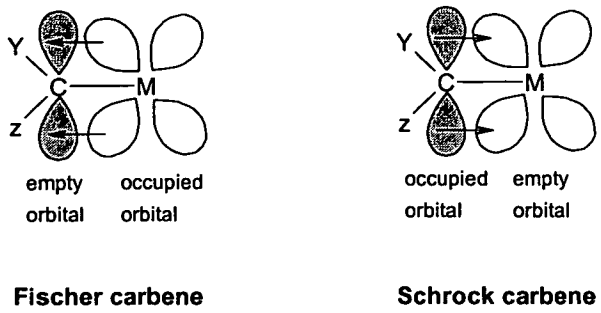


Figure 1.2

Two modes of bonding are present in the reaction between transition metal carbenes and alkenes. The overlap of filled π-bonding orbitals of the alkene with vacant "*dsp*" hybrid orbitals on the metal forms σ-donor bonds. In addition, filled *d* orbitals of the metal can overlap with the vacant π*-antibonding orbital of the alkene, back donating electron density from the metal to the olefin[10] (Figure 1.3).

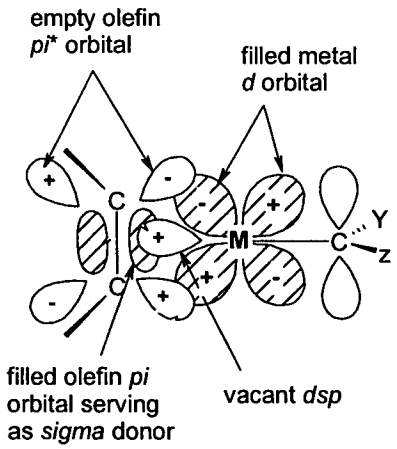
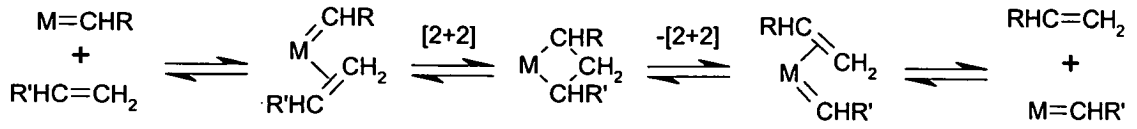


Figure 1.3

The [2+2]cycloaddition / cycloreversion sequence between a metal alkylidene and an alkene is summarised in Scheme 1.7 below.



Scheme 1.7

1.3 Ring opening metathesis polymerisation

1.3.1 Introduction

Ring opening polymerisation of cycloalkenes dates back to 1962 when it was reported that with certain catalysts cyclobutene yielded poly(1-butene).[11] This was later recognised as an example of the alkene metathesis reaction reported by Banks and Bailey in 1964.[12] Ring Opening Metathesis Polymerisation (ROMP) of norbornene and numerous derivatives have been reported using a variety of catalysts ranging across the transition metal series from titanium to rhodium and iridium complexes.[13] The resulting polymers have found applications in industry (Section 1.3.2) and current research is focused on elegant syntheses with ROMP as the key step for preparing materials for diverse applications, outlined in (Section 1.8).

1.3.2 Industrial applications of ROMP

Olefin metathesis has been used in several technical processes and a summary of applications is outlined in the review by Blechert *et al.*[1] An important area of application for olefin metathesis chemistry is the polymerisation of olefins, e.g. the polymerisation of norbornene using a tungsten complex known as the Norsorex process[14] of the CDF-Chemie company, and the Hüls-Vestenamer process which entails the ROMP of cyclooctene[15] (Figure 1.4). Current developments in the area of metathesis polymerisation are discussed in Section 1.8.

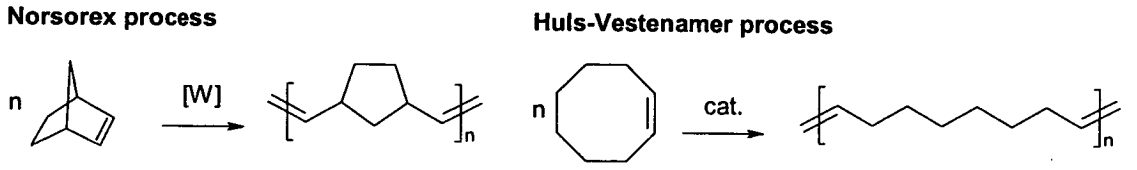
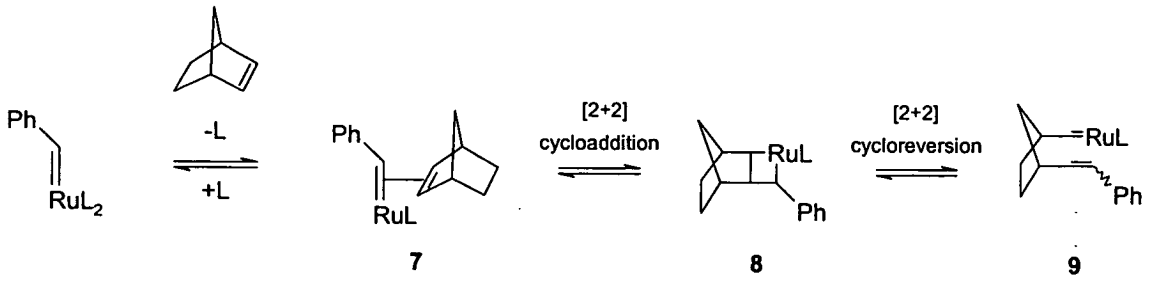


Figure 1.4

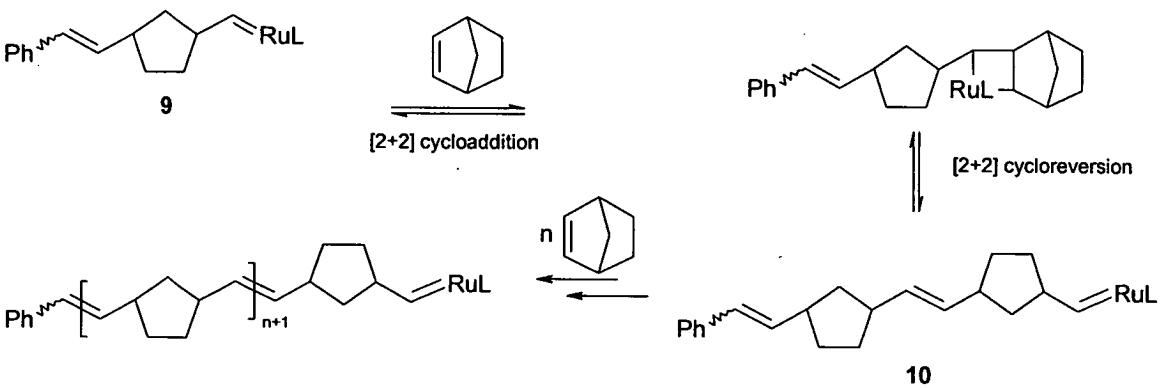
1.3.3 Mechanism of Ring Opening Metathesis Polymerisation

The initiation of the Ring Opening Metathesis Polymerisation reaction exemplified here with norbornene (NBE) and the ruthenium alkylidene **1** is shown in Scheme 1.8. It involves the coordination of norbornene to the ruthenium carbene to give complex **7** which undergoes [2+2] cycloaddition to generate the intermediate metallacyclobutane **8**, followed by [2+2] cycloreversion affording the initiating carbene **9**.



Scheme 1.8

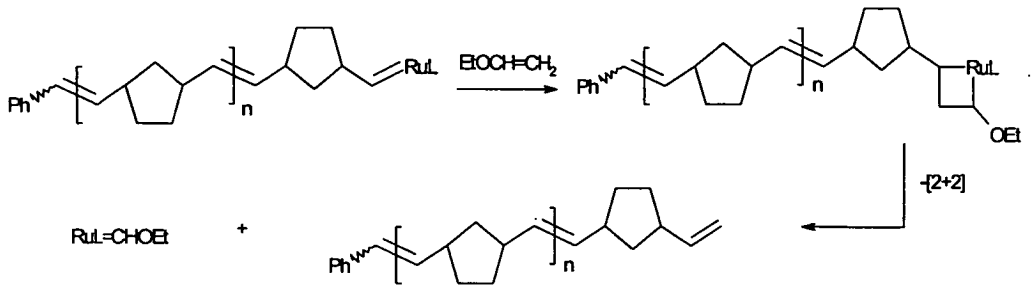
Propagation proceeds via the [2+2] cycloaddition of the initiating alkylidene **9** with another strained monomer unit generating the intermediate metallacyclobutane, which on [2+2] cycloreversion generates a new ruthenium alkylidene **10**. The cycle is repeated until all of the monomer has been consumed (Scheme 1.9) with the ruthenium alkylidene attached to the growing polymer chain.[16] Well-defined initiators such as the Schrock and Grubbs complexes can afford living polymerisations in which termination does not compete effectively with propagation.



Scheme 1.9

A capping agent[17] such as ethyl vinyl ether is usually employed to terminate the polymerisation. The ruthenium carbene reacts with the vinyl ether to give the metal carbene ether and a new vinyl

end group. Thus both the benzylidene and vinylidene termini of the polymer chain can be identified (Scheme 1.10).



Scheme 1.10

The driving force for the ROMP of NBE and norbornadiene (NBD) is the relief of ring strain. Olefins such as cyclohexene have little or no ring strain and are not polymerised because there is no thermodynamic preference for polymer versus monomer. Strained cyclic olefins such as norbornene and norbornadiene have sufficient ring strain to make polymerisation possible.

The polymers produced in the ROMP reaction using well defined catalysts typically have a narrow range of molecular weights, something that is often difficult to achieve by standard polymerisation methods such as free radical polymerisation. The poly-dispersity indexes, PDIs, (the weight average molecular weight M_w divided by the number average molecular weight M_n), are typically in the range of 1.03-1.10.[18] [Polydispersity index, PDI = M_w/M_n; for a monodisperse polymer $M_w = M_n$, hence the PDI = 1.00.] Polymers with such narrow Molecular Weight Distributions (MWD) are said to be mono-disperse.

Another feature of a living system is the ability to synthesise block copolymers (discussed in detail in Section 1.11). For example, norbornene can be polymerised and then a second monomer added after the first is consumed. ROMP is therefore a superior method for making di- and tri-block copolymers and permits the properties of the resulting material to be tailored. However, such materials are only possible if chain initiation and chain propagation are perfectly balanced. Therefore, for functionalised monomers in particular, it is not uncommon to try several different catalysts, solvents, concentrations, temperatures etc. to achieve the best results.[16]

1.3.4 Chain transfer agents

Chain transfer agents are employed to prepare lower molecular weight materials that are often more freely soluble and afford high quality NMR spectra, and yet are truly representative of the higher-molecular weight polymers. For example, oligomers of NBD have been synthesised using hex-1-

ene as a chain transfer agent.[19] This enabled the microstructure of polyNBD to be analysed to the same level as that for polymers of NBE.[20] Chain transfer agents will be discussed in Section 2.6.4.

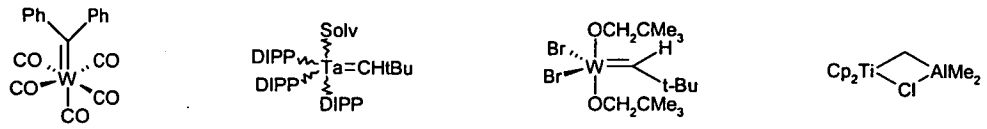
1.4 ROMP initiators

1.4.1 Introduction

From the mid 1950's until the early 1980's the active species for the olefin metathesis reaction were poorly defined multi-component systems consisting of organometallic reagents and an alkyl metal species. These were termed the "classical catalyst systems", e.g. WCl_6/Me_4Sn, $WOCl_4/Cp_2TiCl_2$, $Re_2O_7/SnBu_4$. An example is the use of a cocatalyst such as a tetraalkyltin compound which can form an active species from metal salts such as molybdenum pentachloride and tungsten hexachloride. Alkylation of the metal results in a carbene ligand being formed after the loss of hydrogen chloride (Scheme 1.11).[21]

Scheme 1.11

The harsh conditions and strong Lewis acids that classical catalysts require make them incompatible with most functional groups, thus limiting their use. In addition, the reactions are difficult to control because very little of the active species is formed in the catalyst mixtures. The elucidation of the mechanism of the olefin metathesis reaction developed by Chauvin[8] prompted the discovery of the first single-component homogeneous catalysts for olefin metathesis during the late 1970's and the early 1980's. These new catalysts included (diphenylcarbene)pentacarbonyl tungsten[22] **11**, tris(aryloxide)tantalum carbenes[23] **12**, various dihalo alkoxide alkylidene complexes of tungsten[24] eg **13** and bis(cyclopentadienyl)titanocyclobutanes[25] **14** (Figure 1.5). These single component homogeneous complexes sometimes exhibited higher initiation rates and increased activity than their "classical catalyst" predecessors. In addition harsh conditions were not required to generate the corresponding active species as **11-14** are preformed carbenes. The mechanism could be now studied in detail and detection of propagating species was possible by ^1H NMR spectroscopy.[24]

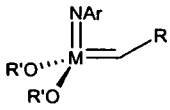


11 **12** **13** **14**

Figure 1.5

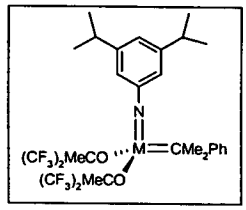
1.4.2 Schrock type initiators

On the basis of the results obtained with these catalysts (**11-14**), the synthesis of well defined high-oxidation state molybdenum alkylidenes of the type $[M(=CHCMe_2Ph)(=NAr)(OR)_2]$ was reported by Schrock and co-workers in 1990[3] (Figure 1.6).



Generic form of Schrock catalyst

M = Mo, W
R = ethyl, phenyl, TMS, CMe_2PH
R' = CMe_3, CMe_2CF_3, $CMe(CF_3)_2$, $C(CF_3)_3$
Ar = 2,6-R''-C_6H_3 (R'' = H, Me, ^{i}Pr)



3

Figure 1.6

These tetra-coordinated alkylidene species constitute potent and well-behaved metathesis (pre-) catalysts which have been thoroughly studied from a mechanistic point of view.[3,26] Among them compound **3** turned out to be particularly active and is now commercially available. This and related complexes are oxo- and hydro-philic and must be handled in rigorously dried solvents using Schlenk techniques. The handling difficulties of this species are compensated with a high reactivity, which is reflected in the ability to polymerise electronically deactivated monomers[27] and ring close sterically demanding and electron poor substrates.[28] At this time the development of single-component catalysts with high reactivity, albeit at the expense of functional group tolerance was a major advance, but there was still room for improvement.

1.4.3 Grubbs type initiators

In attempt to synthesise an initiator with greater functional group tolerance and comparable activity to **3** Grubbs and coworkers[29] investigated the deactivation of catalysts by functional groups in the substrate or the solvent (including water and oxygen). It was believed that the functionality may

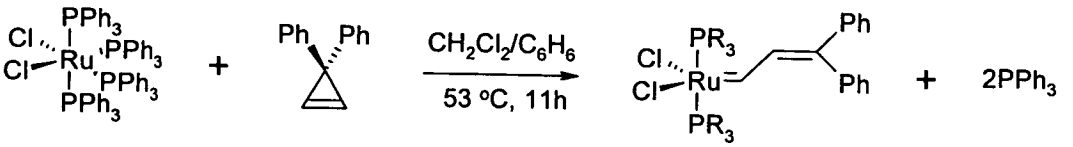
bind competitively to the active metal centre and deactivate the catalyst, or they may react directly with the metal centre and destroy the active species. Improved functional group tolerance would result from the development of a metal carbene that reacted preferentially with olefins in the presence of other functional groups. The advent of single-component catalysts meant that the relationship between structure and reactivity could be more clearly defined. These alkylidene complexes were observed to react more selectively with olefins as the metal centres varied from left to right and bottom to top in the periodic table (Table 1.1).

Titanium	Tungsten	Molybdenum	Ruthenium
Acids	Acids	Acids	**Olefins**
Alcohols/Water	Alcohols/Water	Alcohols/water	Acids
Aldehydes	Aldehydes	Aldehydes	Alcohols/Water
Ketones	Ketones	**Olefins**	Aldehydes
Esters/Amides	**Olefins**	Ketones	Ketones
Olefins	Esters/Amides	Ester/Amides	Esters/Amides

Increasing reactivity

Table 1.1 – Functional group tolerance of early and late transition metal metathesis catalysts.

Initial studies with ruthenium trichloride ($RuCl_3.H_2O$)[30] showed that ROMP under aqueous conditions initiated in 30 mins whereas the analogous reaction in organic media took up to 20 h; thus, not only was the complex water tolerant, but water actually increased its activity. The ability to polymerise functionalised norbornenes, 7-oxanorbornene and norbornadiene monomers with $Ru(H_2O)_6(Tos)_2$ (Tos = *p*-toluenesulfonate)[31] in consistently greater yield with higher molecular weights and lower polydispersities than those prepared with other contemporary catalysts showed real promise. However, at the time Grubbs and coworkers[32] were synthesising tungsten alkylidenes as initiators using 3,3-disubstituted cyclopropenes as carbene precursors. This methodology was adopted in an attempt to make a ruthenium based complex. Thus, the reaction of 3,3-diphenylcyclopropene with either $RuCl_2(PPh_3)_3$ or $RuCl_2(PPh_3)_4$ afforded **15** in essentially quantitative yield (Scheme 1.12).[33]

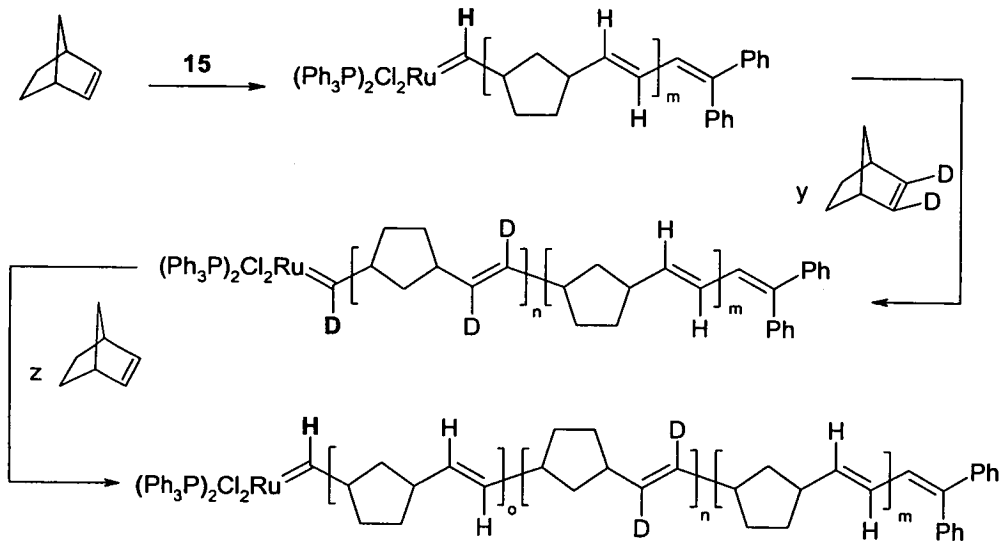


15 R = Ph

16 R = Cy

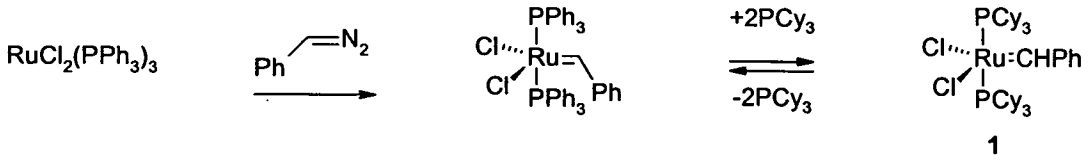
Scheme 1.12

Initiator **15** was found to polymerises NBE (block m) to yield polynorbornene (Scheme 1.13). During the reaction a signal for the propagating carbene was observed in the ^{1}H NMR spectrum at 17.79 ppm. Its identity and stability were confirmed by preparing a block copolymer of 2,3-dideuterio-NBE and perprotio-NBE. When 2,3-dideuterio-NBE was added (block n), the new carbene signal vanishes, but reappears when protio-NBE was added for the third segment (block o). The ability to observe a propagating species on the timescale of the block copolymerisation suggests a living polymerisation.[34]



Scheme 1.13

At this stage complex **15** possessed superior functional group tolerance to Schrock's metal alkylidene **3**, but at the expense of decreased activity. It was known that ligand environment and metathesis activity were related; more specifically, activity increases with more electron-withdrawing ligands.[35] In an attempt to increase the activity of **15**, Grubbs used PCy_3 (Cy = cyclohexyl) in a ligand exchange, which led to the discovery of **16** (Scheme 1.12). However, the multistep synthesis of the carbene precursors (diphenylcyclopropene) and the low initiation rates of **15** and **16** limited their use. In 1995 Grubbs and coworkers[37] described the reaction of $RuCl_2(PPh_3)_3$ with phenyldiazomethane which led to the discovery of **1** (Scheme 1.14), which is now generally referred to as the Grubbs first generation initiator. This ruthenium benzylidene was found to polymerise norbornene in a living manner (PDI = 1.04) due to its high initiation rate, and kinetic studies showed that it initiated polymerisation about 1000 times faster than **15**.



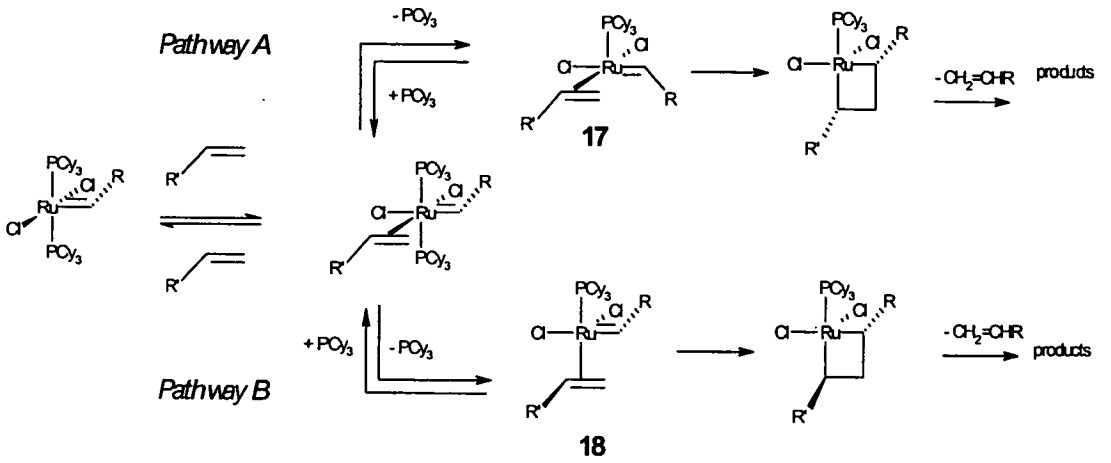
Scheme 1.14

1.4.4 Mechanism of the Grubbs initiators

Initiator **1** is easier to synthesise than Schrock's molybdenum alkylidene **3** and has an overall activity between that of **3** and the original Grubbs carbene **16**.[36] In terms of functional group tolerance, it is equivalent to **16** and, due to its higher activity, **1** has succeeded **16** in popularity in recent years. X-ray crystallography showed that $L_2X_2Ru{=}CHR$ complexes are arranged in a distorted square pyramidal geometry with the alkylidene in the axial position and the *trans* phosphines and halides in the equatorial plane.[37] Grubbs and coworkers[38] carried out extensive kinetic studies on **1** and proposed the following mechanism (Scheme 1.15) which is consistent with activity trends.

The first step involves olefin coordination to the metal centre, presumably *cis* to the alkylidene. Two paths are then possible. In one pathway A, phosphine dissociation and alkylidene rotation occurs to generate the 16-electron intermediate **17**, in which the olefin remains *cis* to the alkylidene. This then undergoes metallacyclobutane formation *cis* to the bound phosphine, followed by cycloreversion to generate the exchanged products. The alternative pathway B involves phosphine dissociation and rearrangement of the olefin *trans* to the remaining phosphine. This intermediate **18** then undergoes metallacyclobutane formation *trans* to the remaining phosphine. This pathway was initially disfavoured because of reversibility considerations, though it is currently being studied in greater detail.

Since establishing that initiation proceeds via phosphine dissociation, several researchers including Grubbs have reported a variety of supporting evidence. This includes i) kinetic data,[38] ii) observation of chelated mono-(phosphine) intermediates during the ROMP of 3-functionalised cyclobutanes,[39] iii) reactivity patterns of imidazoles with $L_2X_2Ru{=}CHR$ complexes,[40] iv) the isolation of a ruthenium catalyst "caught in the act" in which an intramolecularly coordinated olefin has displaced one of the phosphines,[41] v) the observation of mono(phosphine) intermediates by electospray ionisation tandem mass spectrometry,[42, 43] and vi) quantum molecular dynamics studies.[44]



Scheme 1.15

The activity of the Grubbs initiators of the type $(L)_2X_2Ru=CHR$ is governed by the ligand environment and the substituent on the alkylidene moiety. Activity is maximised with L- and X-type ligands with opposite steric demands. Larger and more electron donating phosphines (L) and smaller and less electron donating halides (X) result in optimum activity. The overall activity also depends on the initiation process, which itself is dependent on the nature of the alkylidene moiety.

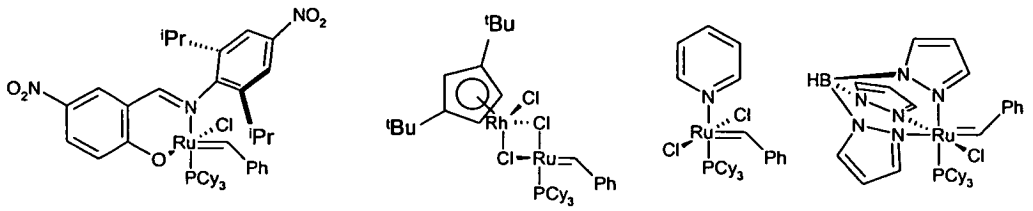
The electron donating phosphine ligand facilitates phosphine dissociation and stabilisation of the vacant trans site in **17**[38, 45] as a result of σ-donation to the metal centre. Consequently, the 14-electron metallocyclobutane intermediate is also stabilised by σ-donation from this ligand. Thus, reactivity increases with phosphine bascity in the order $PPh_3 << P^iPr_2Ph < PCy_2Ph < PPr^i_3 < PCy_3$. Due to the observed increase in activity on going from PPh_3 to PCy_3 it is believed that steric bulk may also contribute to phosphine dissociation by destabilising the crowded bis(phosphine) olefin complex.

In contrast to the trend for phosphines, the halide ligands correlate with decreasing activity as they become larger and more strongly electron donating, in the order Cl> Br>> I. Since the incoming olefin may initially bind *trans* to a halide, a more electron-donating halide should weaken the ruthenium-olefin bond and disfavour olefin coordination.

Rates of initiation (k_i) and propagation (k_p) must be similar in order to facilitate living polymerisations.[16] More efficient initiation was observed alkyl-substituted alkylidenes compared with methylidene complexes $(PCy_3)_2Cl_2Ru=CH_2$.[46] The initiation with an ester-substituted alkylidene $[Ru]=CHCO_2R$ occurs even more rapidly than for alkyl derivatives, but these complexes tend to be less stable.[47] The ruthenium benzylidene **1** seems to be the intermediate case; the phenyl group is somewhat electron withdrawing, but its size may assist phosphine dissociation.

1.4.5 Recent developments in catalyst systems

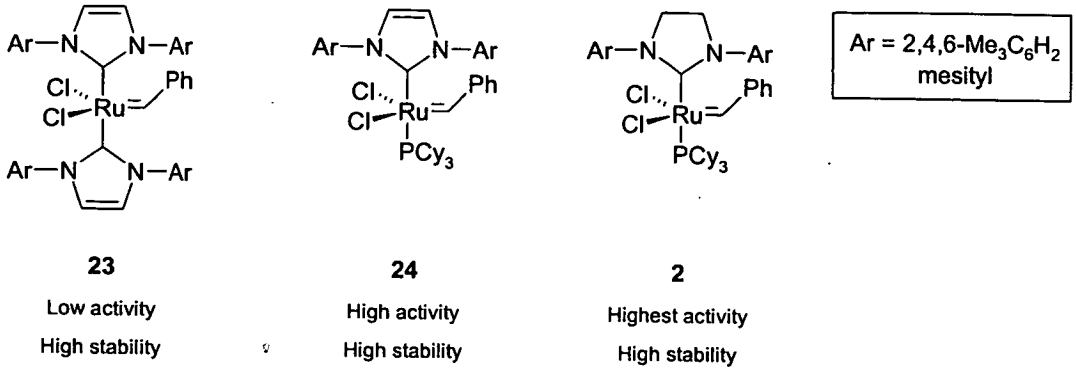
The superior activity of Schrock's complex **3** over **1** has led to the investigation of the ligand environment in the Grubbs initiator. The elucidation of the exact mechanism of olefin metathesis using **1** led to the discovery of the mono(phosphine) intermediate as the active species. Hence, a more bulky and strongly σ-donating ligand could increase the polarity of the Ru=C bond in this intermediate, resulting in a more active catalyst. Recently, several groups have prepared derivatives of **1** based on the following ligands: a bidentate salicylaldimine[48] **19**, a heterobimetallic[49] **20**, pyridine coordinated[49] **21** and tris(pyrazolyl)-borate[50] **22** (Figure 1.7).



19	**20**	**21**	**22**
Low activity High Stablity	High activity Unstable	High activity Unstable	High activity Unstable

Figure 1.7

Although the complexes **19-22** are active to some degree, they tend to have either enhanced stability and low activity, or the reverse, high activity and poor stability. Hermann and co-workers[51] were the first to investigate stable N-heterocyclic carbenes (NHC) with their complex **23** (Figure 1.8), which showed good stability but poor activity. The initiation of the ruthenium initiators of the type $[L_2X_2Ru{=}CHR]$ is dependent upon dissociation of one of the ligands (L). As the dissociation of NHC ligands would be very slow relative to the coordinative labile PCy_3 in **1**, it is not surprising that complex **23** possesses low activity. For optimum activity Grubbs[52] synthesised the ruthenium carbene **24** (Scheme 1.16) adopting the use of one kinetically inert, electron-donating NHC ligand in combination with a less basic PCy_3 ligand.



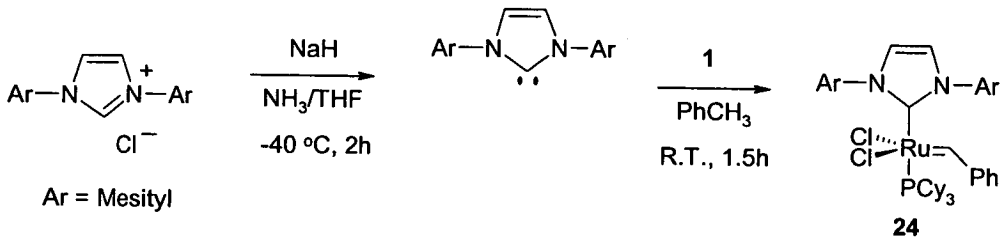
23
Low activity
High stability

24
High activity
High stability

2
Highest activity
High stability

Figure 1.8

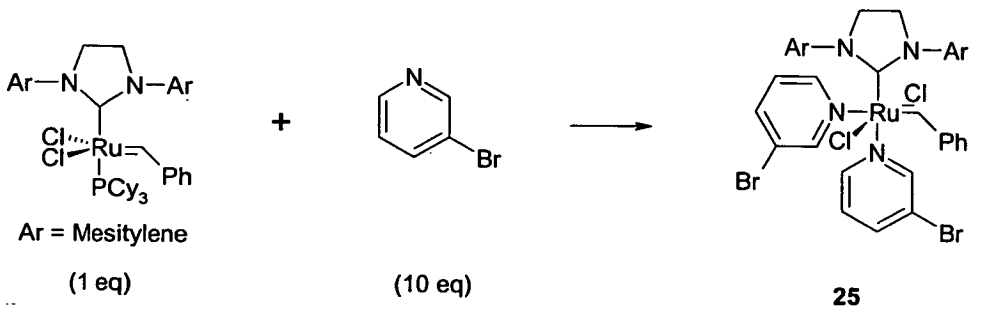
Complex **24** displayed dramatically increased ring-closing activity when compared with **1**. Di-, tri-, and even tetra-substituted cycloalkenes were successfully prepared from the corresponding diene precursors using catalytic amounts of **24**. In certain cases, cyclisation of substrates was possible with low mol percentages of **24** while the corresponding reaction with **1** did not yield any significant amount of cyclized product.[52]



Scheme 1.16

Recently, complex **2** has been prepared which utilises NHC ligands with saturated backbones, this is commonly referred to the Grubbs second generation catalyst.[53] Complexes **2** and **24** rival the activity of Schrock's alkylidene **3** in RCM,[53, 54] but are more active for ROMP[55], while maintaining the functional group compatibility of **1**. However **2** generally gives polymers with uncontrolled molecular weights and broad PDIs, owing to high propagation and slow initiation rates, (low k_i/k_p; k_i = rate constant for initiation, k_p = rate constant for propagation).

As recently as 2002, Grubbs and co-workers developed complex **25** (Scheme 1.17), which shows exceptionally fast initiation, resulting in molecular weight control and a low PDI value for the ROMP products of cycloooctadiene and various functionalised norbornenes.[56]



Scheme 1.17

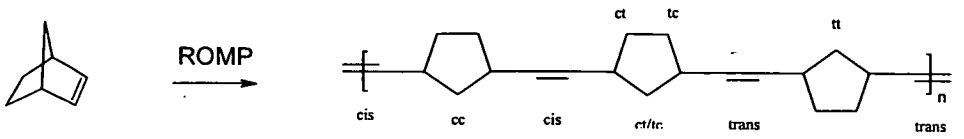
1.5 Stereochemistry of ROMP

1.5.1 Introduction

The stereoregularity of polymer molecules is a microstructural feature of great importance which determines, to a large extent, the bulk properties and hence the commercial value of many polymeric materials. The breadth of this area is such that the reader is referred to the monographs 'Olefin Metathesis and Metathesis Polymerisation'[13] edited by K.J. Ivin and J.C. Mol, 'Ring Opening Metathesis Polymerisation and Related Chemistry'[58] edited by E. Khosravi and T. Szymanska-Buzar and a review "Characteristics of $RuCl_2(CHPh)(PCy_3)_2$ as a catalyst for Ring Opening Metathesis Polymerisation" by Rooney *et al.*[57] The following is a brief overview of the main stereochemical aspects of polymers synthesised via ROMP.

1.5.2 Stereoselectivity

The ratio of *cis* and *trans* double bonds and their distribution is the primary microstructural variant of the products in metathesis polymerisations. The microstructures of the resulting polymers, i.e. the configuration of the double bonds, distributions and tacticities, have been examined extensively making use of ^{13}C and ^{1}H NMR spectroscopy.[59] The ^{13}C NMR spectra of polynorbornene (poly-[1,3-cyclopentylenevinylene]) **26** were first reported and interpreted by Ivin, Laverty and Rooney.[60] Double bond pairs may be cc, ct, tc or tt (c = *cis*, t = *trans*), and assignment of peaks is based on the position of the named carbon from the nearest two double bonds (Scheme 1.18). The ratios tt/tc and cc/ct are denoted by rt and rc respectively, and the fraction of *cis* and *trans* double bonds by σ_c (rc/rt) and σ_t (rt/rc) respectively.



26

Scheme 1.18

Factors which influence the *cis* content (σ_C) such as monomer and catalyst reactivity, steric constraints at the catalyst site, the influence of the stereochemistry of the last formed double bond on the next propagation event and the geometry of the carbene ligand, have been the subject of numerous studies.[57] The ability to determine the amount of *cis* double bonds in the polymer is particularly useful as it gives an indication of activity of the catalyst, as well as any steric hindrance at the metal carbene site. The formation of *cis* double bonds requires more energy than the formation of *trans* bonds. However, the formation of a *cis* junction is sterically less demanding than the formation of a *trans* link. This means that generally an unreactive catalyst will tend to form *trans* links, whereas a more reactive catalyst will allow the formation of equal amounts of *cis* and *trans* links with no discrimination between the two. However, even with more reactive catalysts a very unstrained and unreactive monomer will often form a high proportion of *trans* links. In order to form a high *cis* polymer it is usually necessary to have some form of steric hindrance around the catalyst site to force the transition state to form a less sterically demanding *cis* junction.[61]

Prochiral monomers such as norbornene give polymers containing chiral centres. Adjacent cyclopentane rings may have an isotactic (m) or syndiotactic (r) dyad relationship (Figure 1.9).

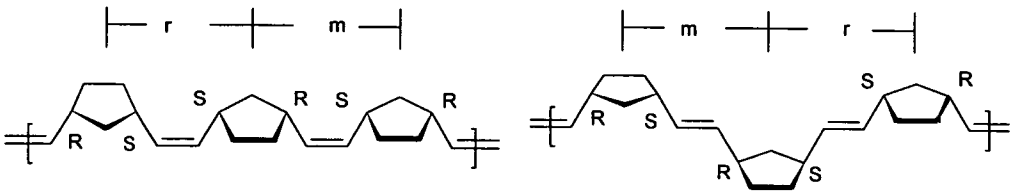


Figure 1.9

Kelly and Calderon[62] devised an entiomorphic sites model that discusses the relative ease of formation of the intermediate *cis* or *trans* metallacycles which determines whether *cis* or *trans* double bonds are eventually formed. The scheme involves a number of assumptions:

1. The propagating species may have left or right handed forms (P_l and P_r), represented here in terms of octahedral symmetry about the metal, with one position vacant for the acceptance of the monomer.

2. Norbornene presents its less hindered *exo* face (the five membered unsaturated ring) to the metal centre.

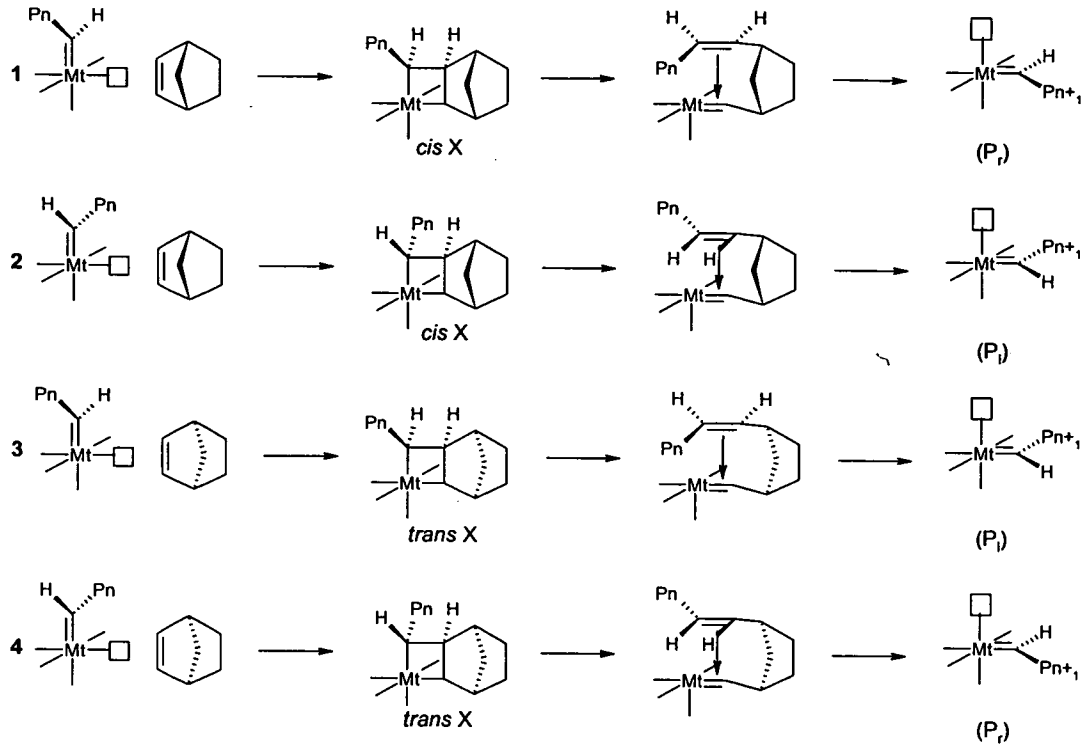
3. The Mt=C and C=C double bonds approach each other in parallel alignment in forming the transition state leading to the metallacyclobutane intermediate, and likewise in the cycloreversion.

4. The configuration P_l or P_r retains its integrity between the successive propagation steps, *i.e.* there is no ligand migration, rotation about the Mt=C double bond, or other significant change of geometry that would result in epimerisation or relaxation to an achiral form.

As discussed by Kelly and Calderon there are four ways in which the intermediate metallacyclobutane may form since, as viewed from the rear of the approaching monomeric unit, the P_n may lie to the left or right, and so may the bridging CH_2 (Scheme 1.19). The four possible modes of addition are summarised in Table 1.2.

Entry	**1**	**2**	**3**	**4**
Orientation of P_n as seen by monomer	Right	Left	Right	Left
Orientation of CH_2 bridge	Right	Left	Left	Right
Orientation of P_{n+1} relative to the vacated ligand	Left	Right	Right	Left
Structure of of C=C in P_{n+1}	*cis*	*cis*	*trans*	*trans*
Configuration of ring in P_{n+1}	r	l	l	r

Table 1.2 – Modes of addition



P_n denotes a chain containing n monomer units.

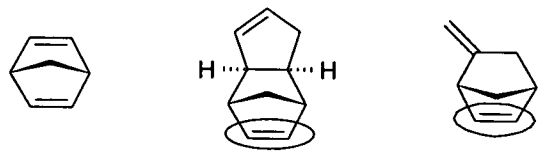
Scheme 1.19

1.5.3 Regio- and site-selectivity

If it is assumed that attack on the double bond occurs exclusively on the *exo* face, selectivity falls into three different categories:

1.5.3.1 Reactivity of diene monomers

In the case of diene monomers the double bonds may have different reactivities, due to their position on the monomer. The more reactive alkene in each example is circled in Figure 1.10.



27 **28** **29**

Figure 1.10

Each alkene unit in NBD **27** has identical reactivity, whereas in dicyclopentadiene **28** the double bond of the norbornenyl unit is more reactive than that of the cyclopentenyl due to strain energy differences. Finally, the methylenyl double bond in 2-vinylnorbornene **29** is less reactive than the norbornenyl alkene again due to strain differences.

1.5.3.2 Steric constaints and electronic effects

Structurally similar double bonds may show differential reactivities due to steric constraints of substituents (Figure 1.11).

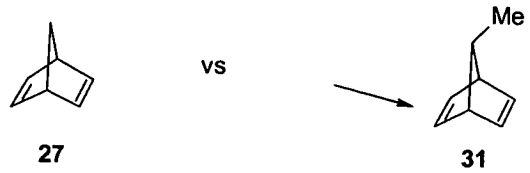


Figure 1.11

For example, reaction with the alkene units of NBD **27** is equally possible at either side of the methano-bridge. For 7-methylnorbornadiene **31**, however, the double bond *anti* to methyl group on the bridgehead is more reactive than its *syn* counterpart. Increased steric hindrance of the *syn* alkene attributed to the methyl group inhibits the incoming metallacarbene. Special electronic effects can also have an effect on the selectivity of addition to the double bond (Figure 1.12).

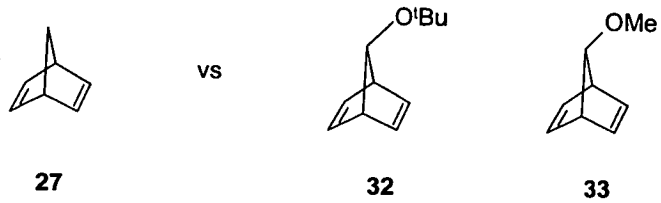
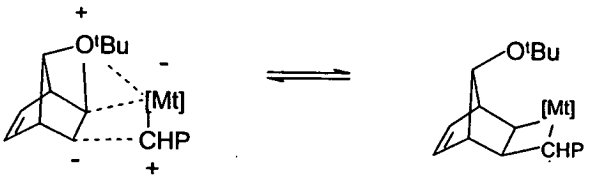


Figure 1.12

Normally the reaction would predominantly occur on the alkene unit *anti* to alkoxy group of **32** and **33**, on the basis of steric hindrance as described above (Figure 1.9). However, with a molybdenum based complex ($MoCl_5/Me_4Sn/Et_2O$) attack can be up to 50% on *anti* double bond due to the oxygen promoted assistance of the [2+2] metallacyclobutanation step, (Scheme 1.20).[63]



Scheme 1.20

1.5.3.3 Head-to-tail bias

The polymerisation of unsymmetrical monomers can lead to head/tail effects. The steric bulk of the substituent and its position relevant to the double bond are important factors, however, so is the nature of the double bond. (Figure 1.13).

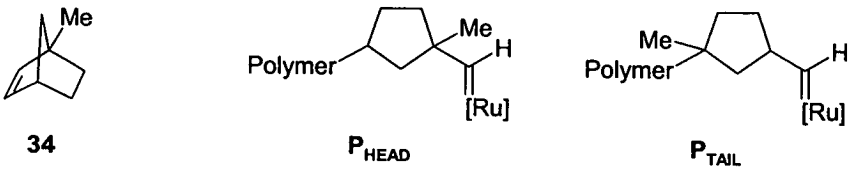


Figure 1.13

Rooney *et al.*[64, 65] investigated the head/tail effects of polymerising 1-methylnorbornene **34** with $RuCl_3$, $OsCl_3$ and **1**. Initiator **1** and $OsCl_3$ gave polymers which were strongly HT biased, whereas the corresponding polymer derived using $RuCl_3$ was completely non-biased (equal amounts of HH, HT, TH, TT). The difference in regioselectivity observed with the classical catalysts ($OsCl_3$/$RuCl_3$) was attributed to a difference in polarity of the Mt=C π bond. The ability of **1** to generate strongly biased HT poly**34** was attributed to the sterics of the PCy_3 ligands of the ruthenium carbene.[38] Thus, propagation by the tail ruthenium alkylidene ($\mathbf{P}_{TAIL}$) is strongly preferred by the incoming monomer resulting in a propensity for HT formation on both the *cis*- and the *trans*-forming cyclobutanation steps.

1.5.3.4 Tacticity

Due to the extent of research that has been carried out on polymer tacticity, it would be impossible to give a full review in this introductory section. Therefore, the reader is referred to an excellent review by *Hamilton*.[66] However, as this is an important area an example is given below.

Rooney, Ivin *et al.*[67] used optically active 5-substituted norbornenes to determine tacticity. Using this monomer, the dyads may have HH, TT, TH or HT structures (H = head, T = Tail) (Figure 1.14). The symbols HT and TH will be used to distinguish olefinic carbons on the head and tail side respectively of an HT structure.

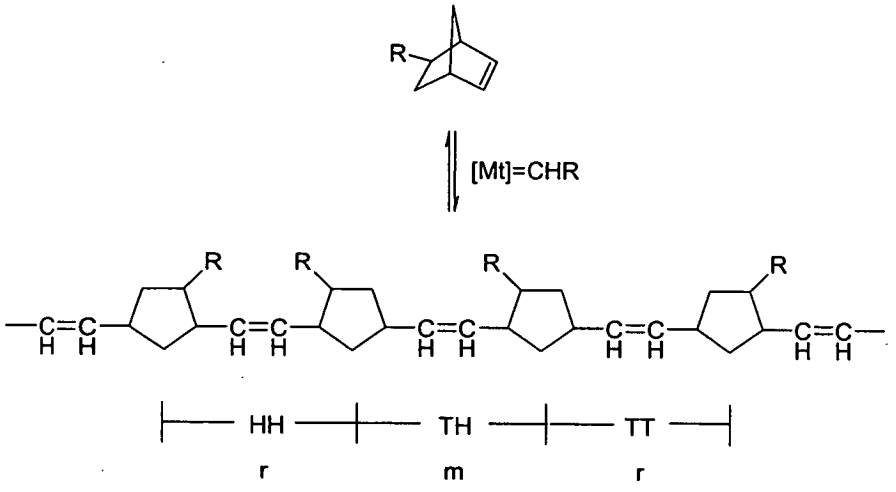


Figure 1.14

By polymerising firstly a racemic mixture of (±)-*exo*-5-methylnorbornene and then the resolved (+)-*exo*-5-methylnorbornene with $ReCl_5$ (σ_C = 1.0) and $RuCl_3$/cyclooctadiene (σ_C = 0.11) a full tacticity assignment was made.

1.6 Nitrile Oxide / isoxazoline chemistry

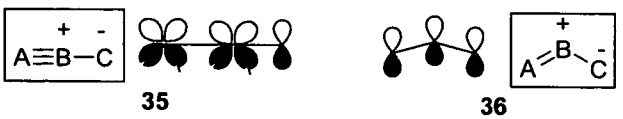
1.6.1 Introduction

The chemistry of 1,3-dipoles, first classified by Huisgen[68] is vast and has been comprehensively reviewed in the two volume monograph entitled '1,3-Dipolar Cycloaddition Chemistry' edited by *Padwa.*[69] Nitrile oxides, in their own right, are much researched and have been shown to be valuable tools in a wide range of syntheses from natural products to polymer chemistry. Only a brief overview of their chemistry will be given here. More detailed discussion can be found in 'The Nitrile Oxides' by Grundmann and Grünager,[70] 'Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis' by Torsell[71] in the review 'Recent Advances in Synthetic Applications of Nitrile Oxide Cycloadditions' by Kanemasa and Tsuge[72] and in the review '1,3-Dipolar Cycloaddition Reactions, Part 1' by Gallos.[73]

Nitrile oxides have an illustrious history. In 1800, Howard[74] prepared the explosive mercury fulminate. The correct structure of fulminic acid and its salts remained unknown for a long time and was the subject of much speculation. It had to wait for nearly 100 years for its elucidation. In 1899 Ley[75] suggested that fulminic acid was the N-oxide of formonitrile, i.e. the parent compound of nitrile oxides. The early knowledge of the chemistry of nitrile oxides can be attributed to contributions by Wieland in the early 1900's, Quilico and associates in the 1940's and Huisgen, who, in the 1960's, systematised comprehensively 1,3-dipolar reactions and arrived at a better understanding of their mechanism.[76] Over the years, this reaction has been developed into a generally useful method of five-membered heterocyclic-ring synthesis. Numerous possibilities for variation are available by changing the structure of both the dipolarophile and the 1,3-dipole.

1.6.2 1,3-Dipoles

The 1,3-dipole is defined as a three atom four π-electron system isoelectronic with heteroallyl anions but with neutral overall charge.[77] They can be divided into two structural types (Figure 1.15), the linear propargyl-allenyl type **35** and the bent allyl type **36**, which differ only in the presence or absence respectively of an additional orthogonal π-bond.



35 **36**

Figure 1.15

Over 18 different types of 1,3-dipoles have been used in dipolar cycloadditions. They can be divided into the two structural classes and then further divided and subdivided according to the elements occupying the A, B and C positions. This is illustrated,[78] together with some representative members of each group, in Table 1.3.

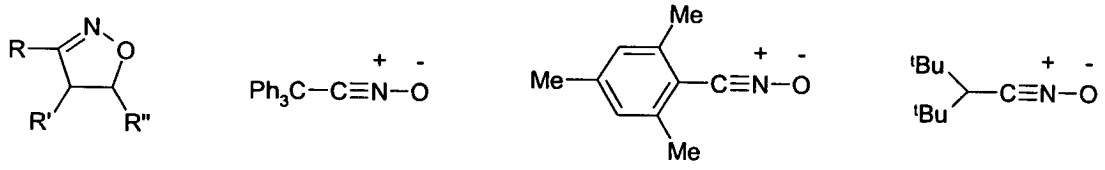
1,3-Dipoles

Propargyl-Allenyl Type		Allyl Type	
Nitrilium Betaines	Diazonium Betaines	Central N	Central O
$RC{\equiv}\overset{+}{N}{-}\overset{-}{X}$	$N{\equiv}\overset{+}{N}{-}\overset{-}{X}$	$R_2C{=}\overset{+}{N}R{-}\overset{-}{X}$	$R_2C{=}\overset{+}{O}{-}\overset{-}{X}$

	Propargyl-Allenyl type		Allyl type	
X	Nitrilium betaines	Diazonium betaines	Central N	Central O
CR_2	Nitrile ylides	Diazoalkanes	Azomethine ylides	Carbonyl ylides
NR	Nitrile imides	Azides	Azomethine imides	Carbonyl imides
O	Nitrile oxides	Nitrous oxide	nitrones	Carbonyl oxides
S	Nitrile sulphides	Dinitrogen sulphide	/	/

Table 1.3 - Common 1,3-dipoles.

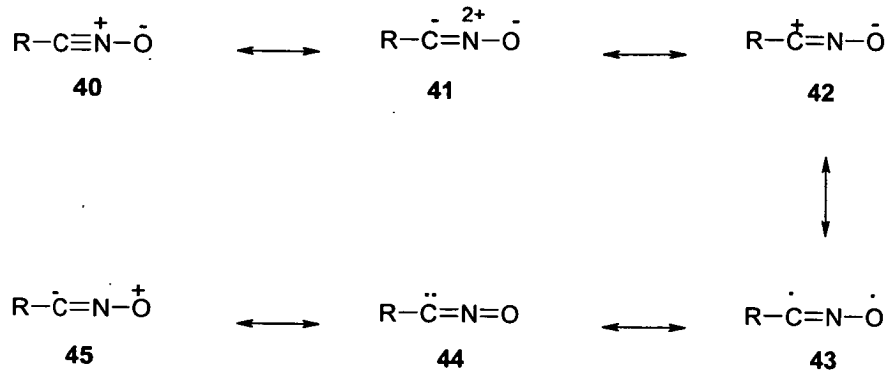
As this project is primarily concerned with the synthesis of 2-isoxazolines (4,5-dihydroisoxazoles) which are the cycloadducts of nitrile oxides and alkenes, the chemistry of nitrile oxides is discussed in more detail. Most nitrile oxides are transient species, which dimerise to 1,2,5-oxadiazole-2-oxides (furoxans), although there are a few examples of isolable nitrile oxides such as **37**,[79] **38**[80] and **39**[81] which are resistant to dimerisation, an effect attributable to steric factors (Figure 1.16). For synthetic purposes, nitrile oxides are therefore generated *in situ* in the presence of the dipolarophile.



2-Isoxazoline **37** **38** **39**

Figure 1.16

Nitrile oxides **40** are members of the nitrilium betaine class of 1,3-dipoles and are best represented as a hybrid of resonance forms **41-45**, depicted in Scheme 1.21.

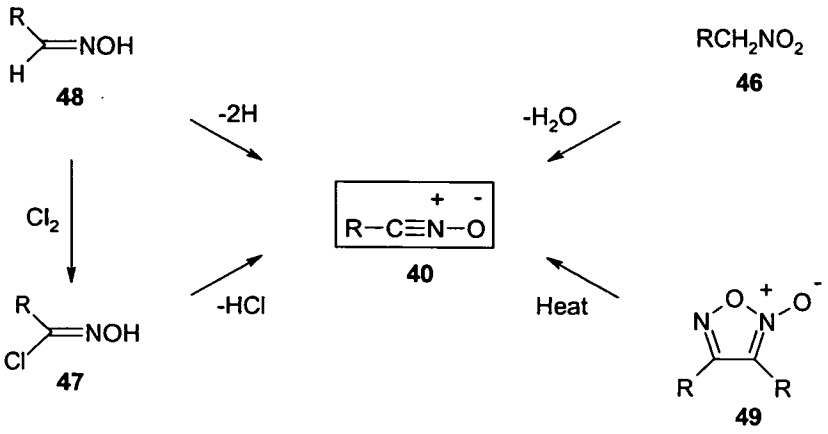


Scheme 1.21

1.6.2.1 Generation of nitrile oxides

There are four common precursors to nitrile oxides as outlined in Scheme 1.22. A popular entry point to nitrile oxides is the Mukaiyama dehydration[82] of primary nitro compounds **46** using an isocyanate as the dehydrating agent and a catalytic amount of base. An alternative route involves the dehydrohalogenation of hydroximoyl halides **47**, commonly carried out by treatment with a base, usually triethylamine[83] or potassium fluoride.[84] Thermal generation is also possible by heating in an inert solvent.[85] The conversion of aldoximes **48** to nitrile oxides is another common strategy. The reaction often involves *in situ* synthesis of the hydroximoyl halides using sodium hypochlorite,[86] conversion of the aldoxime to the hydroximoyl chloride using chlorine gas[87] or milder methods such as using NCS[88] followed by base catalysed dehydrohalogenation.

A less common route to nitrile oxides is thermal cycloreversion of the furoxan dimers **49**.[89] This often requires temperatures greater than 200 °C. However, for ring strained furoxans (e.g. trimethylenefuroxan)[90] and furoxans with bulky substituents, such as di-t-butyl(2-methylsiloxyprop-2-yl) furoxan, cycloreversion is more facile taking place at 120-165 °C.[91]



Scheme 1.22

1.6.3 1,3-Dipolar cycloaddition reactions

The most important reaction undertaken by 1,3-dipoles, from a synthetic point of view, is a [3+2] cycloaddition to a dipolarophile, a multiple-bond containing system, to form a five membered heterocycle, (Scheme 1.23).

D=E = Alkene, imine, carbonyl, nitrile, alkyne, etc.

Scheme 1.23

Although the mechanism of such 1,3-dipolar cycloadditions has been an area of controversy, and the conclusions drawn from the theoretical calculations have tended to conflict, it is now generally accepted that,[92] under normal conditions, 1,3-dipoles react via a concerted, but not necessarily synchronous, one-step process. Huisgen proposed that the reaction proceeds via a parallel-plane orientation complex, which permits π-orbital overlap of reactants and subsequent formation of the new σ-bonds of the product.[93]

Stepwise diradical[94] and stepwise zwitterionic mechanisms[95] have also been considered. However, the observed retention of reactant stereochemistry, the negligible solvent effect and the large negative entropy of activation of such reactions provide strong evidence in favour of the concerted process.[96]

1.6.4 Frontier molecular orbital theory of 1,3-dipolar cycloadditions

The regioselectivity of 1,3-dipolar cycloaddition reactions have also been interpreted by FMO theory. The magnitude of the orbital coefficients in the 1,3-dipoles and dipolarophiles vary with substituent. As a consequence of the principle of maximal orbital overlap[97] the major regioisomer results from the interaction of orbitals of matched size, i.e. large-to-large and small-to-small (Figure 1.17). Steric factors can also play an important role, and orbital control may be over-ridden in intramolecular cycloadditions where sterically it may not be possible for the preferred overlap to take place.

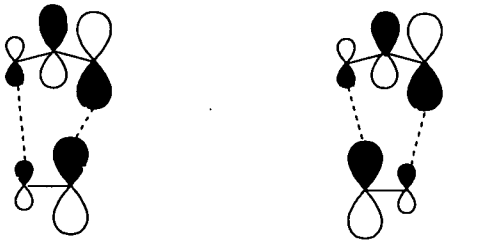
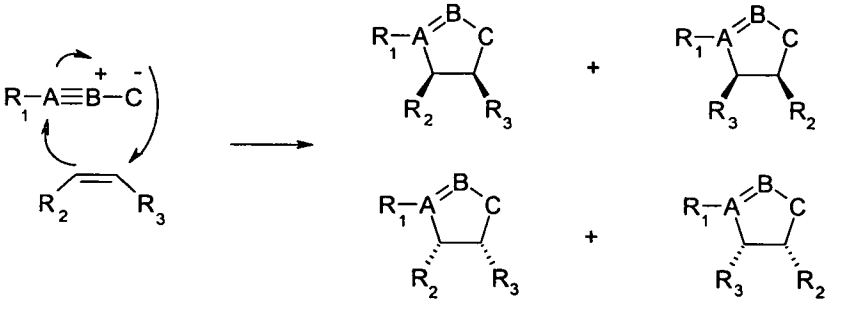


Figure 1.17

1.6.4.1 Stereochemistry

The addition of 1,3-dipoles to dipolarophiles is a concerted process and proceeds with the retention of dipolarophile stereochemistry. When the two faces of the dipolarophile are open to attack, two stereoisomers for each regioisomer are produced (Scheme 1.24). The stereochemical control that is seen in 1,3-dipolar cycloadditions is influenced by steric factors, with the dipole generally attacking from the least hindered face.



Scheme 1.24

1.7 1,3-Dipoles in polymer chemistry

1.7.1 Introduction

1,3-Dipolar cycloaddition reactions are suitable for use in polymer synthesis, since a wide range of difunctional monomers can be synthesised and many of the dipolar cycloadditions are achieved in good yield. Stable polymer production is enhanced by the fact that five membered heterocycles with aromatic character are often the products of such 1,3-dipolar addition reactions.

Macromolecules bearing pendant isoxazole (or isoxazoline) residues could show interesting physical and chemical properties owing to the polarity, basicity and co-ordinating power of such a ring. Besides, the ring's characteristic reactivity may allow it to be transformed into non-cyclic 1,3-difunctional systems, e.g. β-hydroxy ketones and γ-amino alcohols. The isoxazole nucleus could be a useful protecting group in the synthesis of polyfunctional polymers.[98] There are three ways in which nitrile oxide / cycloaddition chemistry can be used in polymer synthesis.

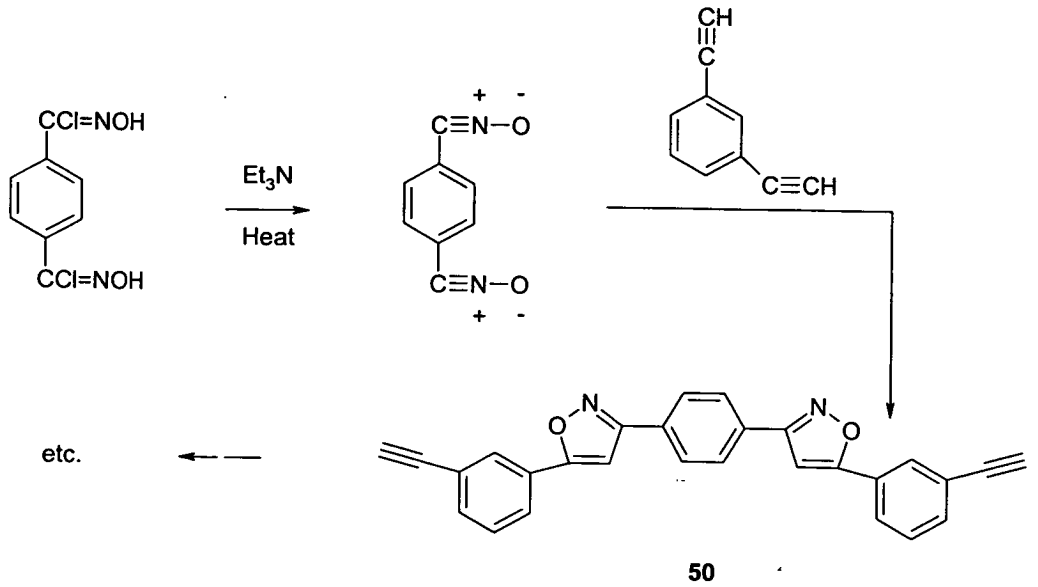
a) 1,3-Dipolar cycloaddition for polymerisation step.

b) 1,3-Dipolar cycloaddition to modify an unsaturated polymer.

c) Polymerisation of vinyl substituted heterocycles incorporating C=N-O formed via cycloaddition reactions of nitrile oxides.

1.7.2 1,3-Dipolar cycloaddition as polymerisation step

Thermally stable polyisoxazoles **50** have been produced by the reactions of bis-nitrile oxides with bis-acetylenes[99] (Scheme 1.25). The difunctional nitrile oxides were usually generated by the dehydrochlorination of the hydroximoyl chlorides. Overberger and Fujimoto[100] prepared polymers containing isoxazole rings by treating 1,3-diethynylbenzene with terepthalonitrile di-N-oxide in benzene. The polymer, which was stable in air below 400 °C, was obtained in high yields. These results suggested that the isoxazole ring has good thermal and oxidative stability.



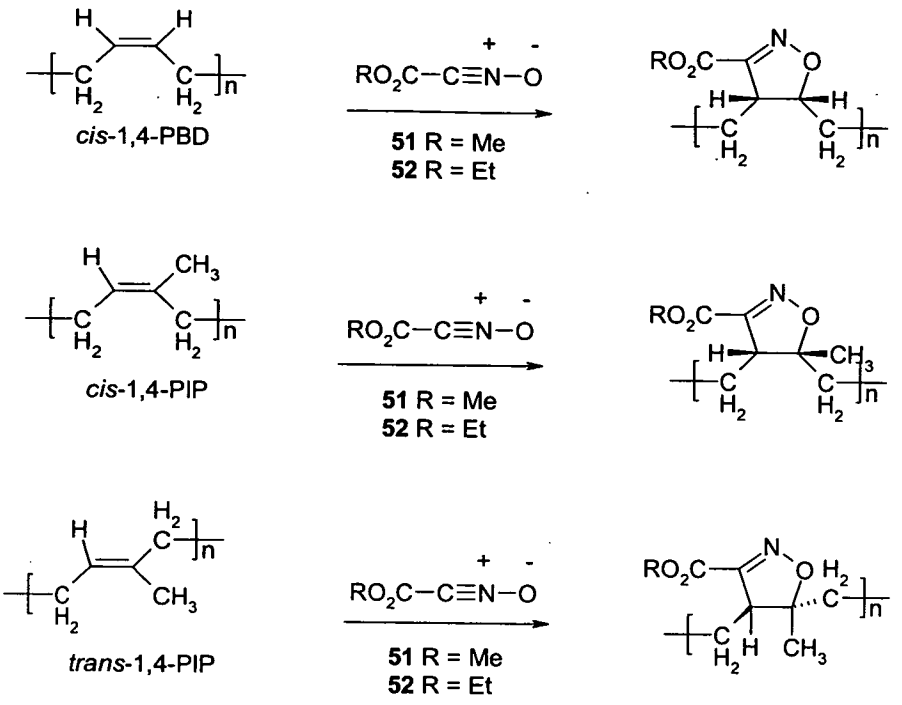
50

Scheme 1.25

1.7.3 1,3-Dipolar cycloadditions to unsaturated polymers

Previous work in the group[101] investigated the addition of nitrile oxides **51** and **52**, generated by thermal dehydrohalogenation from the corresponding hydroximoyl chlorides, to *cis*-1,4- and *trans*-1,4-polyisoprene (PIP) and to *cis*-1,4-polybutadiene (PBD) (Scheme 1.26).

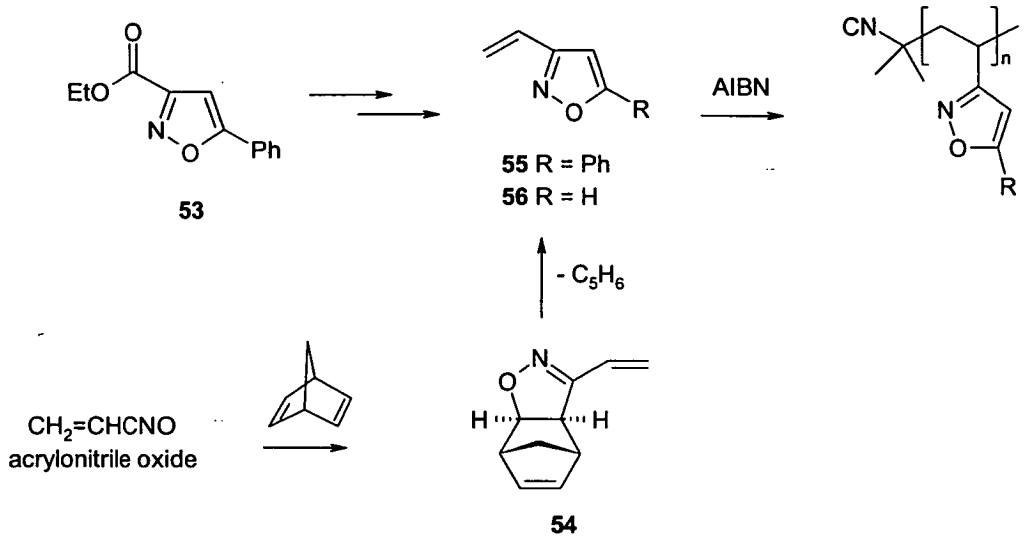
The products were examined by ^{1}H and ^{13}C NMR spectroscopy by comparison with the cycloadducts from the reaction of the same nitrile oxides with the simple alkenes. These cycloadducts were selected as models for the unsaturation present in the PBD and PIP. The degree of modification of the polydiene depended on the initial ratios of [alkene]:[hydroximoyl chloride] and the substituent in the corresponding nitrile oxide. For PBD, degrees of modification as high as 86% were observed. The corresponding figure for PIP was lower (66%), an effect attributed to steric factors. ^{13}C NMR spectroscopy confirmed the presence of both the isoxazoline rings and the pendant ethoxycarbonyl and methoxycarbonyl groups.



Scheme 1.26

1.7.4 Polymerisation of 3-vinylisoxazole

Paton, Tout *et al.*[102] investigated the synthesis of 3-vinylisoxazoles as possible monomers for free radical polymerisation. The first of the two approaches studied entailed the synthesis of 3-vinyl-5-phenylisoxazole **55** from reduction of 3-ethoxycarbonyl-5-phenylisoxazole **53** to the aldehyde followed by Wittig olefination. The second route involved the cycloaddition of acrylonitrile oxide to norbornadiene (NBD) to yield the isoxazoline adduct **54** which was subjected to flash vacuum pyrolysis (FVP) to yield the 3-vinylisoxazole **56**. The adducts **55** and **56** were then polymerised under free radical conditions (using AIBN as the initiator) (Scheme 1.27). Copolymers of **55** with styrene, vinyl acetate and methyl methacrylate were also prepared under free radical conditions.



Scheme 1.27

The work reported in this thesis provides another method in which 1,3-dipolar cycloaddition chemistry can be used in polymer chemistry. Novel aspects of this work will be the functionalisation of unsaturated polymers prepared by olefin metathesis using 1,3-dipolar-cycloaddition chemistry and the preparation of novel isoxazolino-/isoxazolidino-fused NBEs as novel monomers for ROMP.

1.8 Recent applications of ring opening metathesis polymerisation

1.8.1 Introduction

The ability to synthesise functionalised polymers is dependent on the monomer and the tolerance of the initiator to its functionality. Recent developments in catalyst systems pioneered by Schrock and Grubbs have seen an array of complexes able to polymerise monomers with varying functionality. Monomers are generally based on functionalised norbornenes (Figure 1.18), which are prepared via the Diels-Alder reaction of cyclopentadiene or furan and a functionalised dieneophile. Norbornene is a strained ring system which is in many ways ideally suited for exploitation in polymer synthesis. Among the features of this class of compound are:

- Ease of synthesis by Diels-Alder reactions of cyclopentadiene and furan.
- Conformational rigidity that results in well-defined locations for substituents.
- The presence of alkene bonds in the resulting polymer where further chemistry can be carried out.
- High reactivity due to the strain energy of approximately 100 kJ/mol (NBD = 110 kJ/mol, compared with 27 kJ/mol for cyclopentene).

Figure 1.18

1.8.2 Functionalised polymers

The classical catalyst systems (*e.g.* WCl_6/SnR_4) were the first to be employed for the polymerisation of functionalised NBEs as outlined in Section 1.8.2.1. More recently the highly active Schrock alkylidene **3** and the functional group tolerant Grubbs first generation initiator **1** have enabled the synthesis of polymers with numerous functional groups resulting in a range of polymeric structures with control over polymer microstructure such as *cis/trans* content and tacticity. Due to the advent of these well-defined ROMP initiators, functionality incorporated into the polymer backbone can be very diverse.

1.8.2.1 Functionalised polymers using classical catalyst systems

Examples of functionalised polymers prepared the using classical catalyst systems are as diverse as high temperature polymers ($WCl_6/SnMe_4$),[103] hydrogels ($OsCl_3$),[104] tubular polymers bearing monohedron tapered side groups ($RuCl_3.xH_2O$)[105] and pentafluorophenyl-imide functionalised polymers (WCl_6, $MoCl_5/SnMe_4$) [106] as outlined in Figure 1.19.

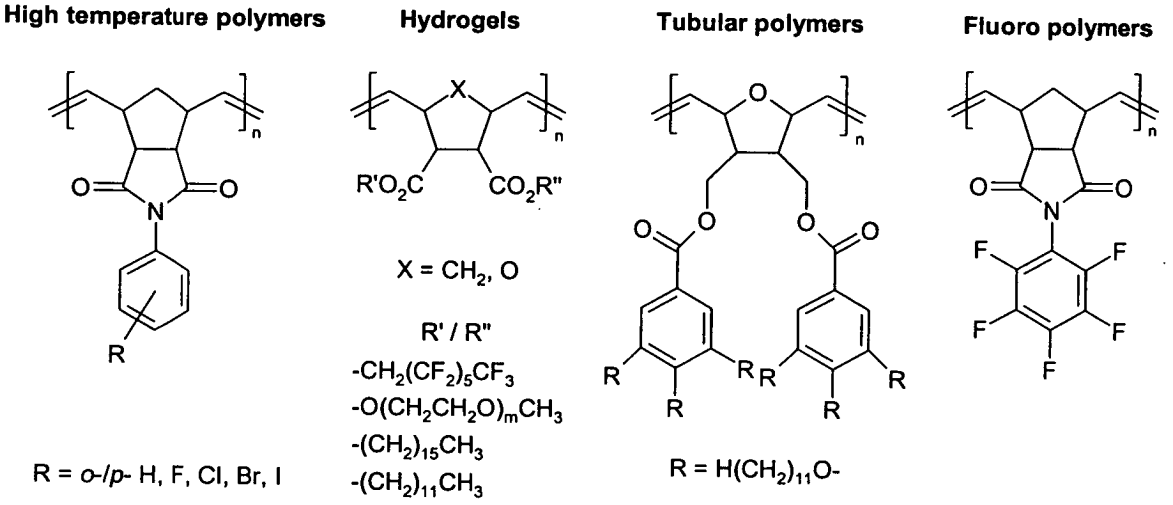


Figure 1.19

1.8.2.2 Functionalised polymers using the Schrock initiators

The Schrock initiator **3** has also been used to synthesise polymers with diverse functionality such as comb polymers, polyelectrolytes and carbohydrates[109] (see Section 1.11.2) as outlined in Figure 1.20. The comb polymer was prepared by synthesising oligomers of norbornene with **3** which were end capped with norbornene through an ester linkage. Polymerisation of the NBE functionalised polynorbornene produced the macromonomer in almost quantative yield with low molecular weight distributions (PDI = 1.03-1.17).[107] Polyelectrolytes were prepared by the polymerisation of norbornene dicarboxylic acid and 7-oxanorbornene dicarboxylic acid that contain a suitable protecting group (tetrahydropyran and 2-methylpropenoyloxy). The resulting polymers were deprotected and treated with glycidyl methacrylate to yield the polyelectrolyte which was used as a component in dental adhesives.[108]

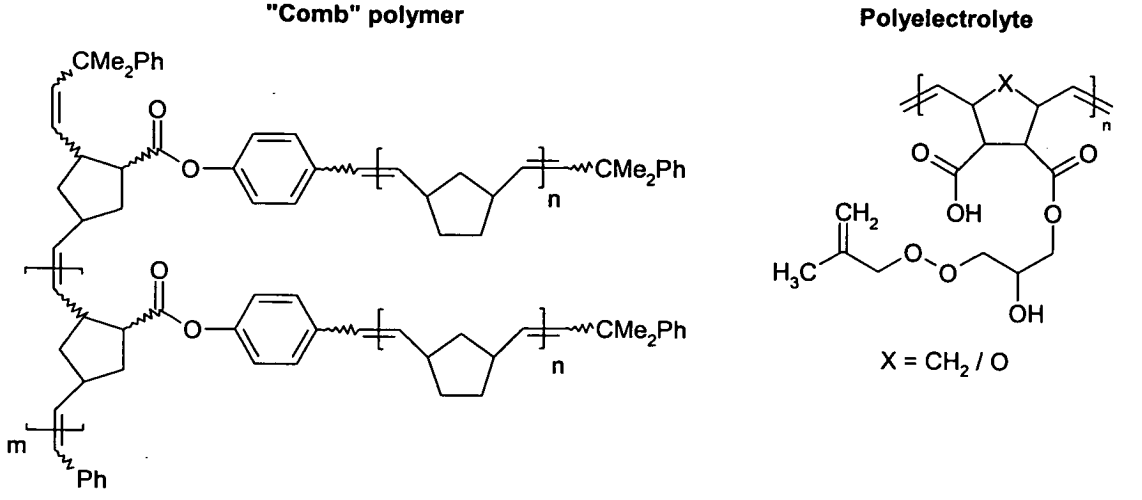


Figure 1.20

1.8.2.3 Functionalised polymers using Grubbs initiator 1

The ruthenium carbene **1** has been used to generate an array of polymers with diverse functionality (including biologically active residues as outlined in Section 1.9.1). Monolithic rigid rod materials,[110] fire resistant polymers,[111] telechelic polymers[112] and side chain liquid crystal polymers.[113] are illustrations of functionalities tolerant of the ruthenium alkylidene **1** as outlined in Figure 1.21.

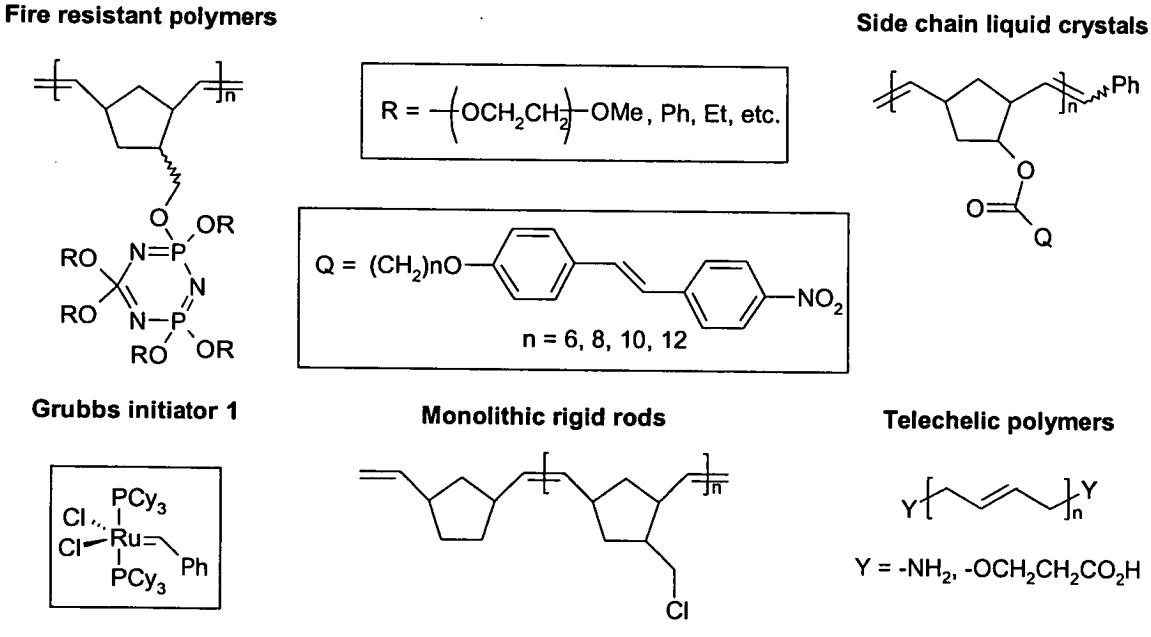


Figure 1.21

1.8.2.4 Functionalised polymers using Grubbs initiator 2

The second generation ruthenium complex **2** has been used recently by Sleiman *et al.*[114] to generate adenine-containing homopolymers and b lock copolymers via ROMP. These were synthesised as potential biomolecular sensors and DNA delivery agents (Figure 1.22).

Adenine-containing homopolymers and block copolymers

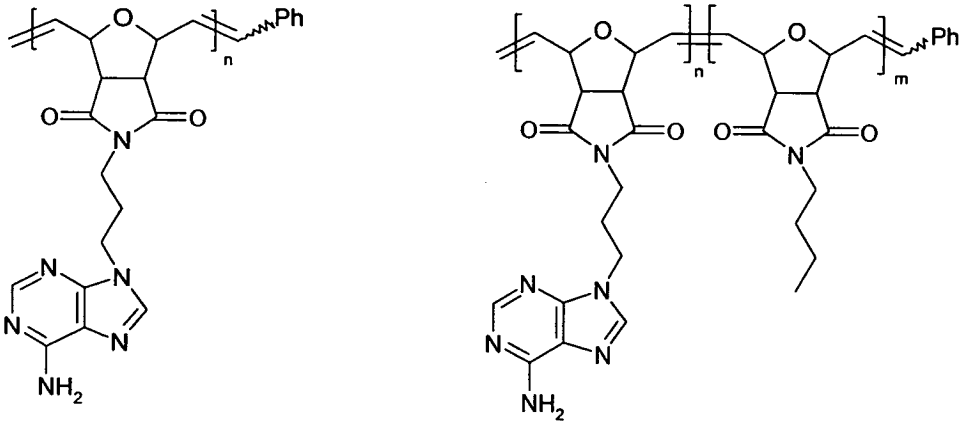
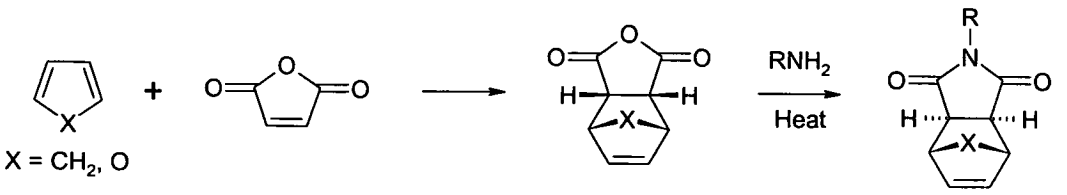


Figure 1.22

1.9 Applications of functionalised polymers for biological applications

1.9.1 Current biologically active polymers prepared via ROMP

The well-defined ruthenium carbene **1** has been used to polymerise a variety of functionalised norbornenes via ROMP. Monomers based on maleimide fused NBEs can be easily synthesised from the Diels-Alder reaction between maleic anhydride and cyclopentadiene or furan. Heating the resulting endo-cycloadduct with the corresponding amine affords the *exo*-maleimide fused norbornene as shown in Scheme 1.28.



Scheme 1.28

Many research groups are currently interested in polymers functionalised with biologically relevant side groups synthesised via ROMP. These include carbohydrates,[115] peptides,[116] nucleic acid bases[117] and even penicillin functionality[118] incorporated onto the polymer backbone (Figure 1.23). The synthesis of these biorelevant materials has been facilitated by the functional group tolerance of ruthenium carbene 1. In addition, this initiator promotes living polymerisation resulting in good control over the molecular weight (M_w, M_n), molecular weight distribution (MWD) and alkene geometry of approximately 70% *trans* content.

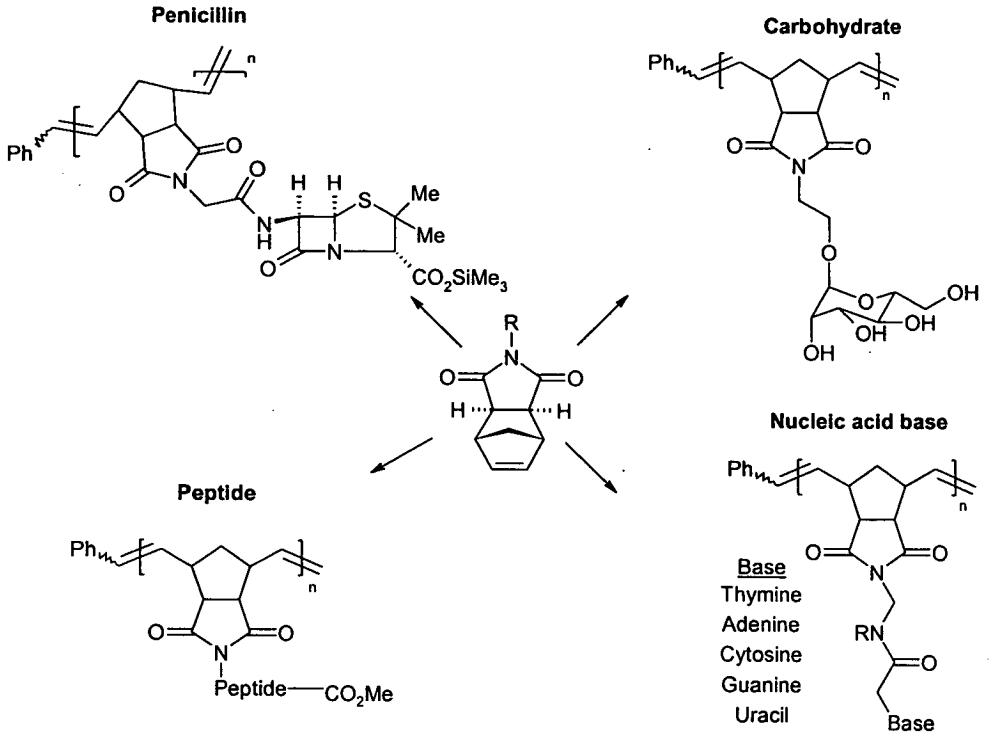


Figure 1.23

Recently, Nguyen *et al.*[119] have developed a series of anti-cancer homo- and co-polymers via ROMP. NBE derivatives containing indomethycin, chlorambucil and 2-(4-aminophenyl)-6-methylbenzothiazole, (residues of known anti cancer activity) were readily polymerised using 1 (Figure 1.24). Random and block copolymers of the NBE derivatives were also prepared.

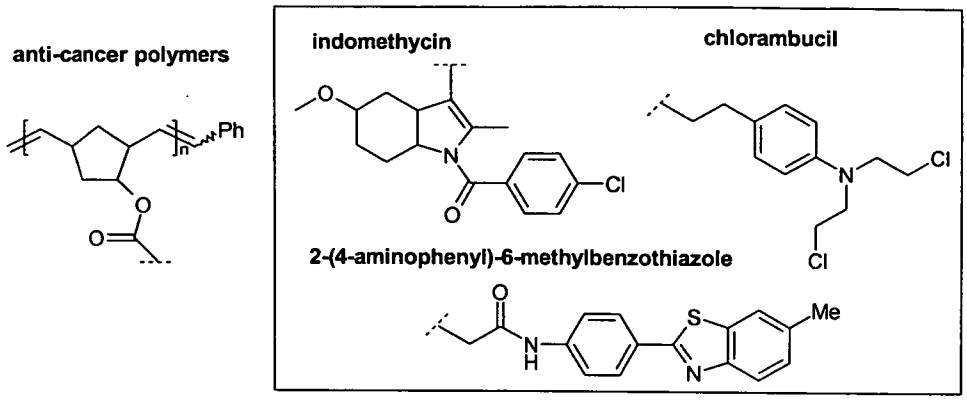


Figure 1.24

Arimoto *et al.*[120] synthesised a multivalent array of vancomycin using the ruthenium initiator 1 (Figure 1.25). The reaction yielded a polymer (n = 10, by SDS-PAGE electrophoresis) and this was shown to have a significant (up to 60 fold) enhancement of antibacterial activities against vancomycin-resistant enterococi compared to vancomycin itself.

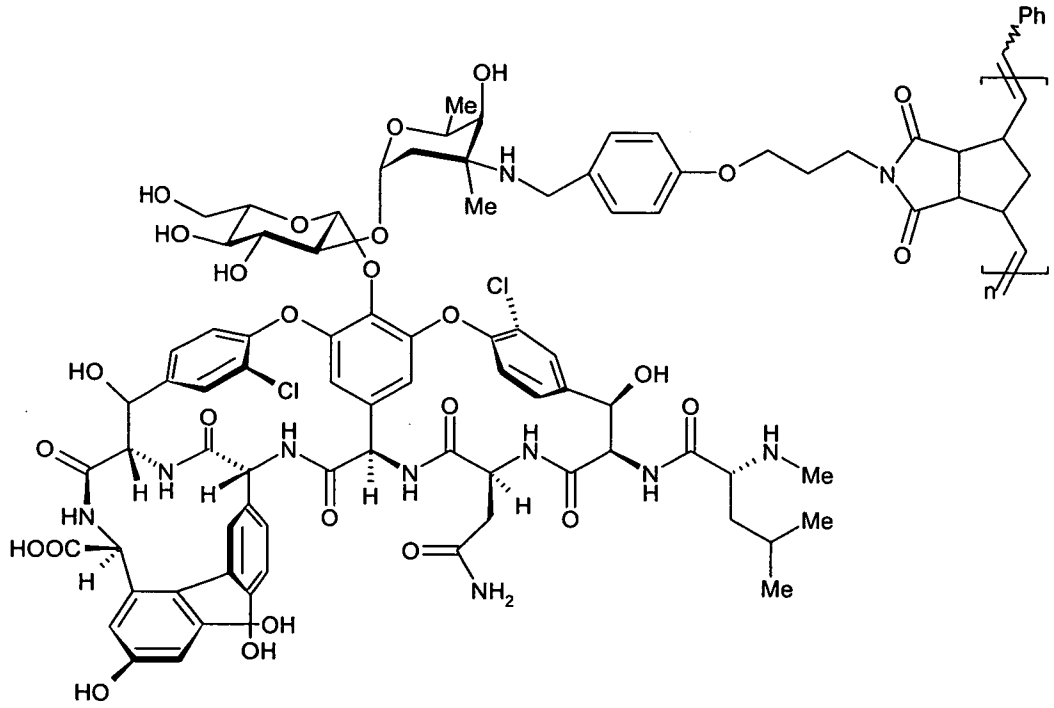


Figure 1.25

1.9.2 Origin of carbohydrate functionalised polymers, "glycopolymers"

The current interest of glycobiology, the study of the role of carbohydrates in the immune system, in tissue repair and in fighting infection, has resulted in a renaissance in carbohydrate biology and

chemistry. As a result, several synthetic analogues[121] have been prepared to mimic the complex assemblies found on cell surfaces that can modulate cellular interactions and are under development as therapeutic agents. In addition, a number of sophisticated and sensitive analytical techniques have been developed (e.g. Surface Plasmon Resonance Spectroscopy, Immunofluorescence microscopy, Fluorescence Resonance Energy transfer) to enable the study of cell carbohydrate functions and biological interactions involving saccharides.

Recognition processes involving carbohydrate-protein interactions are key to numerous biological processes. The proteins involved, generically named lectins, are most frequently found on cell surfaces. They have the ability to bind specifically and non-covalently to carbohydrates.[122] The mechanism of the carbohydrate-lectin interaction and the structures of the glycopolymers involved in these recognition events are still largely unknown. In consequence, carbohydrate based polymers, "glycomimics" are emerging as a well-defined tool for investigating glycopolymer-protein interaction.[123]

1.9.3 Synthetic glycopolymers

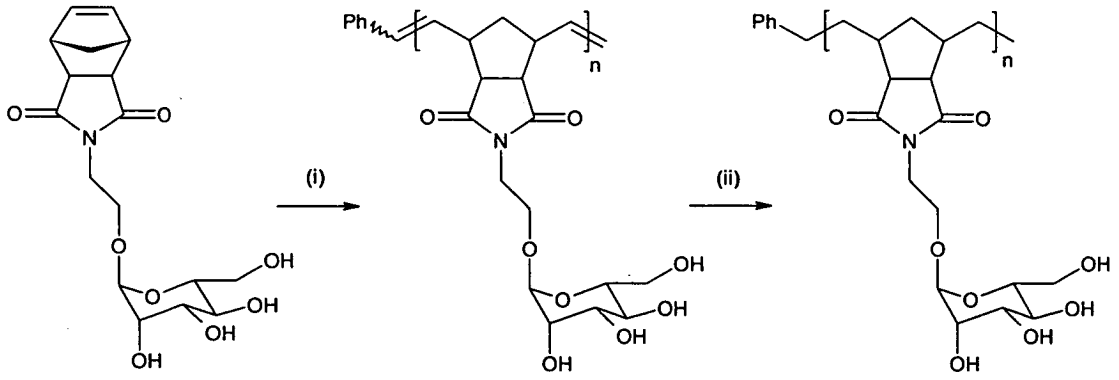
The term glycopolymer is still not clearly defined. For the purposes of this thesis, glycopolymers will be defined as synthetic polymers containing sugar moieties as pendant groups (although it can also mean synthetically modified natural sugar based polymers). In a review of synthetic glycopolymers, Haddleton *et al.*[124] discussed the syntheses of pendant carbohydrate-carrying linear polymers. Saccharide containing polymers that have been tailored to investigate diverse recognition processes have been synthesised by free radical polymerisation, ionic polymerisation, ring-opening polymerisation (ROP), controlled radical polymerisation, nitroxide-mediated radical polymerisation, copper-mediated living radical polymerisation (CMLRP) and more relevantly to this thesis, via ROMP.[124]

1.9.4 Glycopolymers syntheised by ROMP

In hindsight ROMP was an excellent candidate for the preparation of carbohydrate functionalised polymers as it has the potential for control of molecular weight, structure and density of carbohydrate substituents. Due to the living nature of initiators such as **1**, the preparation of copolymers for the synthesis of materials for selective immobilisation of different cell types is possible. Finally, due to the excellent functional group tolerance of the Grubbs ruthenium benzylidene **1**, the preparation of functionalised polymers is possible.[2] The following examples illustrate how synthetic carbohydrate functionalised polymers synthesised via ROMP have the potential to allow understanding and control of a range of biological processes.

1.9.4.1 Cell agglutination inhibitors of Concanavalin A.

Structural studies of lectins reveal that many possess multiple saccharide binding sites separated by large distances (typically 30-70 Å), which can be spanned readily with polymeric backbones. Thus multivalent saccharide bearing polymers (neoglycopolymers) were synthesised by Kiessling *et al.*[115] as cell agglutination inhibitors of Concanavalin A (Con A). The Con A tetramer has two saccharide binding sites on each face, and the orientation of these two sites allows Con A to engage in multivalent interactions.



57 **58** **59**

Reagents: (i) [Ru]=CHPh **1**, DTAB, H_2O/DCE; (ii) $TsNHNH_2$, H_2O, 100 °C

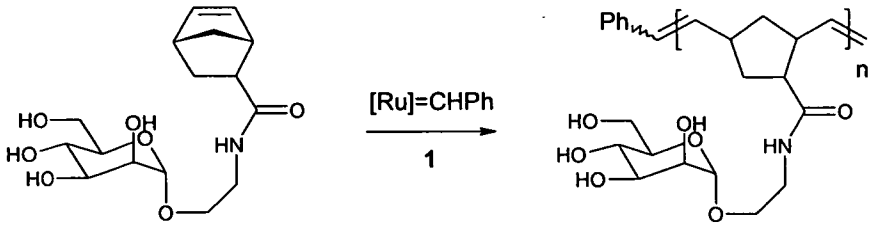
Scheme 1.29

Glycopolymers containing mannose **58** and galactose epitopes, (av DP = 10, 25, 143) were synthesised via ROMP of the corresponding norbornenyl monomer **57** using **1** (Scheme 1.29). The concentration of mannose residues required to inhibit Con-A promoted erythrocyte agglutination was determined for each structure. Kiessling *et al.* studied the dependance of Con A binding on the lengths of neoglycopolymers. A plateau in the hemagglutination inhibition was reached with polymer n = 52 or higher. To provide an insight into the impact of polymer backbone flexibility on activity, the neoglycopolymers were reduced to produce a series of polymers with saturated backbones **59**. Despite the differences in backbone flexibility, the most potent ligands in each series had approximately the same efficacy.

1.9.4.2 Cell aggregation by scaffold receptor clusters

The aggregation of cells by lectins or antibodies is important for biotechnological and therapeutic applications. Lectins however, due to their quaternary structure are limited in their ability to cluster cells. By increasing the number of ligand binding sites e.g. by arranging the lectins on a polymer

backbone, the clustering of cells would be possible. Kiessling *et al.*[125] proposed the synthesis of a series of mannose functionalised neoglycopolymers **61** via ROMP as potential scaffolds to assemble multiple copies of the tetravalent protein Con A noncovalently, (Scheme 1.30). Thus norbornenes incorporating mannose epitopes **60** were oligomerised (av DP = 21, 38, 65, 142) using the Grubbs initiator **1**.



60 **61**

Scheme 1.30

The ability of Con A scaffolded clusters to aggregate cells of a T cell leukaemia line (Jurkat) was tested.[125] Con A was added to fluorescently labelled Jurkat cells and cell aggregation occurred (visualised by fluorescence microscopy). However, upon the addition of a pre-mixed s olution of neoglycopolymer **61** (n = 142) and Con A, an enhancement of cell aggregation of 60% over Con A alone was measured. Recently, receptor clustering has been investigated using random carbohydrate functionalised copolymers. This is discussed in Section 1.11.3.

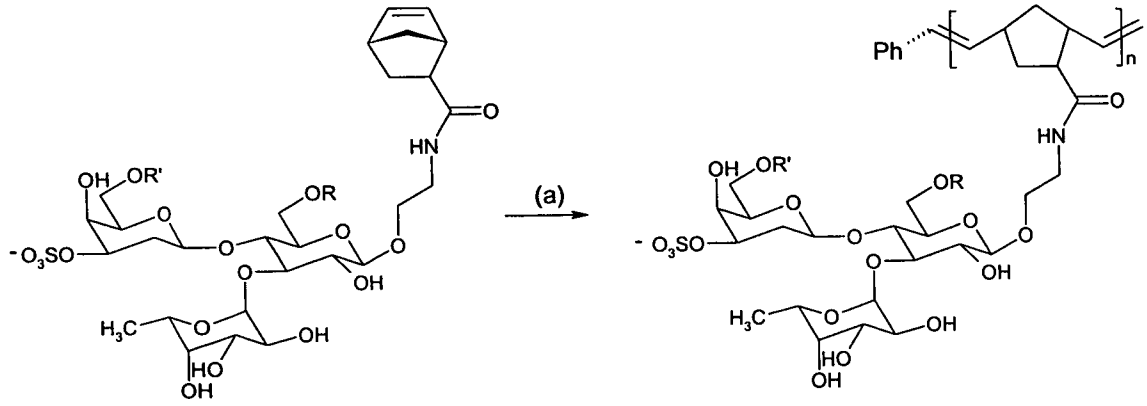
1.9.4.3 Glycopolymers as anti-inflammatory agents.

Carbohydrate thereapeutics have been prepared to treat a variety of disorders caused by excess inflammation, including arthritis, allergies and the tissue damage (reperfusion injury) suffered following lung injury or heart attack.[126] Recently Kiessling *et al.*[127] prepared glycopolymers (Scheme 1.31) bearing analogues of sialyl Lewis X (sLe^x) which is known for its role in inflammatory responses.[128] The recognition of sLe^x by E-selectin (present on the walls of blood vessels) encourages white blood cells (leukocytes) to move into sites of injury or infection from the bloodstream, via a three step migration.

The blocking of this migration with soluble sLe^x mimics is seen as a way of counteracting excess inflammation. In addition, sLe^x is believed to be decisive in the migration of cancer cells through the body and subsequent initiation of secondary tumours (metastasis).[129]

Synthetic carbohydrate and glycoprotein mimics, prepared from the oligomerisation of norbornene monomers displaying sulphated tri-saccharide residues **62** and **63**, were designed to investigate their L-selectin inhibitory properties under static and flow conditions.

The multivalent glycoprotein analogues **64** and **65** (n = 15) were tested for their ability to inhibit the binding of L-selectin to immobilized heparin (a polysulfated oligosaccharide which is known to bind L-selectin in a calcium dependent manner) in a static binding inhibition assay. The results showed that the neoglycopolymers **64** and **65** had an 80-fold increased inhibitory potency over sLe^x. **64** and **65** were then tested in a cell rolling inhibition assay with sLe^x. The mimics were tested for their ability to block the L-selectin-mediated rolling on GlyCAM-1 (immobilised L-selectin ligand). **65** was approximately 1000-fold more potent than sLe^x at inhibiting L-selectin-mediated rolling. Surprisingly, **64** showed no inhibition of rolling even at increased concentrations. This result proves that the position of the substituents on sLe^x has a profound effect on the activity of the corresponding glycopolymer.



62 R' = SO_3Et_3NH, R = H

63 R' = H, R = SO_3Et_3NH

64 R' = SO_3Na, R =H

65 R' = H, R = SO_3Na

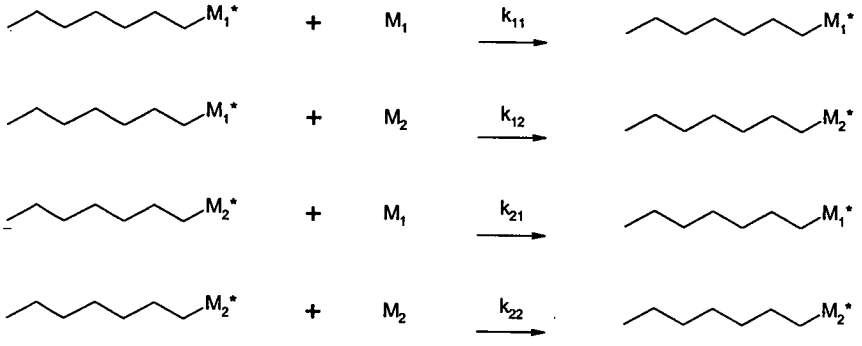
Reagents: (a) [Ru]=CHPh **1**, DTAB, DCE, pH 6.0 bis-tris, 60 °C

Scheme 1.31

1.10 Aspects of copolymerisation

1.10.1 Introduction

Copolymerisation is the polymerisation of two different monomer units of which the distribution can be predefined by experimental procedures. As there are two different monomers present in the feed stock (M_1 and M_2) there are two different propagating species present (M_1* and M_2*) resulting in four distinct propagation reactions. M_1 can react with a polymer chain end derived from an M_1 unit or from an M_2 unit and likewise for M_2; these permutations are summarised in Scheme 1.32 where k_{11}, k_{12}, k_{21} and k_{22} are the rate constants of the propagation reactions.



Scheme 1.32

^{13}C-NMR spectroscopy can be used to characterise the copolymer. There are five aspects of the copolymer that that must be considered, namely the composition of the copolymer and four layers of microstructure which will all be considered in turn.

1.10.2 Composition of copolymers

The composition of the copolymer is a measure of the proportion of each monomer unit in the copolymer. This information can easily be obtained from the ^{13}C NMR spectrum of many copolymers and gives an indication of the reactivity of the catalyst used. It has been previously seen that most catalysts regardless of their reactivity will polymerise strained olefins such as norbornene;[130] however to polymerise less strained monomers such as cyclopentene or cycloheptene a more active catalyst is required. Therefore the copolymerisation of two monomers with differing strain energies gives an indication of the catalyst activity from their incorporation in the copolymer. A less reactive catalyst will incorporate a large amount of the more reactive

monomer relative to the less reactive monomer. A more reactive catalyst is able to polymerise more of the less reactive monomer and incorporate it into the copolymer.

The first layer of microstructure that can be determined from the ^{13}C-nmr spectrum of the unsaturated copolymer is the distribution of the two monomer units along the polymer chain. This will indicate whether the monomers have been polymerised in a random, blocky or alternating manner. The distribution of units (alternating, random or blocky) along the polymer chain can be quantified by the r_1r_2 parameter.

1.10.2.1 Quantifying the distribution of dyads in a copolymer

The distribution of dyads in a copolymer can be shown in graphical form by plotting the mole fraction of one of the two monomers in the feed stock (f_1) against the proportion of that unit, derived from the ^{13}C-NMR spectrum, in the copolymer (F_1). This method is particularly useful if the copolymer is highly ordered, in other words almost perfectly alternating or blocky or if the copolymer is random. The plots that result from copolymers with each of the distributions are shown in Figure 1.26 and examples of each are given in table 1.4.

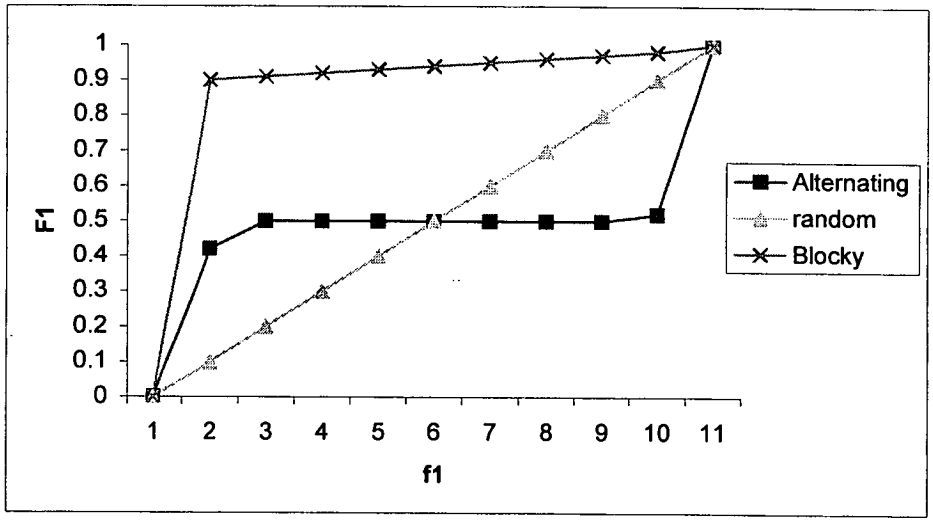


Figure 1.26

A quantative measurement of the distribution of the dyads along the chain can be obtained from the product of the reactivity ratios.[131]

r_1r_2	Copolymer distribution	Example
<1.0	Alternating	Styrene / Maleic anhydride
1.0	Random	Ethene / Vinyl Acetate
>1.0	Blocky	Styrene / Butadiene

Table 1.4 – Dependence of distribution on r_1r_2.

The yield of copolymer is of the utmost importance when considering the distribution of dyads. If any meaningful conclusions are to be drawn from copolymerisation experiments it is necessary to use only polymerisations which are as low as yield as possible. One monomer may be polymerised preferentially as the yield of the reaction increases the ratio of the monomers present in the solution changes. If this ratio changes by a significant amount then at higher yield the resulting copolymer is that produced under differing reaction conditions to those specified at the start of the reaction. A yield of 10% is thought to be the maximum at which copolymerisation results can be considered reliable.[132]

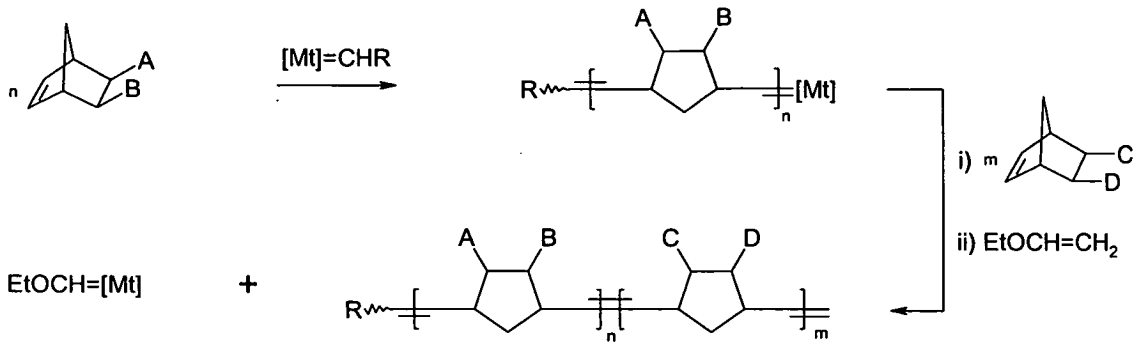
1.10.3 Copolymer Stereochemistry

Copolymer stereochemistry is governed by the same principles as outlined in Section 1.5. However, in almost all cases the tacticity of copolymers cannot be determined due to complexities of the spectra and this type of analysis tends to be reserved for homopolymers.

1.11 Synthesis of copolymers

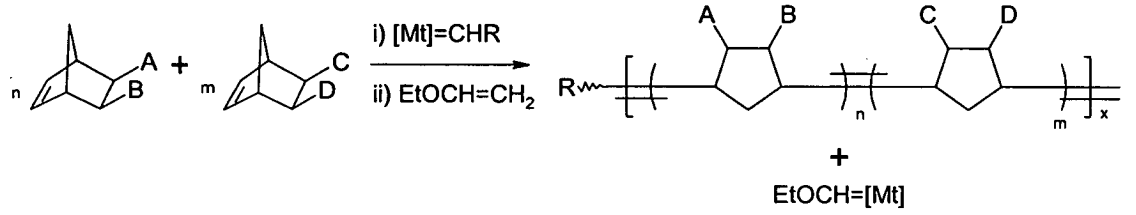
1.11.1 Introduction

Due to the living nature of the preformed initiators in ROMP (i.e. the metal alkylidene remains at one end of the polymer chain after total consumption of the monomer), it is possible to synthesise more complex polymer architectures such as AB block copolymers, formed by sequential addition of the monomers to the reaction (Scheme 1.33). Previously, block copolymers could only be formed by living anionic polymerisation or using controlled radical polymerisation.



Scheme 1.33

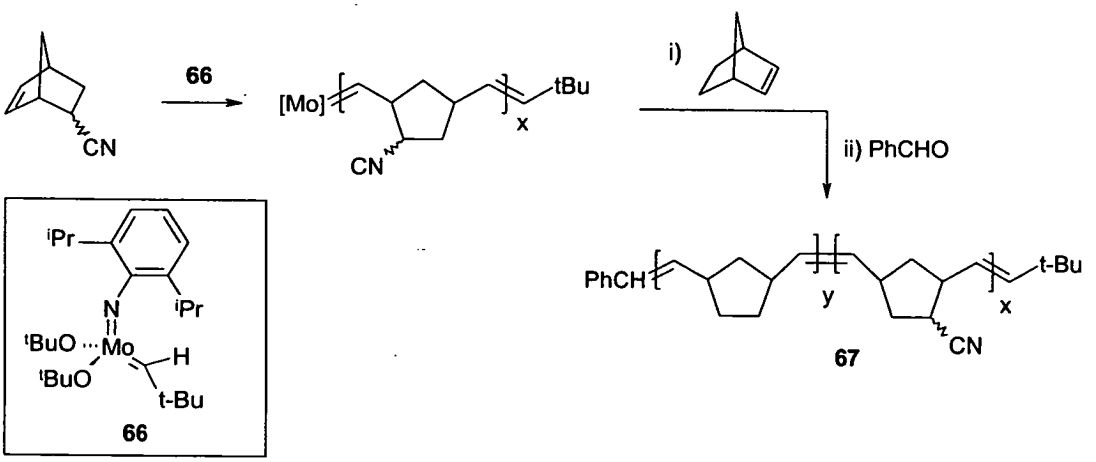
The methodology required for the synthesis of random copolymers is the same as that of homopolymers with the exception that a comonomer mixture is prepared before addition of the initiator. The concentration of each monomer (assuming similar reactivity as in Scheme 1.34), in the final copolymer is then dependent on its concentration in the initial feedstock



Scheme 1.34

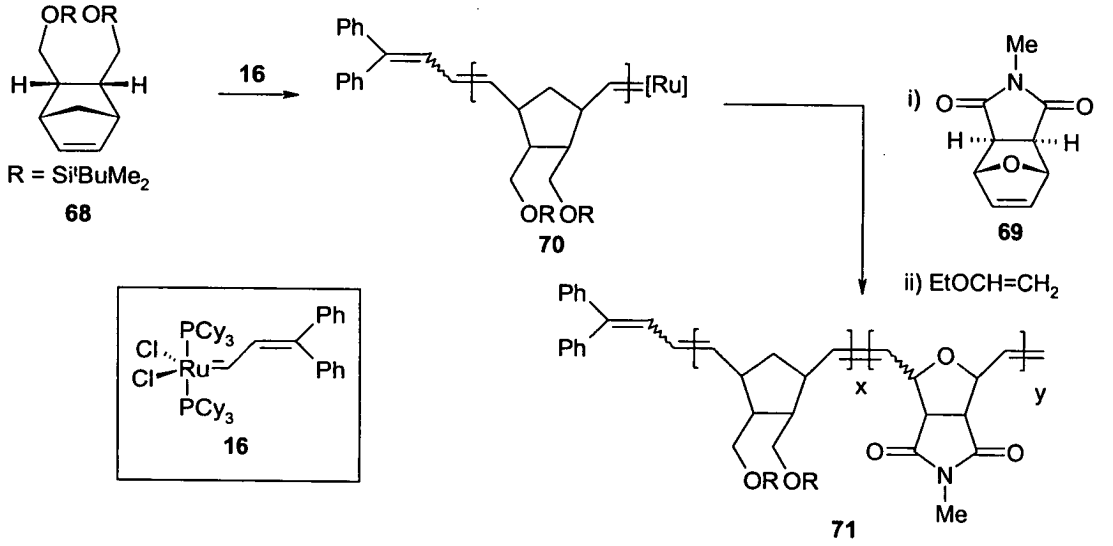
1.11.2 Functionalised block copolymers

Schrock and co-workers[133] were the first to investigate the potential of block copolymerisation by synthesising a copolymer of 2-cyanonorborn-5-ene and norbornene using the initiator Mo(CH-t-Bu)(N-2,6-i-$Pr_2C_6H_3$)(O-t-Bu)$_2$ **66**. The cyanonorbornene was polymerised using the molybdenum initiator **66** followed by the addition of NBE. Termination with benzaldehyde resulted in the diblock copolymer **67** (Scheme 1.35). Evidence of diblock synthesis was an increase in molecular weight between the first and second block measured by GPC analysis. The GPC trace was unimodal with a PDI = 1.05 which implies a process in which no chain transfer or termination occurs on the same timescale of initiation and propagation, *i.e.* a living polymerisation.



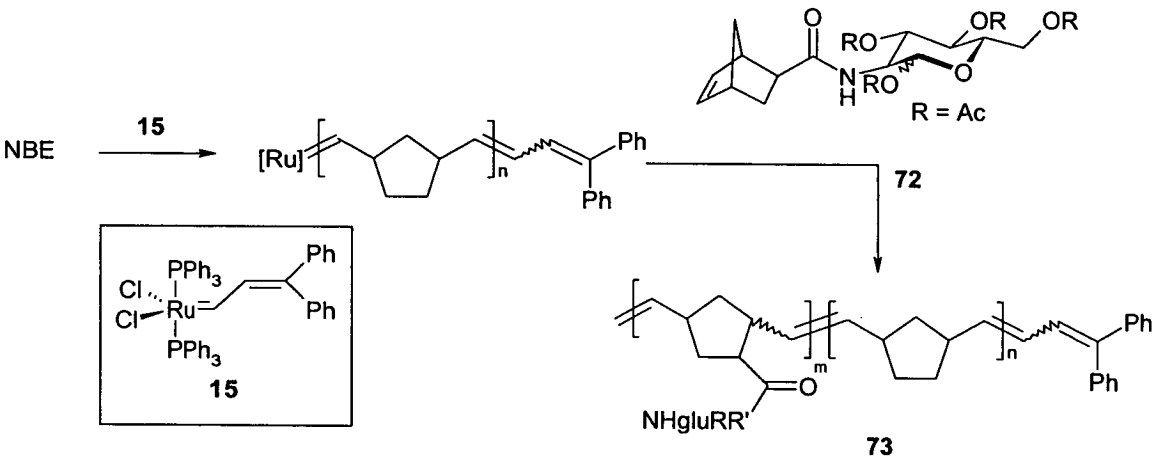
Scheme 1.35

Grubbs *et al.*[134] used initiator **16** to synthesise a silicon-containing block copolymer. It was proposed that this copolymer may be employed as a photo-resist by varying the lengths of the silicon functionalised blocks in the copolymer. Thus, a silicon containing norbornene **68** and a maleimide fused norbornene **69** were sequentially polymerised using the ruthenium propylidene complex **16** (Scheme 1.36). Termination with ethyl vinyl ether afforded the diblock copolymer **71**. Evidence of the copolymerisation was via GPC. Interestingly, the MWD of the copolymer **71** (PDI = 1.26) was narrower than that of a homopolymer of **68** (PDI = 1.75). Initiation via carbene **70** is likely to be faster than by the original carbene **16**. Thus, a living polymer results with a narrower PDI.



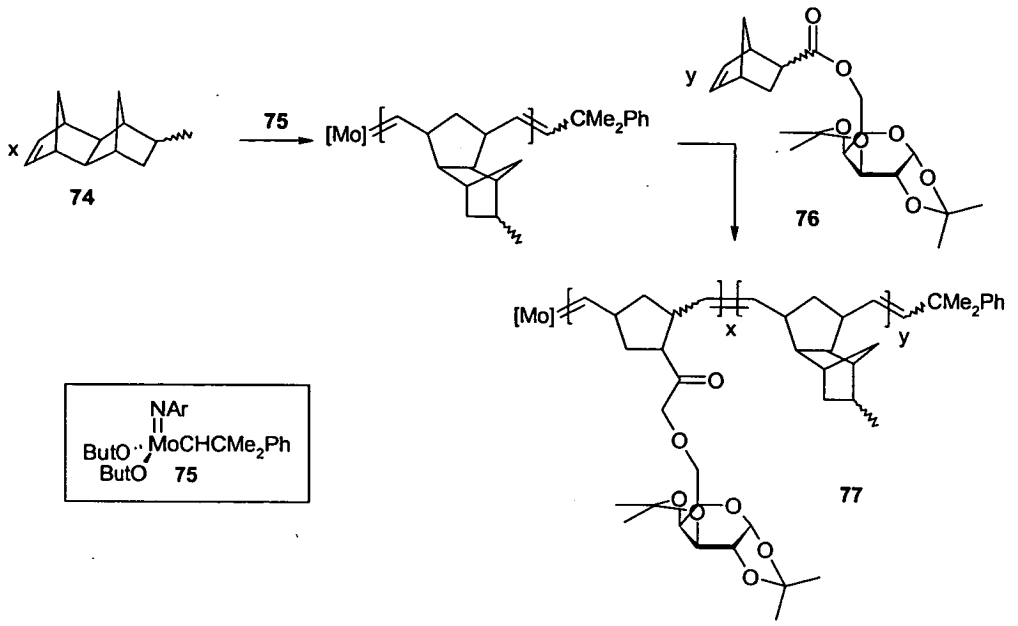
Scheme 1.36

Most therapeutic treatment strategies rely on a combination of multiple drugs to achieve optimum benefit,[135, 136] hence well defined block copolymers which are simultaneously functionalised with a high density of two or more drugs may be an extremely useful means of drug delivery. Grubbs *et al.*[137] were the first to propose the synthesis of a block copolymer for carbohydrate-based applications in which one block possesses pendant sugar moieties for recognition with other features incorporated into the second block for enhanced solubility, biocompatibility, drug delivery etc. Thus norbornene was polymerised using the ruthenium propylidene initiators **15** followed by addition of the acetate-protected glucose substituted-norbornene **72** to yield the block copolymer **73** (Scheme 1.37). The best deprotection results were achieved using ammonium fluoride in THF on triethylsilyl-protected glucose-containing polymers.The polymerisation of an unprotected sugar monomer was effected using initiator **1** under emulsion conditions. Digitized gel permeation chromatography was used to analyse the diblock copolymers (PDI = 1.35), where evidence of synthesis was a molecular weight increase on going from the homopolymer to the copolymer.



Scheme 1.37

Schrock *et al.* also investigated the potential of synthesising "sugar coated" block copolymers containing a first block of variable functionality.[109] Methyltetracyclododecene **74** was polymerised using $Mo(CHCMe_2Ph)(NAr)$-$(O\text{-}t\text{-}Bu)_2$ **75** followed by addition of the acetal protected galactose substituted norbornene **76** (Scheme 1.38). Evidence of synthesis of the carbohydrate functionalised copolymer **77** was via GPC from which the PDI values (1.03-1.18) where calculated. Other sugar functionalised norbornenes examined included a ribonic-γ-lactone- and a mannose (furanose form)-substituted monomer. Facile hydrolysis of the acetal protected galactose-containing polymers was achieved using a mixture of trifluoroacetic acid/water over a period of 15 mins to yield the deprotected analogues.



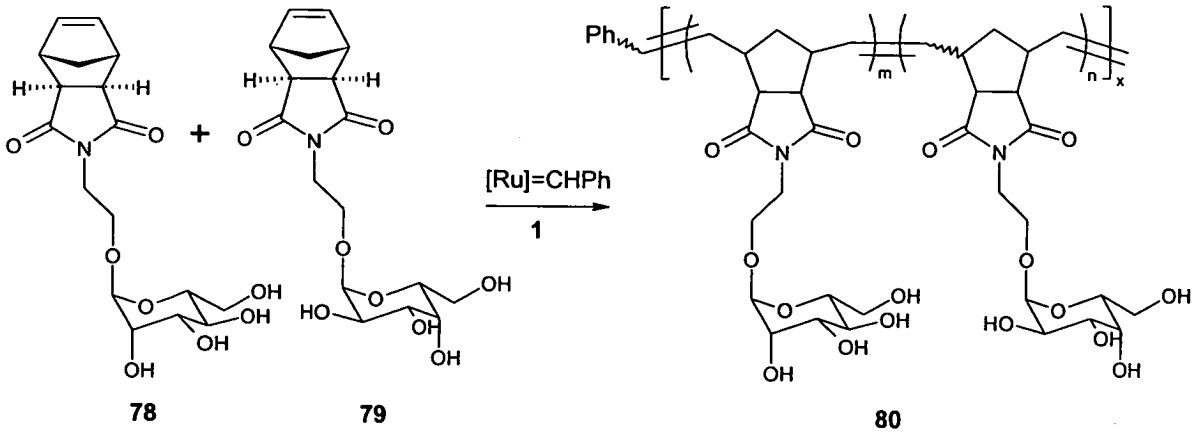
Scheme 1.38

1.11.3 Functionalised random copolymers

As stated previously, a comonomer system with differing reactivity gives a blocky copolymer as the more strained monomer polymerises preferentially. However, if a comonomer system based on two monomers of similar reactivity is polymerised, the percentage of one of the comonomer residues present in the final copolymer is proportional to its % in the feedstock.

Kiessling *et al.*[138] prepared sugar containing random copolymers using a comonomer system based on mannose- **78** / galactose- **79** functionalised norbornenes (Scheme 1.39). It is known that Con A binds mannose, but does not recognise the sterically similar galactose;[139] consequently copolymers **80** with varying percentages of mannose- and galactose-substituted monomers were used to examine the influence of epitope density on the formation of Con A clusters. The investigations showed that the density of binding epitopes (mannose) presented by a glycopolymer influences the ability of the copolymer in receptor clustering.

Copolymers with a high proportion of the active mannose residues might be expected to recruit many receptors to a single molecule; however, steric effects prevent the binding of every residue. They found that a copolymer with a lower % of mannose epitopes binds fewer total receptors per molecule, thus increased spacing between residues, allows for more efficient binding.



Scheme 1.39

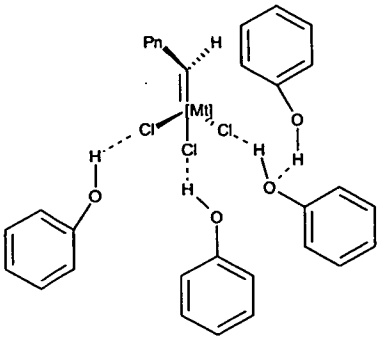
1.12 Alternating copolymers

Perfectly alternating copolymers are difficult to form with monomers of similar polarity due to polymerisation cycles that must be set up that alternatively favour polymerisation of one monomer while excluding the second and subsequently polymerising the second monomer while excluding the first.

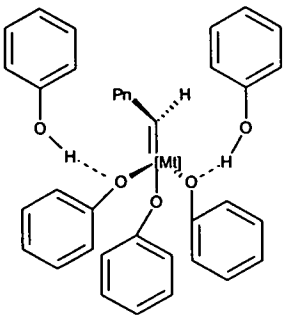
Previously, monomers with dissimilar polarities were polymerised using Ziegler-Natta copolymerisation of CO/ethene[140, 141] and styrene/ethene.[142] However, the synthesis a copolymer with monomers of similar polarity was very rare.[143]

1.12.1 Alternating copolymer using phenolic solvent cage

Rooney *et al.* developed a system based on $RuCl_3$ to synthesise an alternating copolymer of norbornene (NBE) and cyclopentene (CPE). The activity of this and other classical Ru-based ROMP initiators are rather sluggish, therefore ligand exchange with harder acidic ligands was investigated in order to increase the polarity of the π component in the ruthenium carbene and thus the activity. Phenol solvents were noted to act as potential ligands and showed not only greatly enhanced catalyst activity but also a remarkably high degree of alternating distribution of CPE and NBE units.[144] It was postulated that a Ru-carbene complex bearing η^1–coordinated phenoxide ligands forms *in situ* by the action of excess phenol on $RuCl_3$ (Figure 1.27).



M = H-bonding between metal chlorides and phenol ligands



N = Substituted phenoxide ligands

Figure 1.27

A cage is formed around the metal centre such that the differential steric effects of cyclopentylene and pentylene chain ends are greatly emphasised with respect to the incoming monomer NBE and CPE respectively. The process is therefore governed by the steric demands of the chain end coupled with the different steric and electronic properties of the approaching monomers and it is envisaged that propagation involves different metallacarbenes P_N and P_C, (N = cyclopentylene, C = pentylene.) as outlined in Figure 1.28.

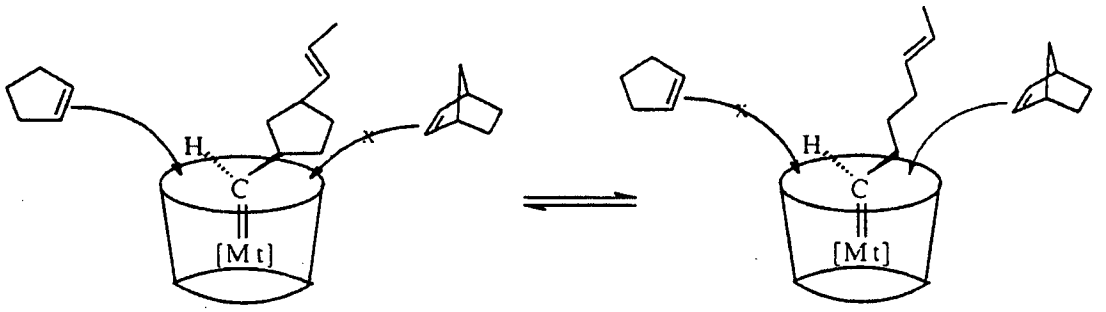
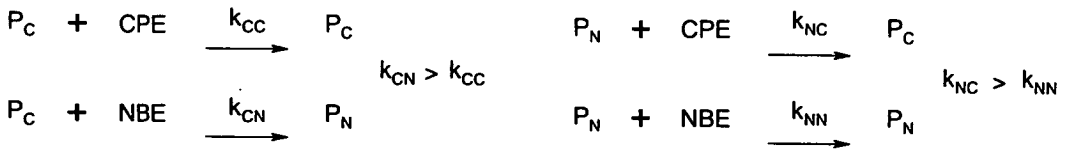


Figure 1.28

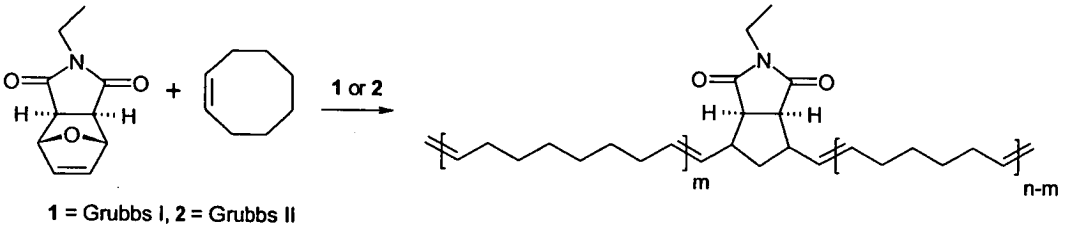
Thus, with P_N the bulky norbornene is denied access to the site and the much less bulky CPE has the opportunity to react leading to P_C. The less sterically constrained P_C is now relatively accessible to both monomers but reacts preferentially with NBE due to its much more reactive double bond thus generating P_N. The sequence of events can be described by the following kinetic (Scheme 1.40).



Scheme 1.40

1.12.2 Alternating copolymers from comonomers of differing polarity

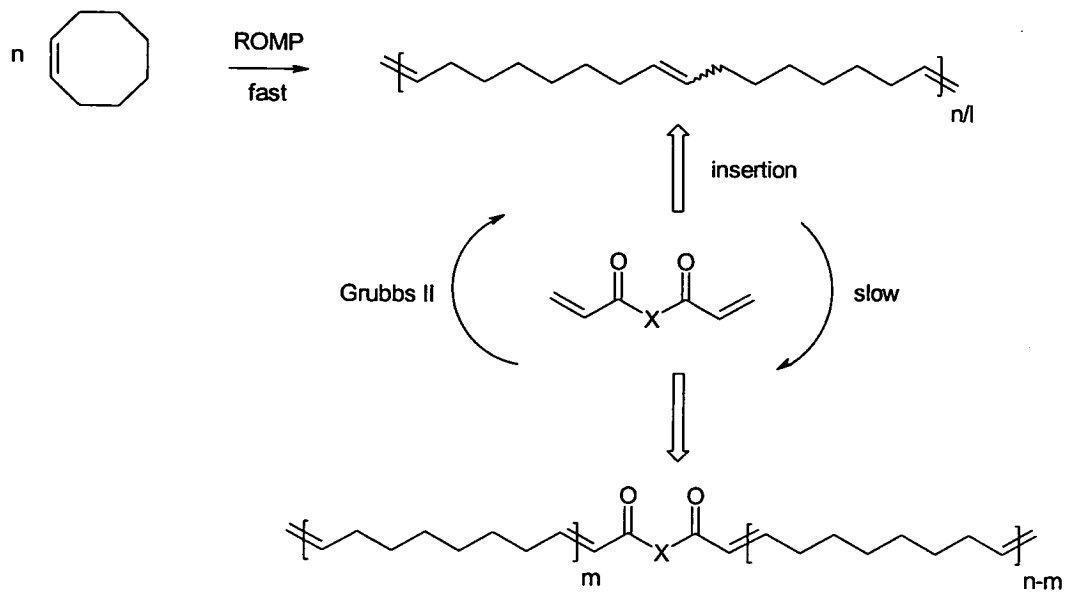
Alternating copolymers of monomers of differing polarity has been achieved by the copolymerisation of maleimide-fused oxanorbornenes and cyclooctene, with the *endo* isomer generally giving a higher % alternation[145] (Scheme 1.41).



Scheme 1.41

1.12.3 Alternating copolymers via Ring Opening Insertion Metathesis Polymerisation (ROIMP)

Recently, Grubbs *et al.*[146] have presented a novel method of synthesising alternating copolymers by ring opening insertion metathesis polymerisation (ROIMP). Cycloalkenes are homopolymerised (e.g. cyclooctene, cycloheptene) and then an α,β-unsaturated carbonyl compound (e.g. a diacrylate) is inserted into the polymer scaffold by cross-metathesis (Scheme 1.42). The resulting copolymers had a range of narrow PDI values 1.43-2.06, with a % alternation between 94-99.



Scheme 1.42

1.13 Concluding remarks

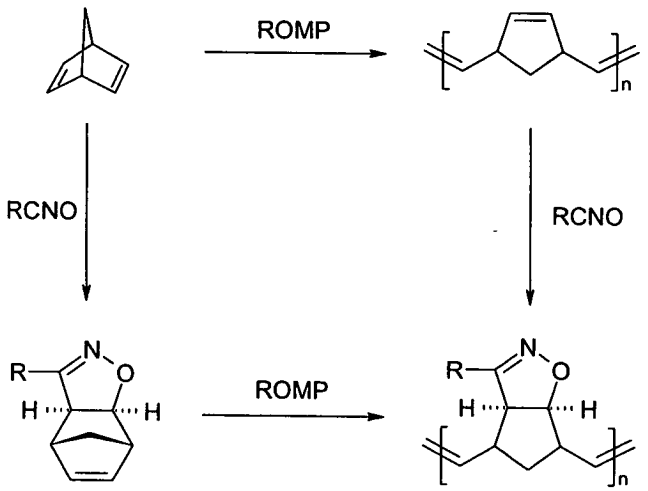
The successful polymerisation of a range of functionalised NBEs by the heteroatom tolerant ruthenium alkylidene **1**, as highlighted by the above applications and previous work in the group on nitrile oxide/1,3-dipolar cycloaddition chemistry, have prompted an investigation into synthesising functionalised polymers from isoxazolino-/isoxazolidino-fused NBEs with various substituents on the heterocycles. The findings are discussed in the following section.

2.0 Results and discussion

Part 1 – Functionalised polymers and copolymers

2.1 Introduction

The principal objective of the present work has been to examine the feasibility of preparing functionalised polymers using a combination of nitrile oxide cycloaddition chemistry and ring opening metathesis polymerisation (ROMP). To this end two approaches were selected for initial investigation. The first involves the synthesis of isoxazoline functionalised polymers with simple substituents (ester/phenyl) by cycloaddition of nitrile oxides to unsaturated polymers such as polynorbornene (polyNBE) and polynorbornadiene (polyNBD). The second route entails initial cycloaddition of nitrile oxides to norbornadiene NBD and ROMP of the resulting functionalised norbornene. These approaches are summarised for norbornadiene as the starting material in Scheme 2.1.



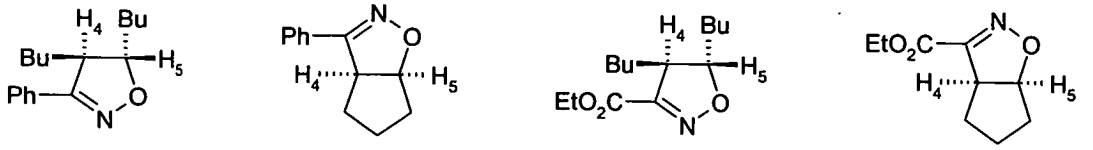
81 R = Ph
82 R = CO_2Et

83 R = Ph
84 R = CO_2Et

Scheme 2.1

Before attempting modification to the polymers themselves, preliminary studies were carried out with model alkenes in order to develop synthetic techniques that could be used for polyNBE/NBD and to provide well defined model systems for comparison purposes. *trans*-Dec-5-ene and cyclopentene were chosen to mimic the "in chain" and "ring" double bond present in the polymers respectively. The cycloaddition of benzonitrile oxide **95** and ethoxycarbonylformonitrile oxide **96**

to *trans*-dec-5-ene yielded the "in chain" mimics **85** and **87** whereas the cyclopentene adducts **86** and **88** were prepared by the addition of **95** and **96** to cyclopentene.



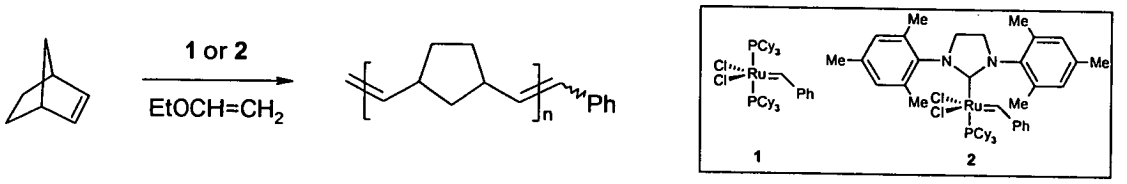
85 **86** **87** **88**

Figure 2.1

2.2 Polymers of norbornene (NBE) and norbornadiene (NBD) synthesised via ROMP

2.2.1 Synthesis of polyNBE and polyNBD

Samples of polyNBE and polyNBD were prepared by the method described by Rooney *et al.*[57] Thus, a solution of the monomer was prepared and to this was added the ruthenium initiator **1** or **2** dissolved in cyclohexane. The reaction mixture was stirred for approximately 2 hours followed by termination with ethyl vinyl ether. The resulting polymer was dissolved in chloroform and precipitated three times in methanol. The polymerisation of NBE with **1** ([70]:[1]) (Scheme 2.2) afforded 1,3-(cyclopentylenevinylene) as a fine white powder (92%) with a molecular weight M_n = 2.10x10^4 and a polydispersity index, PDI = 2.58. The analogous experiment performed using **2** yielded polyNBE (99%) with a M_n = 12.28 x10^4 and PDI = 2.16. Norbornadiene was polymerised with **1** to afford polyNBD as a hard brown solid (95%). Their structures were confirmed by NMR comparison with the literature of previous polymerisations of NBE[19] and NBD[20].



Scheme 2.2

2.2.2 Synthesis of oligomers of NBE and NBD using a chain transfer agent

The synthesis of lower molecular weight oligomers was achieved by the inclusion of hex-1-ene as chain transfer agent (CTA). The reaction was carried out as above with the exception of the chain transfer agent being added to the monomer solution before addition of the initiator. The

polymerisation of NBD and NBE in the presence of hex-1-ene results in oligomers **89**, **90** and **91** with vinyl and hexenyl termini (Figure 2.2).

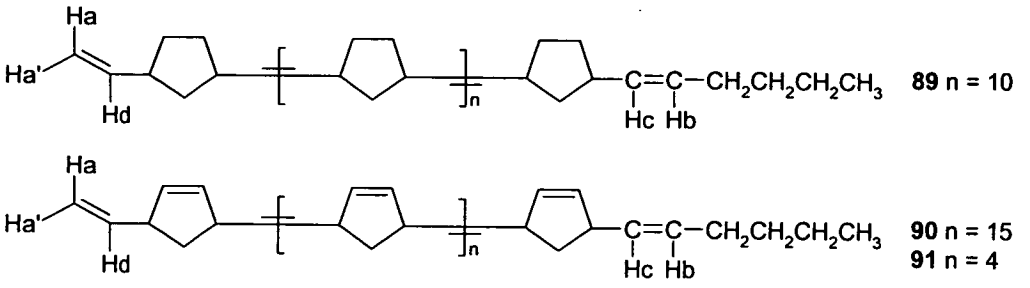


Figure 2.2

Interpretation of the ^{1}H NMR spectra allowed the end groups of the polymers to be identified and thus the average degree of polymerisation (av DP) estimated (Figure 2.2). A vinyl terminus was identified by its characteristic ^{1}H NMR signals. Peaks were observed at 4.90, 5.05 and 5.84 ppm for protons $H_{a'}$, H_a and H_d, with the expected coupling $J_{a,a'}$ = 2.1 Hz, $J_{a,d}$ = 17.1 Hz and $J_{a',d}$ = 10.2 Hz. Also present were signals at 1.62-2.08 and 0.92 ppm attributable to the butyl group. Determination of the stereochemistry of the protons H_c and H_b was hampered by the overlap of signals for the olefinic protons H-2/H-3. Signals attributable to the vinyl and hexenyl end groups were also detected in the ^{13}C NMR spectrum. Peaks at 143.9 and 112.3 ppm were assigned to the vinyl group and peaks at 30.2, 27.2, 22.8 (3xCH_2) and 14.3 ppm (CH_3) to the butyl group. Polymers of NBE and NBD were both synthesised using varying molar ratios of chain transfer agent. Tables 2.1 and 2.2 show the effect of varying the concentration of chain transfer agent on the molecular weight (M_n) of the oligomers. The M_n value was calculated by integrating the peaks for the protons of the in-chain alkene units against the peaks attributable to the protons of the vinyl end group. The yields were calculated as a percentage of the monomer used.

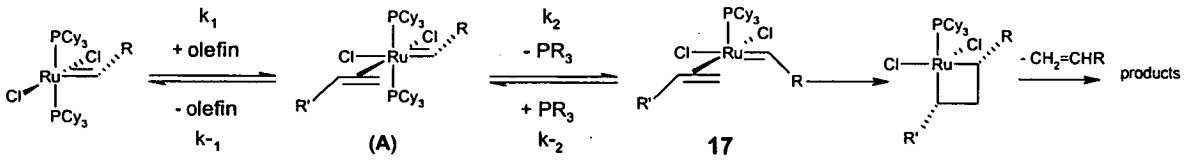
Sample code	hex-1-ene / %	yield / %	M_n x 10^{-4}	av DP
JM012	1	92	1.41	149
JM011	5	93	0.68	71
JM006	10	>98	0.11	10
JM053	15	98	0.06	5

Table 2.1 – Polymers and oligomers of NBE using initiator **1**

Sample code	hex-1-ene / %	yield / %	M_n x 10^{-4}	av. D_p
JM016	1	>98	nd	nd
JM015	5	94	0.20	21
JM005	10	>98	0.16	15
JM052	15	83	0.05	4

Table 2.2 – Polymers and oligomers of NBD using initiator **1**

Norbornene was polymerised with the first generation Grubbs initiator **1** to give a product with a *cis* content $\sigma_C = 0.17$, whereas polymerisation with the second generation ruthenium initiator **2** yielded a product with a *cis* content $\sigma_C = 0.59$. As discussed in the Introduction (Section 1.4.4) initiation using the Grubbs initiators proceeds via an associative mechanism[38] as outlined in Scheme 2.3. The ruthenium carbene binds olefins to generate a 16-electron species (**A**) before the loss of a phosphine ligand to give complex **17**. This is then capable of metallacycobutane formation and cycloreversion to afford the initiating species which polymerises the substrate before deactivation by rebinding of the phosphine ligand.



Scheme 2.3

Grubbs and coworkers have reported[147] that initiator **2** shows greater olefin metathesis activity than the first generation initiator **1**. This higher activity can be explained on the basis of the k_1 to k_2 ratios of these initiators which show that the N-heterocyclic carbene ligand (NHC) ligand in **2** increases selectivity for binding olefinic substrates over free phosphine by four orders of magnitude.

Rooney *et al.*[58] have proven that by increasing the polarity of the π component in the [Ru]=CHP moiety, and thus its reactivity in the [2+2] cycloaddition step, will lead to an increase in the *cis* content (σ_C) of the polymer. Thus, on going from phosphine to the more basic (NHC) ligand there is greater electron donation by this harder ligand resulting in a more polar [Ru]=CHP moiety. This results in the observed increase in *cis* content (σ_C) of polynorbornene from 0.17 to 0.59 on going from **1** to **2**.

2.3 Model compounds

2.3.1 Introduction

Several problems may be encountered when trying to examine reactions involving polymers due to their high molecular weight, compared to an equivalent low molecular weight compound. The most obvious problem is purification. Following reaction on a polymer containing a large number of the same functional groups per molecule, the reacted polymer molecule will contain, not only the primary desired product, but also unreacted functional groups and often groups resulting from unwanted side reactions. These will be impossible to separate. This effect presents particular difficulties if the reaction proceeds at low to medium yields, when identification and subsequent analysis becomes more difficult. This is further exacerbated by the fact that polymers are not susceptible to a number of classical analytical techniques. For example, for amorphous polymers melting points do not exist [although softening temperatures can be determined by differential scanning calorimetry (DSC)], there is a spread of molecular weights rather than one identifiable value. Some spectroscopic techniques (eg ^{1}H and ^{13}C NMR) are sometimes hampered by poor resolution[148] and low solubilities and require great care to obtain good data.

In order to cope with some of these practical problems, extensive use was made of model compounds selected to mimic as closely as possible the polymer structural units, (Figure 2.2). All reactions were first attempted on the model compounds in order to determine the optimum experimental conditions. If a reaction would not proceed in good yield on the model compound it was considered unlikely a good yield would be achieved with the polymer (provided the model was well chosen). However, the main use of the model compound was to aid structural analysis of the modified polymers. The model adducts can be purified and unequivocally analysed by accepted techniques. Comparison of the spectroscopic data (particularly ^{13}C NMR) of the model compound and the equivalent modified polymer, provides evidence for the structure of the product. Although the reactions on model compounds and polymers are expected to proceed by the same mechanism, the reaction with polymers may be less facile for special reasons.

- As the reaction proceeds, partial conversion of functional groups on the polymer chain often results in significant changes in the solubility of the polymer in the reaction medium. The polymer may well precipitate from solution well before complete reaction, therefore limiting any further reaction.[149]
- For reactions that proceed to high yield on polymers, there are likely to be neighbouring group effects. The 1,3-dipolar cycloaddition to an alkene group, adjacent to one that has already been substituted, is likely to be effected by both steric and electronic effects.

It is clear that no model compound can be expected exactly to parallel the reactivity of a polymer, however cyclopentene and *trans-dec-5-ene* were considered to imitate most closely the reactive sites on the polyenes as shown in Figure 2.3.

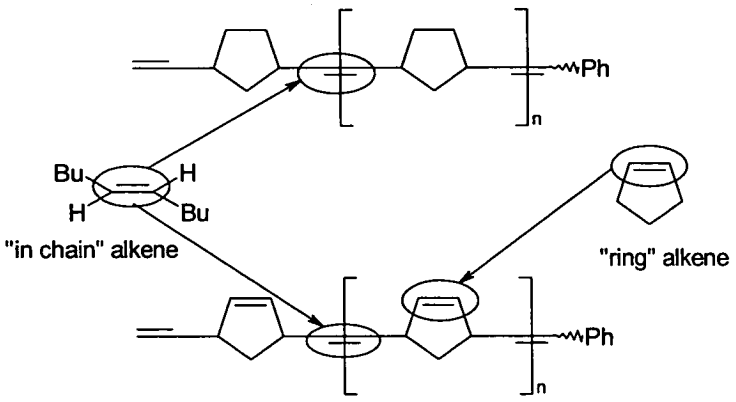
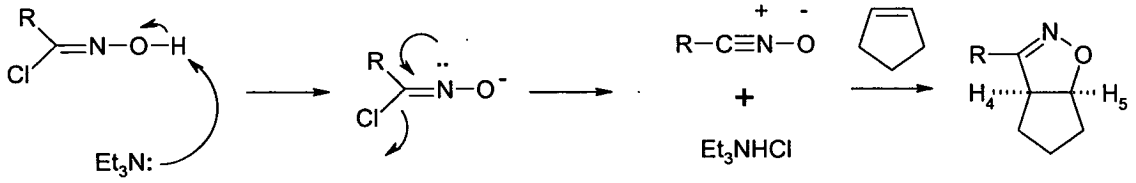


Figure 2.3

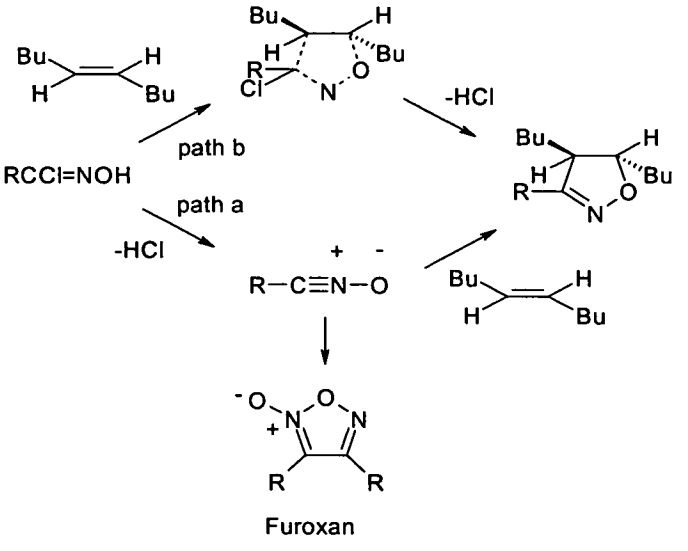
2.3.2 Generation of nitrile oxides

Model isoxazolines were synthesised by two methods. The first method used for generating the nitrile oxides involved the dehydrochlorination of the hydroximoyl chloride using triethylamine (Scheme 2.4). Triethylamine hydrochloride, the by-product, is insoluble in ether and is easily removed by filtering through celite.



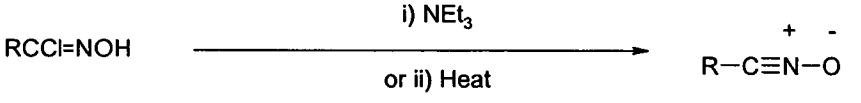
Scheme 2.4

In the second instance nitrile oxides were generated *in situ* by thermal dehydrochlorination of the corresponding hydroximoyl chloride.[150] In refluxing toluene (in which HCl has a low solubility) the reaction proceeds slowly and there is therefore a low standing concentration of nitrile oxide in the presence of excess dipolarophile. This favours adduct formation greatly over dimerisation of the nitrile oxide and is particularly useful for the reactions with unreactive dipolarophiles.[101] The formation of nitrile oxide cycloadducts using this technique has been explained in terms of either a classical nitrile oxide generation and cycloaddition (path a) or by direct interaction of the hydroximoyl chloride precursor with the dipolarophile (path b) as illustrated in Scheme 2.5. As furoxans are often formed as by-products, path a is considered the more likely.



Scheme 2.5

The nitrile oxides used in this part of the project and their method of generation from the corresponding hydroximoyl chloride are summarised in Figure 2.4.



92 R = Ph (Benzohydroximoyl chloride)

93 R = EtO_2C (Ethyl chlorooximidoacetate)

94 R = MeO_2C (Methyl chlorooximidoacetate)

95 R = Ph (Benzonitrile oxide)

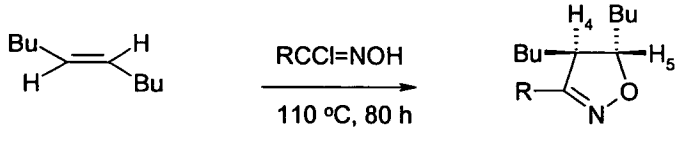
96 R = EtO_2C (Ethoxycarbonylformonitrile oxide)

97 R = MeO_2C (Methoxycarbonylformonitrile oxide)

Figure 2.4

2.3.3 Synthesis of model compounds

The *trans*-dec-5-ene cycloadducts **85**, **87** and **98** were prepared by dissolving the nitrile oxide precursor and *trans*-dec-5-ene in toluene and heating at reflux for 4 days. The solvent was removed *in vacuo* and the resulting liquid was heated at 50 °C under high vacuum (0.01 mmHg) to remove excess dipolarophile (Scheme 2.6).



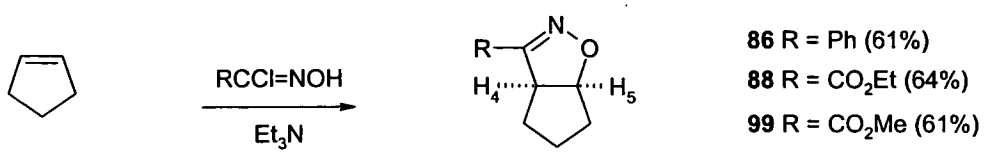
85 R = Ph (42%)

87 R = CO_2Et (48%)

98 R = CO_2Me (44%)

Scheme 2.6

In the second case, cyclopentene was reacted with nitrile oxide generated *in situ* from the corresponding hydroximoyl chloride by addition of triethylamine to afford the 2-isoxazolines **86**, **88** and **99** as in Scheme 2.7.



86 R = Ph (61%)
88 R = CO_2Et (64%)
99 R = CO_2Me (61%)

Scheme 2.7

The key to elucidating the structure of the modified polymers is through identification of the isoxazoline protons and carbons. Table 2.3 lists the key absorptions from the ^1H and ^{13}C NMR spectra which are characteristic of the CH groups at the 4- and 5-positions of the isoxazoline rings from 1,3-dipolar cycloaddition to *trans*-dec-5-ene and cyclopentene. Full assignments of peaks are shown in the experimental section 3.2.2 and 3.2.3. A noteworthy feature of the data is the difference in chemical shifts for H-4/H-5 of the *trans*-dec-5-ene cycloadducts compared with those of the cyclopentene adducts ($\Delta\delta$ ~ 0.9 ppm for H-4 and ~ 0.7 ppm for H-5). The large differences in chemical shift between *trans*-dec-5-ene and cyclopentene adducts facilitates the assignment of isoxazoline peaks in the NMR spectra of the modified polymers of polyNBD, when modification is occurring at both the "in chain" and "ring" alkenes.

In contrast there is little difference for the corresponding carbon peaks in the ^{13}C NMR spectra. The model compounds revealed peaks at approximately δ_C 51 (C-4), 89 (C-5) and 150 ppm (C-3) which is additional evidence for the presence of an isoxazoline ring. The presence of peaks at similar chemical shifts in the spectra of a modified polymer would be evidence of modification.

Isoxazoline	Alkene	R	H-4	H-5	C-4	C-5
85	*trans*-dec-5-ene	Ph	3.25	4.43	52.3	86.4
87	*trans*-dec-5-ene	CO_2Et	3.08	4.45	51.2	88.9
98	*trans*-dec-5-ene	CO_2Me	3.10	4.45	52.5	89.1
86	cyclopentene	Ph	3.99	5.16	51.6	87.3
88	cyclopentene	CO_2Et	3.94	5.35	50.6	90.3
99	cyclopentene	CO_2Me	3.96	5.21	51.2	90.8

Table 2.3 – Isoxazoline chemical shifts (ppm) for *trans*-dec-5-ene and cyclopentene model compounds

2.3.4 Relative reactivity of the alkene units

2.3.4.1 Introduction

Polynorbornadiene contains three types of alkene double bond: those in the cylopentene ring and the *cis* / *trans* units in the main chain as shown in Figure 2.3, and they are likely to have different reactivities. The reactivities of alkenyl dipolarophiles in cycloaddition reactions with various nitrile oxides have been reported by Grünager *et al.*[70] and the relative dipolarophile reactivities in the cycloaddtions of benzonitrile oxide have been determined by Huisgen *et al.*[151] The dipolarophile was generated *in situ* in ether (0-5 °C) in the presence of a variety of olefinic and acetylenic dipolarophiles and the relative rates determined by competition experiments. A selection of the rate constants relative to ethene is given below in Table 2.4, which shows that there are substantial differences in reactivity.

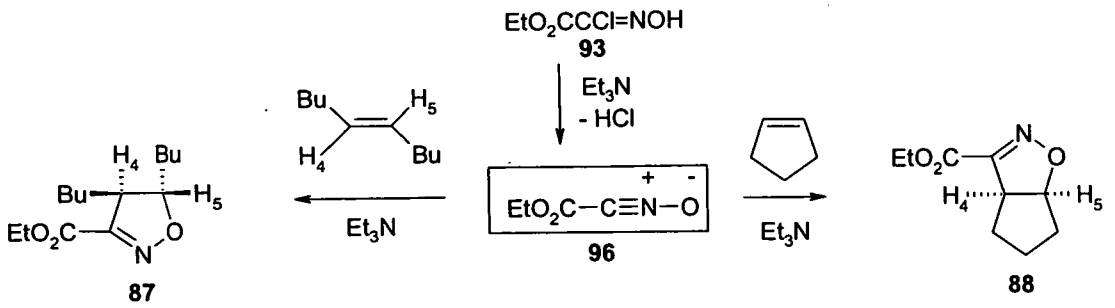
Dipolarophile	Rate constant[a]
Norbornene	15.3
Methyl acrylate	8.3
Styrene	1.15
Ethene	1.00
Hex-1-ene	0.31
Cyclopentene	0.21
Cyclohexene	0.0025

[a]Data taken from references [69, 70]

Table 2.4 – Relative rate constants for the reaction of benzonitrile oxide with dipolarophiles.

The differences in reactivity can be attributed to both electronic and steric effects. For example, substituted alkenes such as hex-1-ene are less reactive than ethene itself, whereas the ring strained norbornene is much more reactive.

It has previously been established within the group[152] using competition experiments that typical mid-chain trans alkenes such as *trans*-dec-5-ene are more reactive (~4:1) than their *cis*-isomers in cycloaddition reactions with ethoxycarbonylformonitrile oxide **96**. However, a comparison of *trans* alkenes with cyclopentene has not been previously reported. A competition experiment using cyclopentene and *trans*-dec-5-ene was therefore carried out as in Scheme 2.8.



Scheme 2.8

2.3.4.2 Competition experiment

For the competition experiment a solution of triethylamine in ether was added over 8 h (using a motorised syringe pump) at room temperature to a stirred solution of the two dipolarophiles (5 equivs.) and the hydroximoyl chloride (1 equiv.). The resulting solution was filtered through celite and the solvent was evaporated *in vacuo*. The resulting crude mixture of adducts was examined using ^{13}C and ^{1}H NMR spectroscopy and the characteristic peaks for the two isoxazolines were identified by comparison with those of the authentic adducts. The ^{13}C NMR spectra were used to determine the adduct ratio from the intensities of the C-4 and C-5 peaks which have very similar chemical environments in the two products. Table 2.5 shows the calculated ratios.

Compound	Ratio from C-4 / %	Ratio from C-5 / %
88	84	83
87	16	17

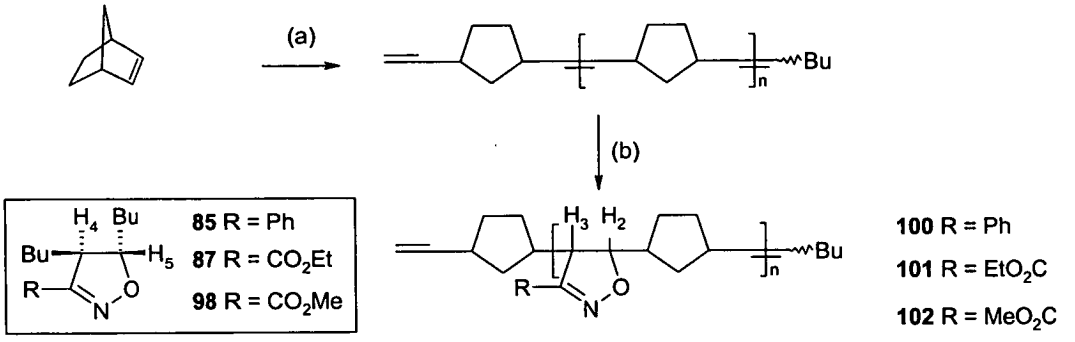
Table 2.5 – Measured yields for the reaction of ethoxycarbonylformonitrile oxide **96** with cyclopentene and *trans*-dec-5-ene.

These results show that cyclopentene is a more reactive dipolarophile (to the order of ~ 5 times) than *trans*-dec-5-ene in the 1,3 dipolar cycloaddition with ethoxycarbonylformonitrile oxide **96**. The electron withdrawing $-CO_2Et$ group tends to lower the orbital energy levels of the dipole and leads to more LU-controlled type reactions. This would be expected to give faster reaction rates with electron rich alkenes. Due to steric hindrance of the bulky butyl groups either side of the double bond in *trans*-dec-5-ene it is expected that cycloaddition is slower than that for cyclopentene. In addition, it is assumed that increased reactivity as a result of the ring strain in cyclopentene results in a higher rate of reaction than with *trans*-dec-5-ene.

2.4 Modification of homopolymers

Having successfully carried out the modification to model alkenes via cycloaddition with nitrile oxides **95-97**, the corresponding reactions with polyNBE **89**, polyNBD **90** / **91** were examined as representative examples.

2.4.1 Modification to polynorbornene



Model compounds

Reagents: (a) i) [Ru]=CHPh, CH_2=CHBu; ii) EtOCH=CH_2, (b) RCNO, Tol., 110 °C, 80h

Stereochemistry (HH, HT/TH, TT) in modified polymer not indicated in diagram

Scheme 2.9

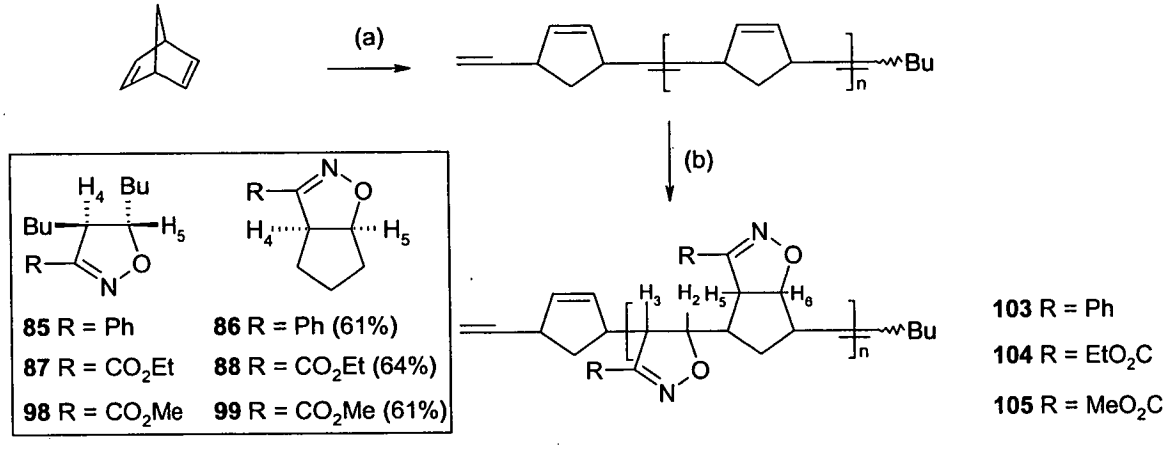
In a typical experiment a solution of polyNBE **89** (n ~ 10; σ_C = 0.17) in toluene was heated at reflux with the nitrile oxide precursor for 80h (Scheme 2.9). After cooling, the solution was reduced to a small volume (ca. 5-10 ml) on a rotary evaporator and the product precipitated in methanol several times. The final traces of solvent were removed from the modified polymer by heating at 40 °C under high vacuum (0.02 mmHg). The resultant solid was analysed by NMR spectroscopy and elemental nitrogen analysis. Polynorbornene has only one type of alkene unit albeit a *cis/trans* mixture which can undergo 1,3-dipolar cycloaddition with the nitrile oxides **95-97**. The presence of isoxazoline signals in the ^{1}H and ^{13}C NMR spectra of the modified polymer at comparable chemical shifts to those of the model compound provides strong evidence of modification. For this purpose the chemical shifts of H-2/H-3 and C-2/C-3 in the modified polymer are compared with those of H-5/H-4 and C-5/C-4 in the model respectively (Scheme 2.9 and Table 2.6). ^{13}C NMR peaks attributable to the C=N of the isoxazoline were also detected at ~ 151 ppm. The starting material contained predominantly *trans* alkene units which are known to be more reactive in cycloaddition reactions with ethoxycarbonylformonitrile oxide **96** than their *cis* counterparts.[152] It is therefore concluded that the isoxazoline units in the product have mostly *trans* configurations.

R	Modified polymer (**100**, **101**, **102**)				Model compound (**85**, **87**, **98**)			
	H-2	H-3	C-2	C-3	H-5	H-4	C-5	C-4
Ph	4.32	3.39	86.3	50.4	4.43	3.25	86.4	52.3
CO_2Et	4.39	3.20	90.7	54.1	4.45	3.08	88.9	51.2
CO_2Me	4.39	3.20	90.1	53.8	4.45	3.10	89.1	52.5

Table 2.6 – Chemical shifts of isoxazolino protons and carbons in the modified polymers and model compounds. For numbering see Scheme 2.9 above.

2.4.2 Modification to polynorbornadiene

A solution of polyNBD **90** (n ~ 15; $\sigma_C = 0.18$) in toluene was heated at reflux with the nitrile oxide precursor for 80h (Scheme 2.10). After cooling, the solution was reduced to a small volume (ca. 5-10 ml) on a rotary evaporator. Precipitation in methanol several times afforded the product. The modified polymer was analysed using the same methods as for polyNBE (Section 2.4.1).



Reagents: (a) i) [Ru]=CHPh, CH_2=CHBu; ii) EtOCH=CH_2, (b) RCNO, Tol., 110 °C, 80h
Stereochemistry (HH, HT/TH, TT) in modified polymer not indicated in diagram

Scheme 2.10

Polynorbornadiene possesses three different alkene bonds, i.e. "*cis* / *trans* in chain" and "ring" alkene units which can undergo 1,3-dipolar cycloaddition with the nitrile oxides **95-97**. NMR examination of the products showed isoxazoline protons H-2/H-3 for "in chain" modification and H-5/H-6 for "ring" modification (Table 2.7). The cyclopentene models **86**, **88** and **99** were chosen to mimic ring modification, therefore H-5/H-6 of the modified polymer are compared to H-4/H-5 of the cyclopentene model. The *trans*-dec-5-ene models **85**, **87** and **98** were chosen as a model for

modification to the chain alkene, therefore H-5/H-4 of the *trans*-dec-5-ene model was compared with H-2/H-3 of the modified polymer.

R	modified polymer				cyclopentene model		*trans*-dec-5-ene	
	"cyclopentene"		"in chain alkene"		**86, 88, 99**		model **85, 87, 98**	
	H-6	H-5	H-2	H-3	H-5	H-4	H-5	H-4
Ph	4.95	3.89	4.39	3.18	5.16	3.99	4.43	3.25
CO_2Et	5.05	3.99	4.47	3.04	5.35	3.94	4.45	3.08
CO_2Me	5.05	3.99	4.42	3.18	5.21	3.96	4.45	3.10

Table 2.7 – Chemical shifts of isoxazoline protons in modified polymer and model compounds. For numbering see Scheme 2.10 above.

Further evidence for the formation of isoxazolino units in the polymer was provided by the ^{13}C NMR spectra (Table 2.8). Of particular note is the similarity of the chemical shifts between the modified polymers and their corresponding model compounds in the ^{13}C NMR spectra.

R	modified polymer				cyclopentene		*trans*-dec-5-ene model	
	"cyclopentene"		"in chain alkene"		model **86, 88, 99**		**85, 87, 98**	
	C-6	C-5	C-2	C-3	C-5	C-4	C-5	C-4
Ph	88.4	50.5	87.6	51.3	87.3	51.6	86.4	52.3
CO_2Et	88.8	50.0	88.1	50.9	90.3	50.6	88.9	51.2
CO_2Me	90.2	50.6	88.9	51.2	90.8	51.2	89.1	52.5

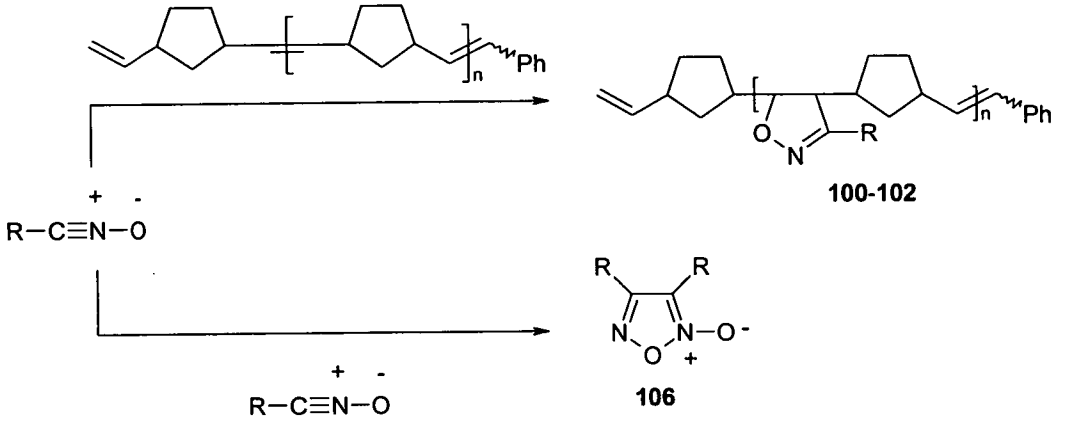
Table 2.8 – Chemical shifts of isoxazoline carbons in modified polymer and model compounds.

In conclusion, the reasonable correlation between the δ_H / δ_C values for isoxazoline protons and carbons in model compounds and the peaks in the modified polymers proves that modification by nitrile oxide cycloaddition has occurred on both alkene junctions.

2.4.3 Determination of degree of modification

The degree of modification and hence the yield of the cycloaddition reactions to the polydienes were determined by two methods: elemental nitrogen analysis and ^1H / ^{13}C NMR spectroscopy. These techniques require that the reacted polymer be thoroughly separated from any starting reagent or furoxan by-product as illustrated in Scheme 2.11. This was achieved by multiple

precipitations of the polymer in methanol. It should be noted that the modified polymer may have a different solubility in methanol than unmodified polymer. Highly modified polymer chains are expected to be more polar than less modified chains and thus be more soluble in methanol. The net result is that the measured yields could be less than the actual yields. Nitrile oxides have a propensity for dimerisation[70] yielding a furoxan **106** by-product. This is in direct competition with modification to the polymer, as outlined for polynorbornene in Scheme 2.11.



Scheme 2.11

2.4.3.1 Elemental nitrogen analysis

The first method of determining the number of isoxazoline units formed during the reaction was by CHN analysis. As the unmodified polymers contained no nitrogen atoms, the % N can be used to determine the degree of modification. Examples for polyNBE and polyNBD are shown in Appendix 1.

2.4.3.2 NMR spectroscopy

The degree of modification was determined by comparing the peak area (integral trace) for unreacted alkene signals with those of the isoxazoline signals. Thus the ratio of unreacted alkene to reacted groups can be calculated. However, it should be noted that the ^{1}H and ^{13}C NMR spectra of the polymers tend to be poorly resolved due to the layers of microstructure: cis/trans dyads, Head/Tail effects etc. as outlined in the Introduction (Section 1.5) and later in Section 2.6.2.2.

2.4.4 Modification results

Tables 2.9, 2.10 and 2.11 summarise the modification results for polyNBE and polyNBD as calculated by elemental nitrogen analyses and NMR spectroscopy.

Entry	RCNO	Code	Initial molar ratio[a]	% N in product	Modification (%) by CHN analysis	Modification (%) by ^{1}H NMR
1	R=Ph	**JM036**	1:1	5.14	53	49
2	R=Ph	**JM007**	3:1	2.07	24	[b]
3	R=Ph	**JM058**	30:1	0.08	1	[b]
4	R=CO_2Et	**JM060**	1:1	5.14	52	67
5	R=CO_2Et	**JM025**	3:1	2.37	26	31
6	R=CO_2Et	**JM061**	10:1	0.59	7	8
7	R=CO_2Me	**JM039**	1:1	3.31	34	31
8	R=CO_2Me	**JM038**	3:1	1.93	20	17

[a]Ratio of alkene units in polymer to nitrile oxide precursors; [b]Not determined.

Table 2.9 – Modification to polyNBE **89** (n ~ 10)

Entry	RCNO	Code	Initial molar ratio[a]	% N in product	Modification (%) by CHN analysis	Total (%) Modification by ^{1}H NMR	Ratio ring:chain
9	R=Ph	**JM020**	1:1	4.63	40	29	61:39
10	R=CO_2Et	**JM026**	1:1	4.31	25	30	71:29
11	R=CO_2Me	**JM051**	1:1	2.71	12	14	64:36

[a]Ratio of alkene units in polymer to nitrile oxide precursors.

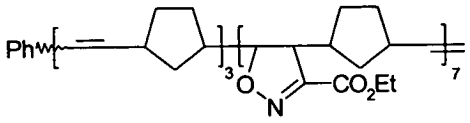
Table 2.10 – Modification to polyNBD **90** (n ~ 15)

Entry	RCNO	Code	Initial molar ratio[a]	% N in product	Modification (%) by CHN analysis	Total (%) Modification by ^{1}H NMR	Ratio ring:chain
12	R=Ph	**JM054**	3:1	1.83	9	19	69:31
13	R=CO_2Et	**JM055**	3:1	3.33	17	24	62:38
14	R=CO_2Me	**JM056**	3:1	2.42	11	[b]	[b]

[a]Ratio of alkene units in polymer to nitrile oxide precursors; [b]not determined;

Table 2.11 – Modification to polyNBD **91** (n ~ 4)

The highest level of modification reported was 67% for polyNBE (n ~ 10) (1 equiv.) with ethoxycarbonylformonitrile oxide **96** (1 equiv.) (entry 4). Thus, the structure of the modified polymer is as described in Figure 2.5 with approximately 3 unmodified units and 7 modified units (though not necessarily in two blocks as may be implied in the diagram).



Stereochemistry (HH, HT/TH, TT) in modified polymer not indicated in diagram

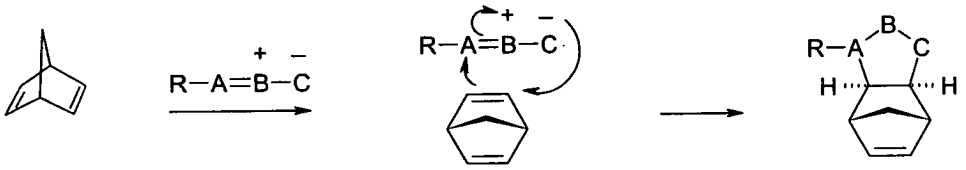
Figure 2.5

There are two noteworthy points from the above nitrile oxide cycloaddition reactions with polyNBE and polyNBD. Firstly, the levels of modification as measured by elemental analysis and ^{1}H NMR are in good agreement and secondly the experiments using polynorbornadiene showed a ring:chain modification ratio of ~ 2:1 as predicted by the model experiments (Section 2.3.4.2).

2.5 Synthesis of isoxazolino- / isoxazolidino- norbornenes as monomers for ROMP

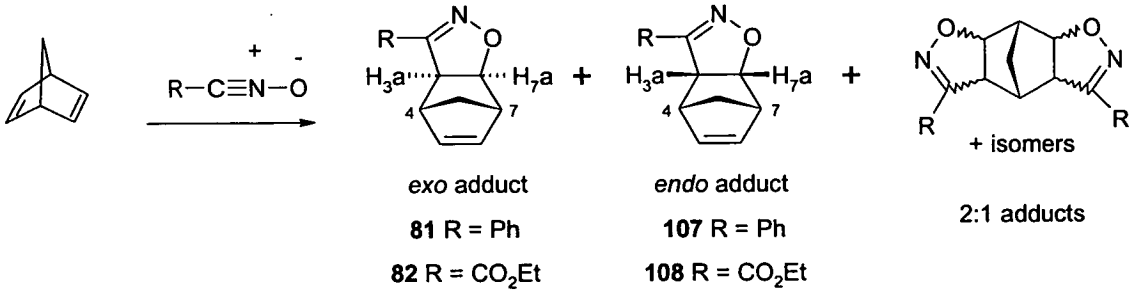
2.5.1 Introduction

Functionalised monomers based on the norbornene {bicyclo[2.2.1]hept-2-ene} ring system have been widely used (Introduction – Section 1.8.1), due to the ease of their synthesis by Diels-Alder reactions (typically of cyclopentadiene and derivatives of maleic anhydride[153]) and their reactivity with the Grubbs initiators.[154] The work in this section of the thesis presents an alternative route to functionalised norbonenes using the 1,3-dipolar cycloaddition reactions of nitrile oxides and nitrones with norbornadiene as highlighted in Scheme 2.12.



Scheme 2.12

2.5.2 Synthesis of isoxazolino norbornenes as monomers for ROMP



exo adduct
81 R = Ph
82 R = CO_2Et

endo adduct
107 R = Ph
108 R = CO_2Et

2:1 adducts

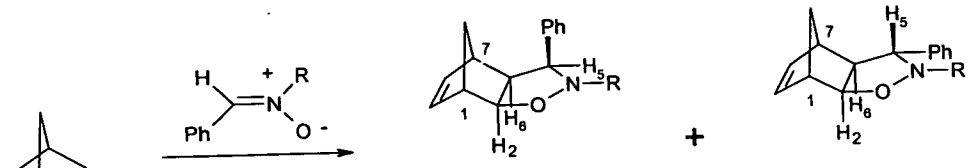
Scheme 2.13

A solution of triethylamine in ether was added over 8 hours to norbornadiene and benzohydroximoyl chloride **92** at 0 °C for one hour and then at room temperature. A large excess of dipolarophile was used in order to minimise furoxan formation and 2:1 adducts (Scheme 2.13). The reaction afforded a mixture of *endo*- and *exo*- isomers **107** (16%) and **81** (54%) respectively, which were separated by chromatography. The corresponding reaction using ethyl chlorooximidoacetate **93** and norbornadiene yielded the *endo*- and *exo*- isomers **108** (15%) and **82** (67%). The *exo* and *endo* isomers of the isoxazolino norbornenes were identified by their characteristic ^1H NMR spectra (Table 2.13). For the *exo*-product **82** the isoxazoline protons 3a-H (δ_H 3.48) and 7a-H (δ_H 4.95, $J_{3a,7a}$ 8.2 Hz) have small couplings to the adjacent bridgehead protons 4-H and 7-H of 1.4 and 1.2 Hz respectively. In contrast, for the *endo*-adduct **108** protons 3a-H (δ_H 4.02) and 7a-H (δ_H 5.39, $J_{3a,7a}$ 9.9 Hz) show larger couplings to 4-H (4.0 Hz) and 7-H (4.2 Hz). The formation of both *endo*- and *exo*- products in 1,3-dipolar cycloadditions to norbornadiene has been noted previously.[155, 156] (*exo*-3-Phenyl-3a,4,7,7a-tetrahydrobenzo[d]isoxazole **81** will now be called phenyl NBE **82**. *exo*-3-ethoxycarbonyl-3a,4,7,7a-tetrahydrobenzo[d]isoxazole **81** will now be called ethoxycarbonyl NBE **82**.)

R	*exo* isomer *J*(x-y)/Hz			*endo* isomer *J*(x-y)/Hz		
	3a-4	7a-7	3a-7a	3a-4	7a-7	3a-7a
Ph	1.4	1.2	8.2	4.0	4.2	9.5
CO_2Et	1.2	1.3	8.3	4.2	4.1	9.4

Table 2.13 – Coupling constants for 2-isoxazoline norbornenes **81** and **82**

2.5.3 Synthesis of isoxazolidino norbornenes

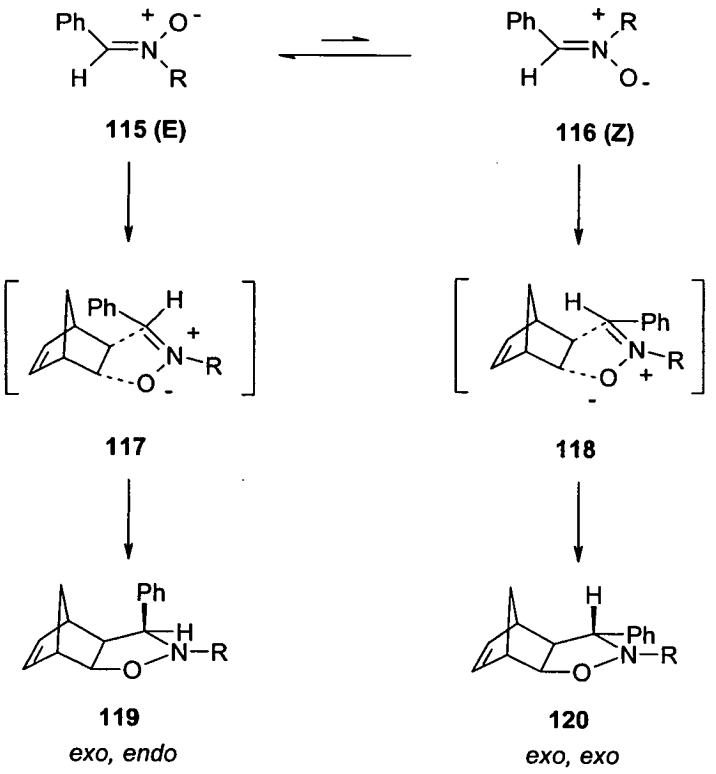


Scheme 2.14

In a typical experiment a solution of the nitrone (1 equiv.) and norbornadiene (4 equivs.) in toluene was heated at reflux for 3 days, and then a second aliquot of norbornadiene (4 equivs.) was added to the reaction. The resulting dark brown solution was evaporated to dryness and the residue extracted repeatedly with ether, filtered, and washed with water to remove any residual traces of nitrone. The ^{1}H NMR spectrum of the product showed that two isomeric isoxazolidines were present in the ratio ~ 7:1 which were separated by chromatography (Scheme 2.14). The reaction between norbornadiene and *C,N*-diphenyl nitrone **109** afforded two *exo*-cycloadducts [*exo, endo* **111** and *exo, exo* **112**] (combined yield 56%) but no *endo*-cycloadducts. The *exo*-cycloadducts, which were formed in a diastereomeric ratio **111**:**112** of 61:39, were separated by preparative thin layer chromatography. The structure of the major *exo, endo* **111** isomer was indicated by the coupling constant $J_{5,6}$ = 8.8 Hz which was similar to that for the *exo, endo* cycloadduct **111** reported by Taniguchi *et al.*[159] ($J_{5,6}$ = 9.0 Hz). The minor *exo,exo* isomer **112** was contaminated with traces of **111**, and it was therefore not possible to calculate the coupling constant for $H_{5,6}$ which was previously reported[159] as $J_{5,6}$ = 7.0 Hz. The corresponding reaction using *C*-phenyl-*N*-methyl nitrone and norbornadiene yielded two *exo* isomers [*exo, endo* **113** and *exo, exo* **114**] (79%). The cycloadducts were separated by preparative TLC and were in a diastereomeric ratio **113**:**114** of 5:95. The minor *exo, endo* **113** isomer was contaminated with traces of the major isomer preventing the coupling constant $J_{5,6}$ being measured. The major isomer had a coupling constant $J_{5,6}$ = 7.2 Hz, which is comparable to that found by Whitham *et al.*[157] ($J_{5,6}$ = 7.5 Hz) for both cycloadducts. The product was assigned structure **114** on the basis of the arguments proposed by Whitham *et al.*[157]

Whitham *et al.*[157] proposed that the *cis-trans*-interconversion of nitrones **115** (*trans*) and **116** (*cis*) results in the formation of a mixture of diastereomeric isoxazolidines **119** and **120** when reacted with norbornadiene (Scheme 2.15). Although there is a significant barrier to rotation in nitrones about the formal C=N bond (approximately 23.2 kcal mol^{-1}), they believe this is not sufficient to prohibit interconversion at 85 °C under the conditions of cycloaddition (ca. $\Delta G^{\ddagger}$ = 29.6 kcal/mol).

This conclusion was in contrast to the explanation given by Buehler[158] who claimed that there is little restriction to rotation about the formal C=N in *C*-phenyl-*N*-methyl nitrone on the basis of the constancy of chemical shift for the *N*-methyl absorption over the temperature range –60 to 100 °C. According to Whitham *et al.*[157] when R = Ph the diastereomeric transition states **117** and **118** are of approximately equal energy, whereas with R = Me the transition state **118** is of lower energy. Since the transition state **118** should be destabilised more than **117** on going from R = Me to R = Ph, due to the *cis*-phenyl-phenyl interaction, it is concluded that the favourable transition state for R = Me is **118** and the predominant adduct is therefore **120**.



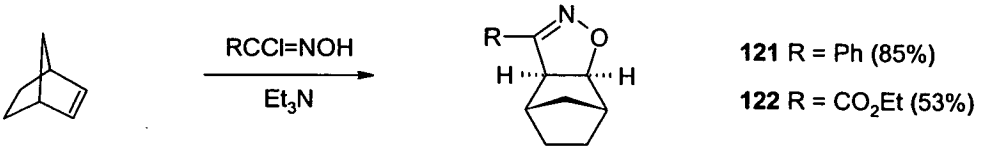
Scheme 2.15

2.6 Homopolymerisations of isoxazoline NBEs 81/82

2.6.1 Test reaction - ROMP of norbornene in presence of *exo*-isoxazoline norbornanes (121 / 122)

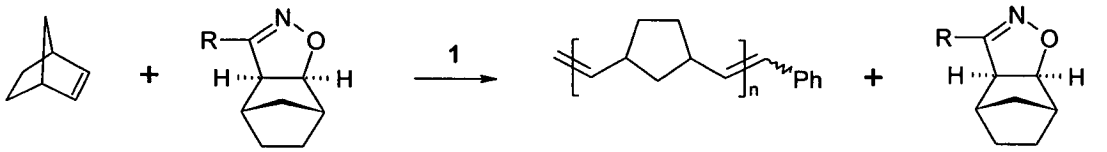
Before preparing the isoxazoline monomers it was necessary to test the stability of the isoxazoline ring under ROMP conditions and to establish that the isoxazolines did not deactivate the initiator. Therefore the *exo*-isoxazoline norbornanes **121** and **122** were chosen as they contain no unsaturation in the norbornane framework. **121** and **122** were prepared in the same manner as the

analogous *exo*-isoxazoline norbornene derivatives **81** and **82**. Previous work in the group[102] and a review found in the literature[160] showed that norbornene is highly reactive in 1,3 dipolar cycloaddition reactions (Scheme 2.16). Thus norbornene and benzohydroximoyl chloride **92** were dissolved in ether and to this triethylamine in ether was added over eight hours. The product was filtered to remove the triethylamine hydrochloride affording the product as a white crystalline solid (85%). *exo*-3-Phenyl-3a,4,5,6,7,7a-hexahydrobenzo[d]isoxazole was formed as only the *exo*-product **121**.[161-166] The isoxazoline protons 3a-H (δ_H 3.47) and 7a-H (δ_H 4.61, $J_{3a,7a}$ 7.1 Hz) have small couplings to the adjacent bridgehead protons 4-H and 7-H of 2.1 and 1.2 Hz.



Scheme 2.16

In a typical experiment a solution of initiator **1** in cyclohexane was added to phenyl norbornane **121** and norbornene in cyclohexane and stirred at room temperature for 2h (Scheme 2.17). The reaction was then terminated by addition of ethyl vinyl ether and the reaction mixture treated with DMSO[167] (50 equivs.) and stirred overnight. The solution was then precipitated in methanol to afford polynorbornene in high yield (99%) and was indistinguishable from an authentic sample. The filtrate was concentrated *in vacuo* and subjected to column chromatography yielding phenyl norbornane **121** (94%). The analogous experiment using ethoxycarbonyl norbornane **122** afforded polynorbornene (99%) and **122** (95%). It was concluded that the Grubbs initiator had no effect on the isoxazoline ring as recovery of starting material indicated that the ring was intact after the subsequent ROMP. In addition, the isoxazoline does not inhibit the polymerisation of norbornene.

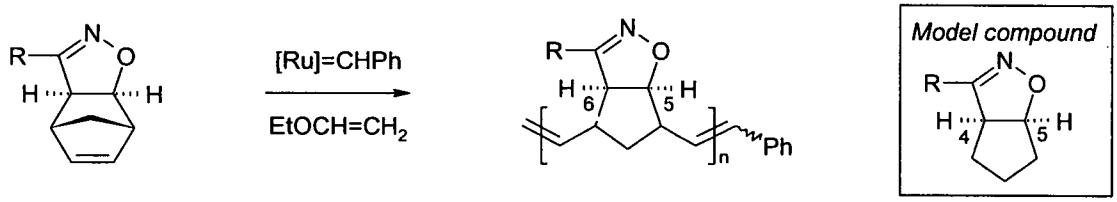


Scheme 2.17

2.6.2 Isoxazoline functionalised polymers

2.6.2.1 Preparation of isoxazoline functionalised polymers and their characterisation using NMR spectrometry

In a standard procedure phenyl norbornene **81** was dissolved in dichlormethane and to this was added a solution of the ruthenium complex **1** or **2.** The reaction was stirred at room temperature for 2h and the reaction was then terminated with ethyl vinyl ether. Precipitation in methanol afforded the product **83** as a dark brown polymeric solid (Scheme 2.18). From the ^{1}H and ^{13}C NMR spectra of the products it was concluded that no starting material remained. The ^{1}H NMR signals for **83** were broader than those of the starting material **81**. Peaks at δ_H 5.44 ppm (HC=CH) and 7.28, 7.63 (PhCH); δ_C 127.9, 128.4, 129.0 (PhCH, PhC), 130.3-134.5 (C=C) and 159.5 ppm (C=N) confirmed the structure of polymer **83**. The ethoxycarbonyl NBE **82** was polymerised in a similar fashion to **81**. The NMR spectra revealed key absorptions at δ_H 1.43 ($CO_2CH_2CH_3$), 4.33 ($CO_2CH_2CH_3$) and 5.42-5.77 ppm (HC=CH); δ_C 14.2 ($CO_2CH_2CH_3$), 62.0 ($CO_2CH_2CH_3$), 130.3-134.5 (C=C), 159.5 (C=N) and 160.5 ppm ($CO_2CH_2CH_3$), confirming the structure of **84**. The chemical shift of the polymeric isoxazoline carbons C-6/C-5 and protons H-4/H-5 of **83** and **84** were compared to those of the cyclopentene model **86** and **88**, respectively as outlined Table 2.12.



81 R = Ph
82 R = CO_2Et

83 R = Ph
84 R = CO_2Et

86 R = Ph
88 R = CO_2Et

Scheme 2.18

		Polymers **83** and **84**				Model compounds **86** and **88**			
R	Initiator	H-5	H-6	C-5	C-6	H-5	H-4	C-5	C-4
Ph	1	4.89	3.77	92.0	58.5	5.16	3.99	87.3	51.6
Ph	2	4.86	3.77	91.6	57.4	5.16	3.99	87.3	51.6
CO_2Et	1	[a]	[a]	[a]	[a]	5.35	3.94	90.3	50.6
CO_2Et	2	5.06	3.65	94.6	57.4	5.35	3.94	90.3	50.6

[a]Did not polymerise

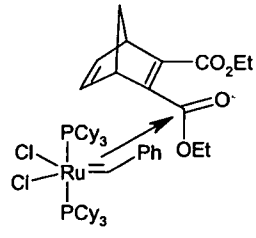
Table 2.12 – Comparison of chemical shift data of polymers **83** and **84** with model compounds **86** and **88**.

As expected the initiator used does not have any great effect on the chemical shifts of the resulting polymers (Table 2.14). There are some differences in the chemical shift data for the polymers from the nitrile oxide cycloaddition modification to polyNBD **103** and **104** and the homopolymers **83** and **84**. Modification levels of less than 50% result in a polymer that consists mainly of cyclopentane units, whereas the homopolymer is composed of repeat isoxazoline units. Consequently, the different chemical environments of **103/104** compared with those of **83/84** results in inconsistent chemical shifts for the isoxazoline protons and carbons (Table 2.13).

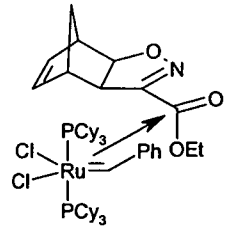
Polymer	R	H-5	H-6	C-5	C-6
81	Ph	3.77	4.86	58.5	92.0
103	Ph	3.89	4.95	50.5	88.4
82	CO_2Et	3.65	5.06	57.4	94.6
104	CO_2Et	3.99	5.05	50.0	88.2

Table 2.13 – Chemical shift data for post modified polymers **103/104** and for isoxazoline polymers **83/84**

It is interesting to note that the first generation initiator **1** does not react with monomer **82** whereas the latter is readily polymerised by the second generation initiator **2**. The ruthenium carbene **1** has been reported before as being unreactive with monomers containing ester functionality.[49, 168] This initiator is nucleophilic and is believed to prefer to complex to the ester **123**, thereby preventing ROMP via [2+2] cycloaddition at the unsubstituted alkene unit as shown in Figure 2.6. It is possible that the same chelation is occurring with ethoxycarbonyl NBE **82**.



123



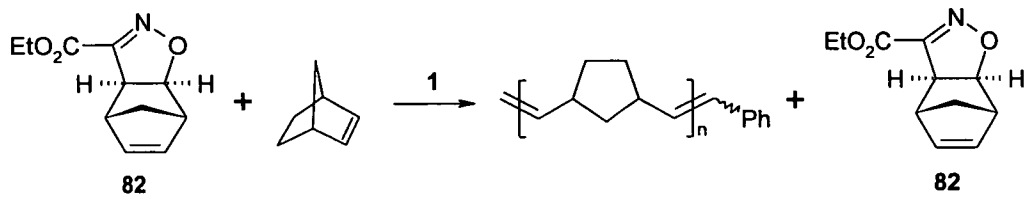
82

Figure 2.6

In contrast, the polymerisation of isoxazoline norbornene **82** with **2** proceeds readily. It is therefore concluded that the ruthenium benzylidene moiety in this initiator ([Ru]=CHPh), which is more

nucleophilic, is able to overcome a "chelation barrier" and [2+2] cycloaddition with the monomeric alkene is more favourable than chelation to the ester.

In an attempt to test this chelation versus polymerisation theory, **82** was stirred with initiator **1** in the presence of norbornene for 2h and then the reaction product was precipitated in methanol. Polynorbornene was afforded in a 99% yield and **82** recovered (95%) from the work up of the methanol mother liquor.



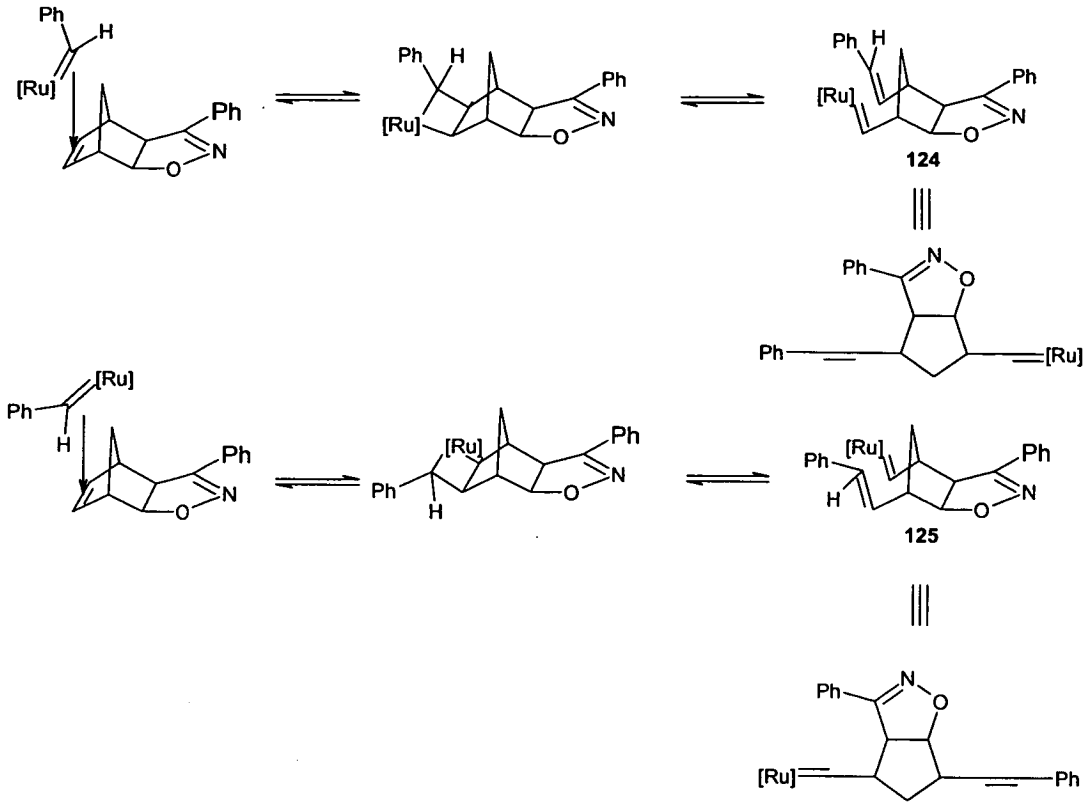
Scheme 2.19

This indicates that initiator **1** reacts with NBE (a sufficiently strained olefin) in preference to coordination to the ester. In contrast, if the reactivity of the catalyst is increased, it preferentially reacts with the olefin of the monomer rather than chelate to its ester group as demonstrated by the facile polymerisation of **82** with **2**.

2.6.2.2 Polymer tacticity

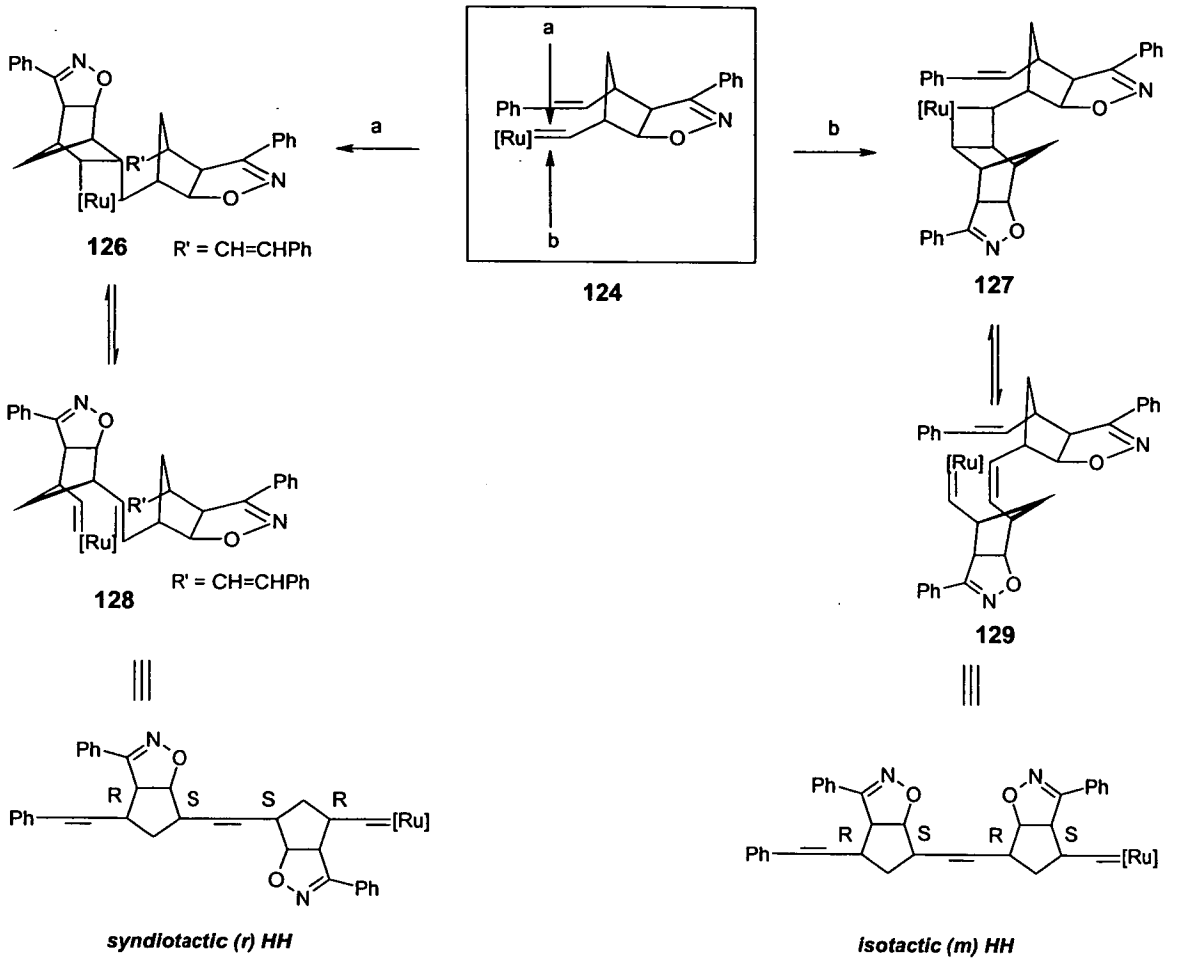
Information concerning the configurational (*cis* / *trans* ratio), tacticity [isotacticity (m), syndiotacticity (r)] and regioregularity (HH, TH/HT, HH) of the ring opened polymers of functionalised norbornenes can be deduced from their NMR spectra. From the ^{1}H NMR spectra of the ROMP product of ethoxycarbonyl NBE **82** the *cis* content σ_C = 0.63 was calculated. The corresponding polymer derived from phenyl NBE **81** had a *cis* content σ_C = 0.62. The tacticity of a metathesis polymer is deduced from the degree and pattern of splitting of main resonances in the ^{13}C NMR spectrum and are most valuable if the tactic and atactic forms are available to make a comparison.

The ROMP of phenyl NBE **81** can be initiated with the ruthenium alkylidene attacking *cis* (phenyl respective to the R substituent) or *trans* to the monomer leading to the first insertion product **124** and **125** respectively, Scheme 2.20.



Scheme 2.20

The attack can occur from above (*exo*) or below (*endo*) the plane of the double bond. The orientation of attack (*cis* or *trans*) with the next monomer unit will dictate whether a head-to- head (HH), head-to-tail (HT), tail-to-head (TH) or tail-to-tail (TT) dyad is formed, (Scheme 2.21). In this case, however the direction of attack, whether above or below the plane of the monomer, will be significant as it will result in syndiotactic (r) or isotactic (m) structure respectively. For example, attack of a second monomer unit above the plane (pathway a) of the *cis* first insertion product gives the metallocyclobutane **126**. A retro [2+2] cycloaddition affords **128**, a syndiotactic (r) HH product. However, if the second monomer unit approaches from beneath the plane of the *cis* first insertion product, the intermediate metallocyclobutane **127** is formed (pathway b). [2+2] cycloreversion affords **129**, an isotactic (m) HH, (Scheme 2.21).



Scheme 2.21

In summary, the ruthenium alkylidene approach to the first monomer unit can be either in a *cis* or *trans* orientation leading to **124** and **125**. Addition of the subsequent monomer unit will be to **124** or **125** either above (*exo*) or below (*endo*) the plane of the monomer and in a *cis* or *trans* orientation thus resulting in eight possible configurations, Figure 2.7.

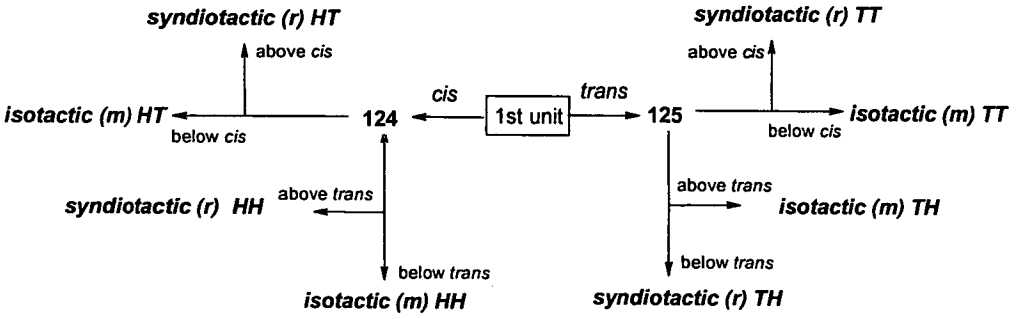


Figure 2.7

The structures of the eight possible configurations described in Figure 2.7 are shown below, Figure 2.8. These configurations are for all *cis* polymers however, as the ROMP product of ethoxy NBE **82** has a *cis* content $\sigma_C \doteq 0.55$ there would be another possible eight for the *trans* junctions, totalling sixteen in all. The ^{13}C NMR spectrum revealed a large multiplet 91.8-94.3 ppm for H-5 (isoxazoline proton) from which no assignments can be made. The alkene units in the polymer were hydrogenated to see if the removal of the *cis*, *trans* layer of microstructure would reveal any further information. However, from the ^{13}C NMR spectrum of the hydrogenated analogue, the H-5 signal was a broad doublet 92.4-93.9 ppm from which no information on tacticity could be deduced.

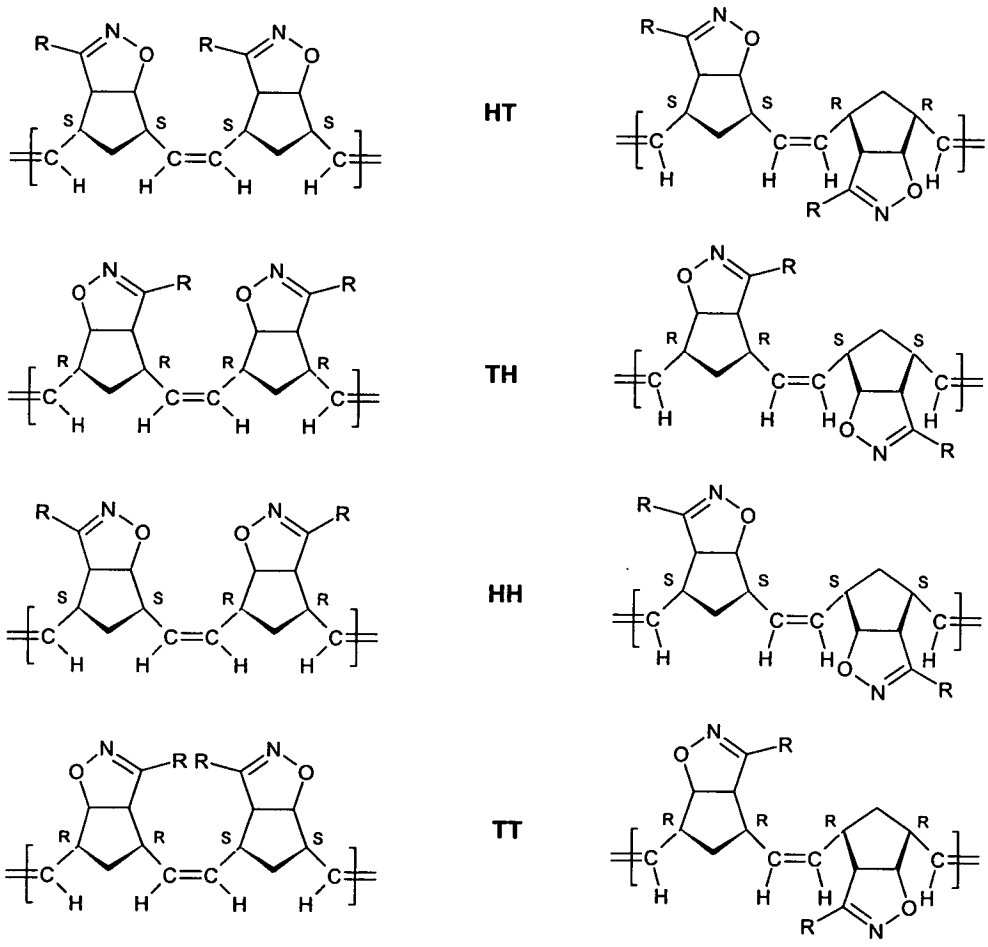


Figure 2.8

2.6.2.3 Molecular weight determination of polymers

The molecular weights of the polymers were measured by GPC analysis and from the results it is interesting to note that using the first and second generation catalysts produce polymers with very different profiles. The ruthenium carbene **2** yields polymers with a much greater M_w and M_n than

initiator **1**, and this can be explained by the greater difference between k_i (rate constant for initiation) and k_p (rate constant for propagation). The carbene **2** has a high propagating rate and slow initiation rate thus giving polymers with uncontrolled molecular weights. The increased k_i/k_p ratio for **1** promotes controlled living polymerisation, which results in lower molecular weight polymers with lower PDI values than those produced with **2**.[56] Complex **2** is a more reactive initiator as, although it dissociates a PCy_3 ligand (initiates) slowly, a small amount of initiated 16-electron species is capable of cycling through multiple olefin metathesis reactions before it is deactivated by the rebinding of PCy_3 (c.f. Introduction Section 1.4.4, Scheme 1.15). In contrast, **1** initiates relatively rapidly, but the rebinding of phosphine is competitive with olefin coordination under typical reactions conditions. As such, the highly active 14-electron intermediate undergoes relatively few turnovers before being trapped by free PCy_3.[147]

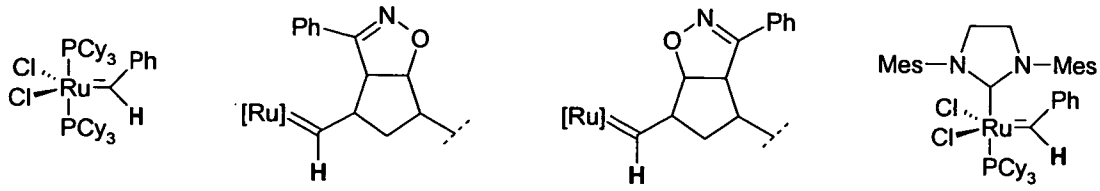
Monomer / code	I	[M]:[I]	yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI[b]	propagating species ppm
81 / JM021	**1**	80:1	63	3.52	1.79	1.97	85	19.4-19.5
81 / JM101	**2**	80:1	62	3.85	3.27	2.18	155	[c]
82 / JM157	**1**	80:1	[d]	[d]	[d]	[d]	[d]	[d]
82 / JM107	**2**	80:1	75	22.86	13.84	1.65	618	[c]

[a]Monomer:Initiator ratio; [b]measured by GPC in THF against polystyrene standards (860 – 2.43 million); [c]not observable; [d]did not polymerise.

Table 2.14 – Selected physical data for polymers from **81** and **82**

2.6.2.4 Monitoring propagating species of isoxazolino norbornenes by ^{1}H NMR spectroscopy

The polymerisation of phenyl NBE **81**, initiated by **1** (1:1 ratio), in $CDCl_3$ was monitored by ^{1}H NMR spectroscopy. In addition to the sharp singlet at 19.9 ppm for unreacted initiator **1**, a broader signal was observable at 19.4-19.5 ppm, which is attributed to the carbene hydrogens of the ruthenium alkylidene end-groups of the propagating polymer.[117, 118, 170] The breadth of the peak can be explained, in part at least, by the presence of regioisomers **130** and **131** (Figure 2.9). The detection of these alkylidene protons corresponding to the propagating species and the low PDI value is indicative of a living type polymerisation. The ^{1}H NMR from the corresponding polymerisation using **2** revealed a signal at 19.08 ppm attributable to the carbene proton of the initiator, but no peaks were detected for the propagating species. This may be attributed to k_p being much greater than k_i.



1 130 131 2

Figure 2.9

The products from the polymerisation of phenyl NBE **81** using the ruthenium carbenes **1** and **2** produced different ^{1}H NMR spectra.[¶] The ^{1}H NMR spectrum (Appendix 2) for the oligomer formed using **1** revealed clearly discernable signals for the end groups (a, b and c) (Table 2.15). This however was not the case with the polymer produced using **2** which is of higher molecular weight with end group signals at baseline intensity.

End group signal (nH)	Structure	δ (ppm)
a (1H)	C*H*=CH_2	8.4
b (5H)	CH=CH*Ph*	7.2-7.4, 7.5
c (2H)	CH=C*H*$_2$	6.1-6.6

Table 2.15 – End group signals for the ROMP product of *exo*-phenyl-isoxazoline **81** with **1**

From the ^{1}H NMR spectrum of the products it is possible to determine the average degree of polymerisation for the living type polymerisations (Table 2.16). The product formed using the ruthenium alkylidene **1** has an av DP ~ 1, whereas the analogous reaction initiated with complex **2** yielded a polymer with chain length n ~ 7. The different behaviour is attributed to the high k_i/k_p of **1** relative to **2**.

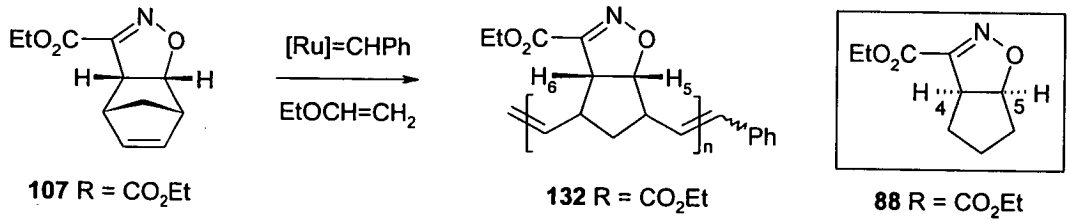
Sample code	[**81**]:[**1**]	yield / %	M_n x 10^{-4}	av DP
JM198	1:1	98	0.04	1
JM194	1:1	99	0.28	7

Table 2.16 – Molecular weights (M_n) from the ROMP of **82** with complexes **1** and **2**.

[¶] Phenyl NBE **81** (10 mg, 0.0048 mmols, 1 equiv.) was dissolved in $CDCl_3$ and the solution transferred to an NMR tube. To this was added the Grubbs initiator **1** (39.2 mgs, 0.048 mmols, 1 equiv.) and the NMR tube shaken, at which point data collection was immediately started. Data were collected every 10 mins and from the resulting ^{1}H NMR spectra, signals attributable to the propagating species 130 and 131 ppm were observed along with a peak for the initiator **1**.

2.6.2.5 ROMP of *endo*-3-ethoxycarbonyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[d]isoxazole 107

As stated in Section 2.5.2 the cycloaddition of ethoxycarbonylformonitrile oxide **96** to NBD yields a mixture of *exo* and *endo* isomers. It is well known that *endo*-isomers of norbornenes are more sterically hindered than the *exo*-isomers and hence are polymerised more slowly.[169] Thus, having isolated a sample of the pure *endo*-3-ethoxycarbonyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[d]isoxazole **107**, an experiment was carried out to polymerise it (Scheme 2.22). The *endo*-isoxazoline NBE **107** was dissolved in dichloromethane and to this was added a solution of the second generation Grubbs initiator **2**. The reaction was stirred for 2 hours and then terminated with ethyl vinyl ether. The product was isolated by precipitation in methanol **132** (96%) which was analysed by ^{1}H NMR spectroscopy. From the spectrum, signals attributable to the ester functionality appeared at 1.27 ppm ($CO_2CH_2CH_3$), 4.20-4.31 ppm ($CO_2CH_2CH_3$) and for polymeric alkene units at 5.39-5.65 ppm. The *cis* content (σ_C) of the product from the ROMP of the *endo*-isomer was indeterminable due to the H-1,4 signals being a broad multiplet between 2.53-3.02 ppm, whereas with the *exo*-isomer the polymer product gave a broad doublet for the H-1,4 signals with a *cis* content σ_C = 0.63. It was noteworthy that **2** not only enables the polymerisation of the ethoxycarbonyl NBE **82** (which is not possible with **1**), but that it is also capable of polymerising the more sterically demanding *endo*-isomer **107**.



107 R = CO_2Et **132** R = CO_2Et **88** R = CO_2Et

Scheme 2.22

2.6.2.6 Monitoring reaction rate of ROMP of isoxazolino NBEs

The polymerisation of ethoxycarbonyl NBE **107** with **2** in $CDCl_3$ was monitored by ^{1}H NMR spectroscopy in order to follow the progress of the reaction. NMR spectra were recorded at t = 1, 10, 25, 30, 40, 45 and 55 mins, and the % reaction completion measured by integrating the monomer alkene signals against the olefinic polymer signals. A plot of % completion against time is shown in Figure 2.10.

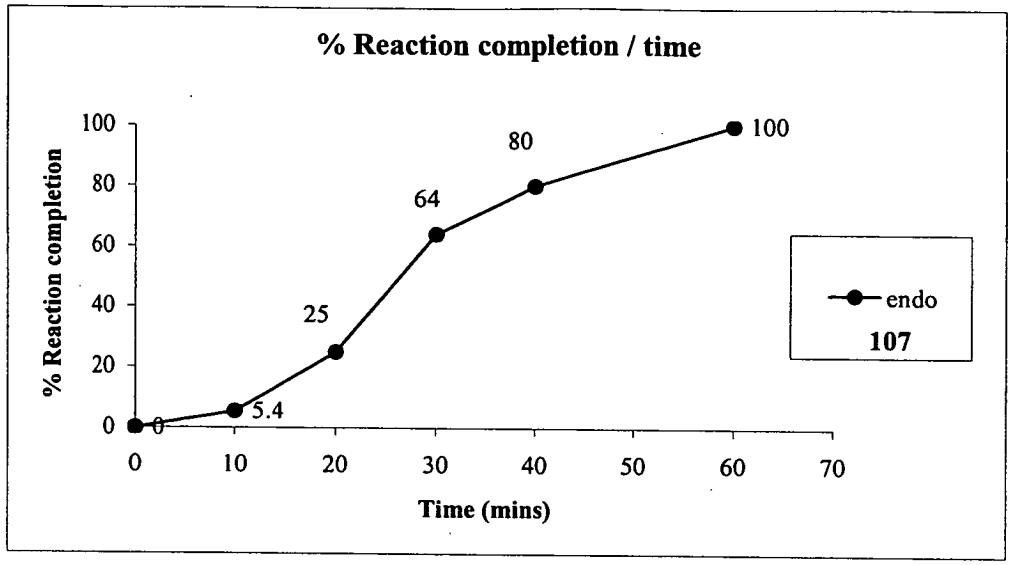


Figure 2.10

The reaction proceeds slowly for the first 20 mins (% conversion at $t_{25\ mins}$ = 25 %), consistent with the slow initiation rates observed for the second generation initiator. However, once the initiating species are formed, the reaction proceeds rapidly and in the next 20 mins the % conversion had risen to 80%. This provides further evidence that the propagation rate for this catalyst is much greater than the initiation rate. As both *endo*- and *exo*-adducts **82** and **107** were available, the relative reactivities in ROMP with initiator **2** were examined. The results are compared in Figure 2.11 below.

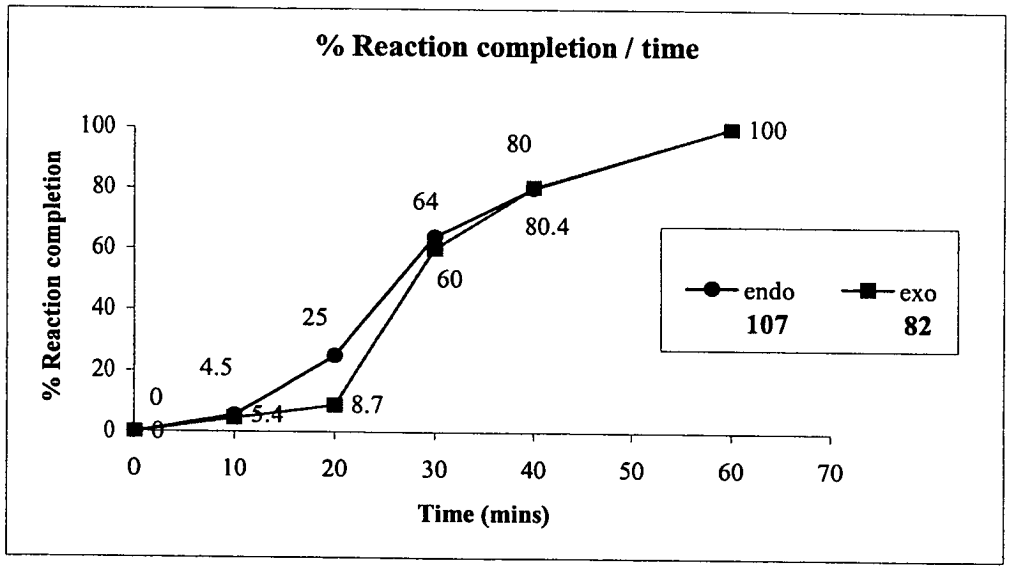
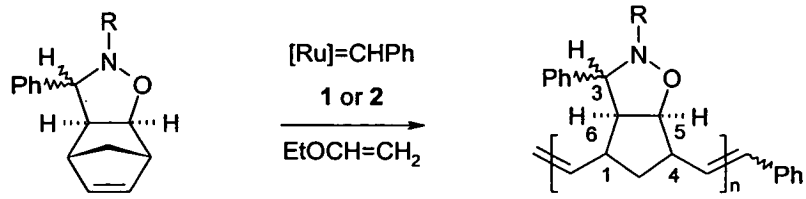


Figure 2.11

From the above graph (Figure 2.11) it is notable that the *exo* and *endo* isomers have comparable reactivity (and if anything the *endo* isomer has a slightly higher reaction rate at the earlier stages). The ruthenium complex **1** has been reported[169] to polymerise *exo* isomers of functionalised norbornenes faster than the corresponding *endo* isomer as they are less sterically hindered. The result above (Figure 2.11) displays the high activity of **2** in polymerising *exo* and *endo* norbornene derivatives **82** and **107** with comparable ease.

2.6.3 ROMP of isoxazolidino norbornenes

Having established that isoxazolino norbornenes are readily polymerised using the ruthenium initiators **1** and **2**, the analogous isoxazolidino norbornenes were used as potential monomers for ROMP. Thus, a solution of the carbene complexes **1** or **2** in dichloromethane was added to the isoxazolidino norbornene (**111/114**) and stirred for 2 h. The polymerisation was terminated using ethyl vinyl ether and precipitation in methanol afforded the product. The resulting polymers bearing *C,N*-diphenyl isoxazolidine **133** and *C*-phenyl-*N*-methyl-isoxazolidine **134** functionality were analysed by NMR spectroscopy. The signals in the ^{1}H NMR spectrum were very broad and contained no peaks from the staring material. The diagnostic peaks for **133** appeared at 4.51-4.47 (H-3,6), 4.87-5.00 (H-5) and 6.96-7.11, 7.21-7.46 ppm (PhCH). The corresponding ^{1}H NMR spectrum for **134** contained signals at 2.50 (NCH_3), 2.99-3.60 (H-3,6) and 4.17-4.40 (H-5). The ^{13}C NMR revealed peaks at 60.8 (C-6), 71.6 (C-3), 88.9 (C-5), 138.0 (PhC) and 150.3 ppm (PhN) for **133** and the analogous spectrum from **134** showed signals at 41.6 (NCH_3), 60.0 (C-6), 80.0 (C-3), 87.6 (C-5) and 138.2 ppm (PhC). These results provide evidence that the isoxazolidine ring was compatible with ROMP conditions. The *cis* content (σ_C) for **134** was calculated as 0.36 when the polymerisation was initiated with **1** and 0.62 using **2**. Due to the peaks for H-1,4 becoming a broad multiplet in **133**, the *cis* content was not able to be calculated. for a polymer initiated with **1**. The first generation initiator **1** normally produces polymers $\sigma_C = 0.10$ due to the low energy ruthenium alkylidene being unable to form the high energy *cis* metallocyclobutanes. The polymerisation of **114** with **1** afforded a polymer **134** with a *cis* content of 36%. The steric hindrance in the monomer **114** due to the phenyl and methyl group must have a crowding effect around the ruthenium alkylidene during the initiation and propagating steps leading to the high *cis* content. Sterically constrained catalysts sites have been reported to generate polymers with high *cis* contents[13].



111 R = Ph
114 R = Me

133 R = Ph
134 R = Me

Scheme 2.23

2.6.3.1 Molecular weight measurements

The molecular weights of the polymers **133** and **134** were measured by GPC analysis. The results show that, as with the isoxazoline functionalised polymers **83** and **84**, using the first and second generation complexes produce polymers with very different profiles as shown in Table 2.17. Initiator **2** leads to higher molecular weight products than complex **1**. This is a result of the larger difference in k_i and k_p of **2** than that of **1** as explained in Section 2.6.2.3.

Isoxazolidine / code	I	[M]:[I]	Yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI[b]	Propagating species ppm
111 JM084	**1**	80:1	95	10.41	6.76	251	1.84	18.6
111 JM101	**2**	80:1	73	42.07	20.04	490	2.37	[c]
114 JM157	**1**	80:1	75	10.5	5.70	234	1.54	19.1
114 JM107	**2**	80:1	76	26.12	11.14	683	2.09	[c]

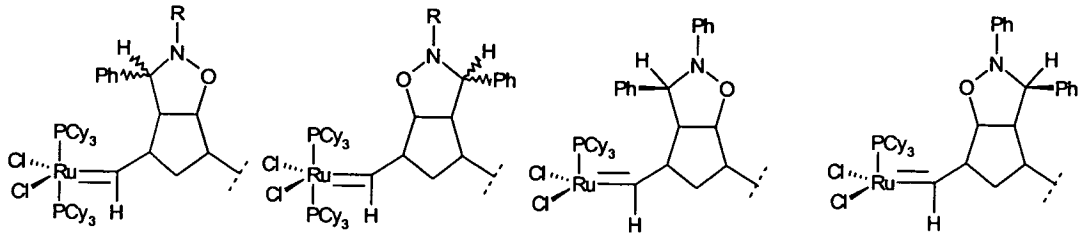
[a]Monomer:Initiator ratio; [b]measured by GPC in THF against polystyrene standards (860 – 2.43 million); [c]not observable.

Table 2.17 – Selected physical data for polymers from **110** and **113**

2.6.3.2 Monitoring of propagating species of isoxazolidino NBEs by ^{1}H NMR spectroscopy

The polymerisation of *C,N*-diphenyl isoxazolidine norbornene **111** and *C*-phenyl-*N*-methyl-isoxazolidine norbornene **114** using the initiator **1** in $CDCl_3$ was monitored by ^{1}H NMR spectroscopy. For the polymerisation of isoxazolidine **111** the main regioisomeric propagating species **135** and **136** were observed at 19.2 ppm along with a sharp singlet at 19.9 ppm attributable to the carbene proton from initiator **1**. At lower chemical shift there were two relatively broad

featureless signals centred at 18.8 and 18.6 ppm. As reported by Ivin *et al.*[170] these may be attributable to carbene protons from the regioisomeric propagating species containing a mono-phophine ligand bound ruthenium centre **139** and **140** (Figure 2.12). The analogous experiment using the *N*-methyl-*C*-phenyl-isoxazolidine **114** revealed peaks at 19.03 and 19.13 ppm which are assigned to **137** and **138** with the carbene proton of initiator **1** at 19.9 ppm.



135 R = Ph **136** R = Ph **139** **140**

137 R = Me **138** R = Me

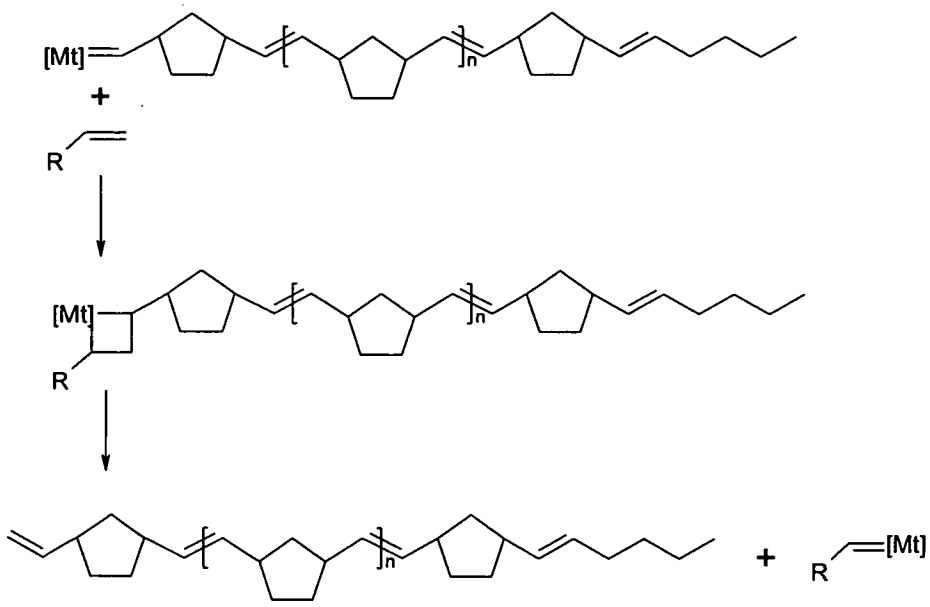
Figure 2.12

The reaction of **111** and **114** using initiator **2** in $CDCl_3$, was also monitored by ^1H NMR spectroscopy. However no propagating species were observed and only a sharp singlet at 19.1 ppm was present. Due to high propagation rates relative to the initiation rate of **2**, propagating species are undetectable using this initiator.

2.6.4 Molecular weight control

2.6.4.1 Introduction

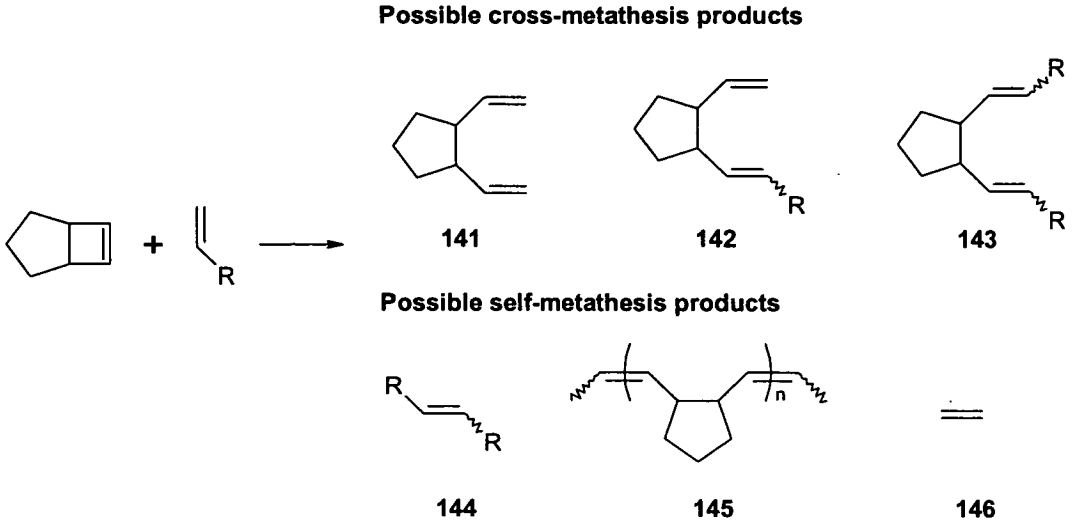
In ring opening metathesis polymerisation, cross-metathesis may occur when a cyclic olefin is polymerised in the presence of an acyclic olefin. For example, in the polymerisation of norbornene reaction at the growing chain end with the acyclic olefin terminates the polymer chain, Scheme 2.24, and this has the effect of lowering the molecular weight of the polymer produced.



Scheme 2.24

There are three different reasons for carrying out such a reaction. Firstly, simply to lower the molecular weight of a polymer in order to aid solubility,[19] in which case the concentration of acyclic olefin in the reaction mixture would be low and the resulting end groups may not even be apparent in the NMR spectrum of the polymer. Secondly, to form oligomers where the end groups can be functionalised and can be detected in an NMR spectrum of the polymer. These telechelic polymers find use as macro-monomers for the formation of block copolymers and networks.[171, 172]
In these two cases the acyclic olefin is known as the chain transfer agent (CTA). Most chain-transfer agents used are unsymmetrical and can produce any one of three different types of telomer. If the alkylidene groups are labelled Q_1 and Q_2 and the cyclic olefin labelled M_1 then the following telomers can be produced $Q_1(M_1)nQ_1$, $Q_2(M_1)nQ_2$ and $Q_1(M_1)nQ_2$ with the first two examples being symmetrical and the third unsymmetrical. A statistical distribution of the different telomers would be 1:2:1 for $Q_1(M_1)nQ_1$: $Q_1(M_1)nQ_2$: $Q_2(M_1)nQ_2$. However, when a terminal olefin such as pent-1-ene is used as a CTA with cyclopentene a strong bias towards the unsymmetrical telomer $[Q_1(M_1)nQ_2]$ was observed in a 1:40:1 ratio with the symmetrical analogues.[173] However, when an internal olefin such as hex-2-ene was used with cyclooctene a much lower ratio of 1:5:1 was obtained for the three possible units.[174]
The third type of cross metathesis reaction produces "dimeric" products, as outlined for a cyclobutene substrate and an alk-1-ene in Scheme 2.25. Despite the many possible products in any one reaction Snapper and coworkers[175] have found some selectivity with only product **142** being

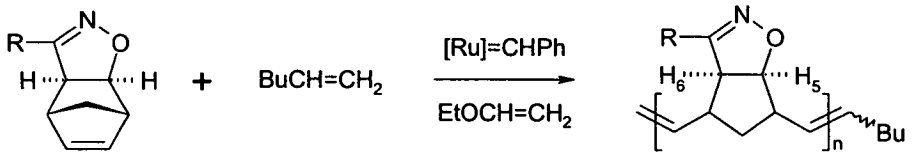
formed before the cyclobutane is consumed, after which **143** and **144** are formed. Even with this degree of product selectivity, there is no stereoselectivity observed.



Scheme 2.25

Although this reaction has enormous potential in synthesis, allowing production of new types of alkenes that would otherwise be difficult to produce, the lack of predictable regio- and stereoselectivity has prevented this method being widely used.[176] However, cross metathesis with alk-1-enes has proved to be well suited for molecular weight control in polymer applications.

2.6.4.2 ROMP of phenyl NBE 81 and ethoxycarbonyl NBE 82 in presence of hex-1-ene



81 R = Ph
82 R = EtO_2C

147 R = Ph
148 R = CO_2Et

Scheme 2.26

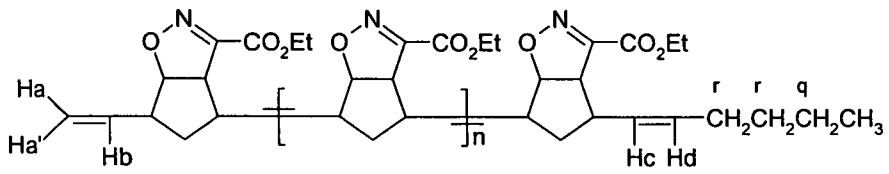
Molecular weight control was achieved through the use of hex-1-ene as a chain transfer agent. Varying amounts of hex-1-ene were dissolved in dichloromethane with *exo*-phenyl isoxazoline **81** or *exo*-ethoxycarbonyl isoxazoline **82** and to this was added a solution of initiator **2**. The reaction was terminated using ethyl vinyl ether and the oligomers afforded from precipitation in methanol.

The ^{1}H NMR spectra of the isoxazoline functionalised oligomers **147** and **148** contained signals for the isoxazoline protons H-6/H-5 and carbons C-5/C-6 which were compared with the cyclopentene model H-4/H-5 respectively (Table 2.18).

	Oligomer					Cyclopentene model				
R	Code	H-5	H-6	C-5	C-6	Code	H-5	H-4	C-5	C-4
Ph	**147**	4.56	3.36	87.7	56.8	**86**	5.16	3.99	87.3	51.6
CO_2Et	**148**	4.91	3.57	93.7	56.1	**88**	5.35	3.96	90.3	50.6

Table 2.18 – Chemical shifts of oligomeric isoxazoline protons compared to CPE models

The oligomer **148** gave NMR spectra in which the signals for the vinyl and hexenyl end groups were clearly discernable (Appendix 3). In the ^{1}H NMR spectrum the vinyl end group signals occurred at 5.9 (=CH), 4.9-5.1 (=CH_2) and the methyl of the hexenyl end group at 0.89 ppm. (The 3xCH_2 from the hexenyl group were overlapping with protons from the cyclopentene from the ring opened product). The signals for the vinyl end group in the ^{13}C NMR appeared at 138.8-139.1 (C-b) and 113.7-115.1 (C-a,a'), with the hexenyl signals at 133.2 (C-c), 128.4 (C-d), 30.4, 30.5, 30.8, 31.1 (2xC-r), 21.2, 21.3, 26.3, 26.4 (C-q) and 12.9, 13.1 (CH_3) (Appendix 3). The average degree of polymerisation (av DP) was calculated using end group analysis by integrating the methyl protons of the hexenyl end group against the internal H-5 isoxazoline proton. The molecular weights for the polymerisation of **82** in the presence of the chain transfer agent using **2** are summarised in Table 2.19, from which it is evident that there is good correlation between the GPC and NMR results.



148

Stereochemistry not inferred (HH, HT/TH, TT) in diagram

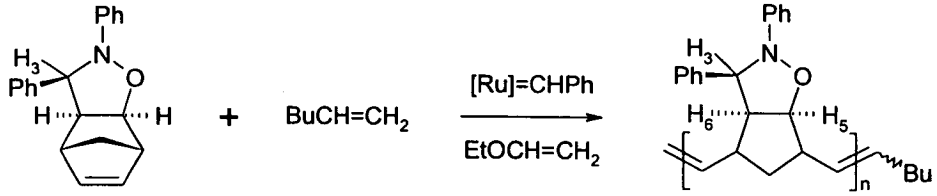
Figure 2.13

Code	[hex-1-ene] / [82]	Yield / %	M_n x 10^{-4}	M_w x 10^{-4}	PDI[a]	av Dp[a/b]
JM105	0.00	75	13.84	22.86	1.65	554[a]
JM110	0.05	96	3.29	4.78	1.45	159[a]/157[b]
JM119	0.10	99	0.34	[c]	[c]	[c]/16[b]
JM132	0.15	93	0.20	0.31	1.55	9[a]/8[b]
JM136	0.25	92	0.09	[c]	[c]	[ca]/4[b]

[a]Determined by GPC analysis in THF against polystyrene standards (860 – 2.43 million); [b]determined by NMR end group analysis; [c]not determined

Table 2.19 - Effect of chain-transfer agent (hex-1-ene) on average degree of polymerisation (av DP) of **148**

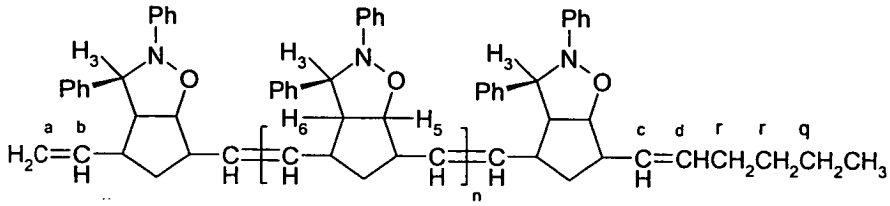
2.6.4.3 Molecular weight control of isoxazolidino norbornenes



111 R = Ph **149** R = Ph

Scheme 2.27

Polymers with controlled molecular weight of *exo-C,N*-diphenylisoxazolidino NBE **111** and *exo-C*-phenyl-*N*-methylisoxazolidine **114** were prepared using, varying amounts of hex-1-ene as chain transfer agent, as described previously for the the isoxazolino norbornenes **81** and **82** in Section 2.6.4.2. The isoxazolidino functionalised monomer (**111** or **114**) was dissolved in dichloromethane with hex-1-ene and to this was added a solution of the Grubbs initiator **1** or **2** (Scheme 2.27). The reactions were terminated with ethyl vinyl ether and precipitation in methanol afforded the oligomers **150** which were analysed by NMR spectroscopy.



150

Figure 2.14

Due to the broad peaks in the ^{1}H NMR spectrum it was difficult to discern the end group signals. A HETCOR experiment was carried out in order to confirm the structure of the oligomer. The isoxazolidino protons were present at 2.97 (H-6), 4.62 (H-5) and 4.72 ppm (H-3a). The ^{13}C-NMR spectrum was more informative with end group signals present at 12.9 (CH_3), 21.3 (C-q), 25.8, 30.8 (2 x C-r), 112.5 (C-a), 116.1 (C-d), 121.4 (C-c) and 149.3 ppm (C-b).

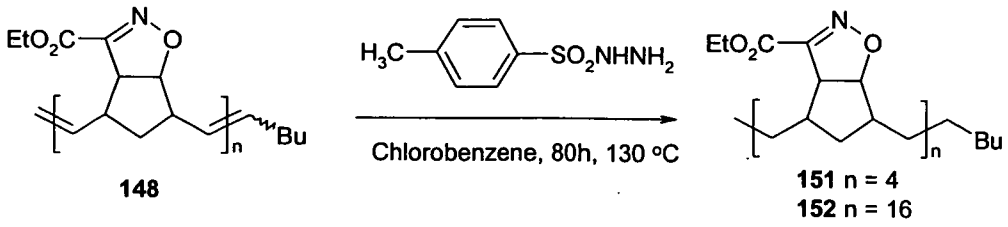
Monomer	Initiator	hex-1-ene / %	Yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI
111	**2**	2	76	1.35	1.25	43[a]	1.08
111	**1**	10	84	0.32	0.26	6[a]/8[b]	1.23
111	**2**	50	89	[c]	0.06	2[b]	[c]

[a]Determined by GPC in THF against polystyrene standards (860 – 2.43 million); [b]determined by end group analysis; not determined

Table 2.20 – Effect of varying [monomer]:[chain transfer agent] on av DP

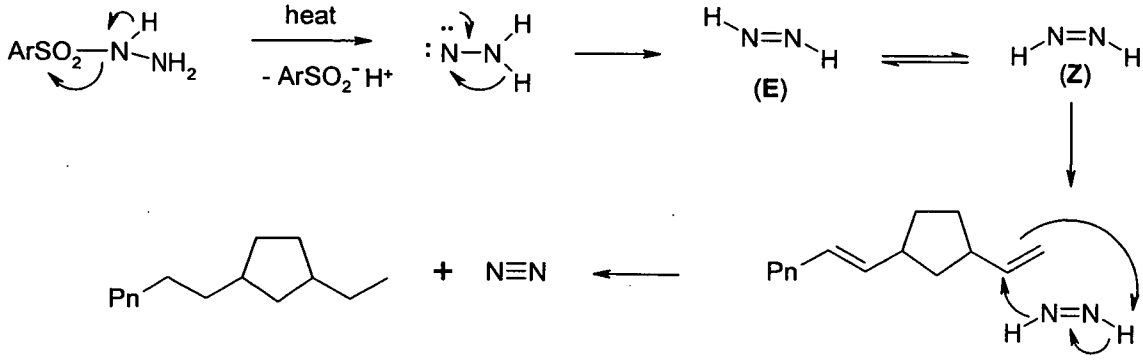
2.6.5 Reduction of homopolymers

Previous work by Hamilton *et al.*[177] established that it is possible to hydrogenate the alkene units in ring-opened polymers of substituted norbornenes by reacting with *p*-toluenesulfonyl hydrazide. They reported[177] the synthesis of polyNBE and polyNBD with *cis* contents = 7 - 98% using a variety of catalyst systems, and subsequent removal of *cis/trans* microstructure by hydrogenation in order to determine the tacticity. For the purposes of this thesis, however, hydrogenation of the isoxazoline functionalised oligomer **148** was carried out to investigate the compatibility of the isoxazolino norbornene with the diimide reducing species. Thus, samples of oligomer **148** (n = 4, 16) were converted into their hydrogenated analogues **152** (85%) by treatment with *p*-toluenesulfonyl hydrazide in chlorobenzene at 130 °C (Scheme 2.28). In the ^{13}C NMR spectrum of the product the absence of olefinic resonances in the region 115-140 ppm and the appearance of new peaks at 30-33 ppm indicated that the reaction had gone to completion. Characteristic signals were also present at 160 (C=O), 153 (C=N), 94 (C-5), 60-61 (OCH_2) and 56 ppm (C-4) demonstrating that isoxazoline moiety is stable to the diimide reduction conditions.



Scheme 2.28

The mechanism of the hydrogenation process as proposed by Cusack *et al.*[178] is shown in Scheme 2.29. The actual reducing species of hydrogenation *via* thermolysis of *p*-toluenesulfonyl hydrazide is diimide and, although both *E* and *Z* forms of diimide are produced, only the *Z* form reduces the double bond.



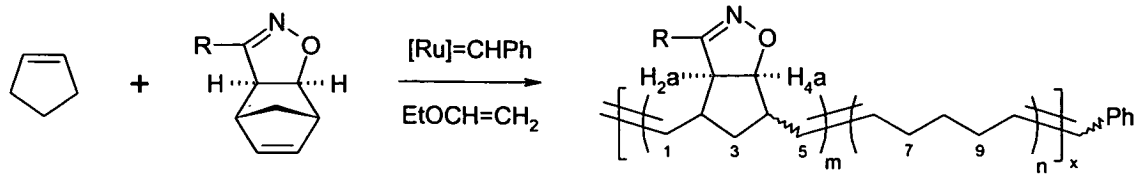
Scheme 2.29

2.7 Copolymerisations

Copolymers with varying molecular architecture can be synthesised by varying the reaction conditions. Copolymers with block distributions (only possible with living polymer systems) are synthesised by the sequential addition of comonomers. Random copolymers are prepared by polymerising a comonomer mixture. An alternating copolymer distribution is the most synthetically challenging and can be achieved by the methods outlined in Section 1.12.

2.7.1 Random copolymers

In order to explore the feasibility of preparing random copolymers involving isoxazoline norbornenes as one of the monomers, a series of experiments were performed using cyclopentene as a representative comonomer at varying ratios as shown in Scheme 2.30.



81 R = Ph

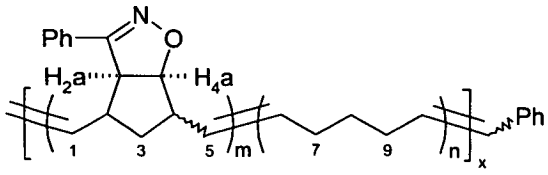
82 R = CO_2Et

153 R = Ph

154-159 R = CO_2Et

Scheme 2.30

2.7.1.1 Cyclopentene (CPE) / phenyl NBE 81



153

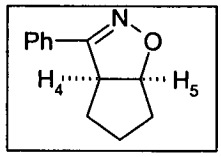
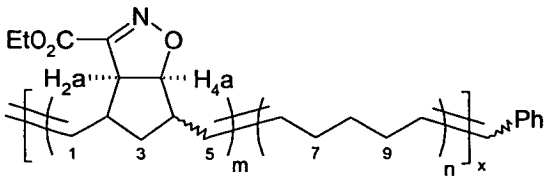


Figure 2.15

According to the standard procedure, a solution of the Grubbs complex **2** in dichloromethane was added to a solution of cyclopentene and phenyl isoxazoline **81** in dichloromethane and the reaction mixture stirred for 20h at room temperature. The reaction was terminated with ethyl vinyl ether and the copolymer **153** (95%) was afforded by precipitation in methanol (Figure 2.15). Signals from the ^{1}H NMR spectra of **153** were discernable at 7.39 ppm and 7.61 ppm (PhCH) and evidence that copolymerisation had occurred was the presence of signals at 1.02-1.96 (H-7,8,9), 3.77 (H-2a) and 4.82 ppm (H-4a). The ^{13}C NMR spectrum contained peaks at 26.7, 29.2 and 31.9 (C-7,8,9), 57.9 (C-2a), 92.5 (C-4a), 127.3–128.8 (PhC) and 159.2 ppm (C=N) providing evidence that copolymerisation had occurred.

2.7.1.2 Cyclopentene (CPE) / ethoxycarbonyl NBE 82



154-159

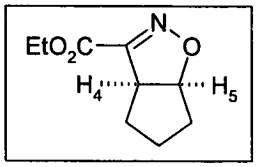


Figure 2.16

A solution of the ruthenium benzylidene **2** in dichloromethane was added to a solution of cyclopentene and ethoxycarbonylisoxazoline NBE **82** in dichloromethane. The reaction was stirred for 20h at room temperature and then terminated with ethyl vinyl ether. The copolymer was isolated by precipitation in methanol (Figure 2.16). From the ^{1}H NMR spectra of the copolymers signals for the ester group were discernable at 1.27 ppm ($CO_2CH_2CH_3$) and 4.26 ppm ($CO_2CH_2CH_3$) and evidence that copolymerisation had occurred was the presence of signals attributable to the pentenylene chain (H-7,8,9) at 1.32-1.95 ppm and also resonances for isoxazoline protons at 3.49 (H-2a) and 4.84 ppm (H-4a). The ^{13}C NMR spectrum contained signals at 25.8, 27.9 and 31.0 ppm attributable to carbons of the pentenylene chain (C-7,8,9) and peaks for the isoxazoline carbons at 56.6 (C-2a) and 93.7 ppm (C-4a). Resonances in the ^{13}C NMR spectrum for the ester group were present at 13.2 ($CO_2CH_2CH_3$), 60.9 ($CO_2CH_2CH_3$) and 159.5 ppm ($CO_2CH_2CH_3$) and confirmation that the isoxazoline moiety was intact was the presence of a peak at 152.8 ppm (C=N). It was not possible to estimate the m:n ratio from the ^{1}H NMR spectrum due to the overlap of the H-3 signal with those corresponding to H-7,8,9. Molecular weight measurements were made on the copolymers using GPC.

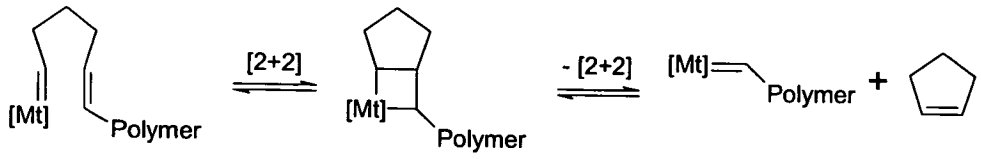
Copolymer	Code	[CPE]:[**82**]:[**2**]	yield / %	$10^{-4}M_w$[a]	$10^{-4}M_w$[b]	$10^{-4}M_n$	PDI
154	**JM155**	20:80:1	95	9.33	-	4.83[c]	1.93
155	**JM152**	40:80:1	91	7.08	0.18	[d]	[d]
156	**JM145**	80:80:1	83	2.82	0.12	[d]	[d]
157	**JM137**	160:80:1	81	[e]	[e]	[e]	[e]
158	**JM144**	320:80:1	69	1.78	0.11	[d]	[d]
159	**JM148**	640:80:1	36	0.12	-	0.07[c]	1.60

[a]M_w of high weight fraction; [b]M_w of low weight fraction; [c]copolymers with unimodal distribution allow for measurement of M_n; [d]unable to calculate PDI of copolymers with bimodal distribution; [e]not determined.

Table 2.21 – Molecular weight determination of random copolymers of ethoxy-NBE and cyclopentene

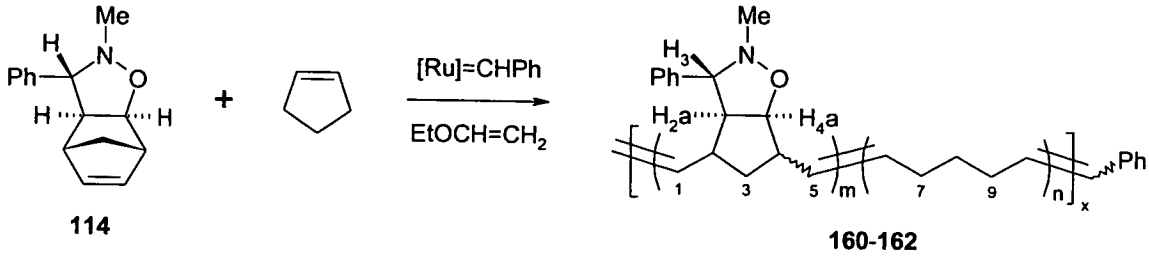
The GPC measurements for the random copolymerisations of ethoxycarbonylisoxazoline NBE **82** and CPE at various ratios produced an unexpected set of results (Table 2.21). Primarily, it was noted that in most cases a bimodal distribution resulted for the copolymer, whereas at the limiting comonomer ratios (i.e. a high excess of one or the other monomer) a unimodal distribution resulted. One possible explanation for the bimodal distribution may be that in certain cases for the ROMP of NBE derivatives with Ru initiators, the intramolecular π complexation of the growing polymer chain competes with propagation. It is this propensity for backbiting that makes **2** such a reactive catalyst for RCM.[53] Bimodal distributions in GPC traces could therefore be attributed to this

secondary metathesis between the growing chain and the adjacent polymer double bond, as illustrated in Scheme 2.31. Such a backbiting process is less likely for the sterically more hindered norbornene derived alkene units.



Scheme 2.31

2.7.1.3 Random copolymers of cyclopentene (CPE) / *exo*-4-methyl-5^{exo}-phenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene (114)



Scheme 2.32

In an analogous experiment to the copolymerisation of isoxazoline NBEs **81** and **82** with cyclopentene, the copolymerisation of *exo*-4-methyl-5^{exo}-phenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene **114** and CPE was investigated. Therefore, a solution of the **2** in dichloromethane was added to a solution of cyclopentene and *exo*-isoxazolidino NBE **114** in dichloromethane and the reaction mixture stirred for 20h at room temperature after which the polymerisation was terminated with ethyl vinyl ether. Precipitation in methanol afforded the product as a brown tar (Scheme 2.32). From the ^{1}H NMR spectra of the random copolymers, signals for the phenyl group were discernable at 7.19-7.50 ppm and evidence that copolymerisation had occurred was the presence of signals attributable to the pentenylene chain (H-7,8,9) at 1.18-1.31 and 1.78-1.92 ppm and also resonances for isoxazolidine protons at 2.49-2.77 (H-2a) and 4.37 ppm (H-4a). The ^{13}C NMR spectrum contained signals at 25.9, 28.3 and 30.9 ppm attributable to carbons of the pentenylene chain (C-7,8,9) and peaks for the isoxazolidine carbons at 63.1 (C-2a), and 87.8 ppm (C-4a) providing evidence that copolymerisation had taken place. The signals for the

isoxazolidine ring were present at 80.1 (C-3), 29.3 (N-CH_3) with resonances for the phenyl group at 126.6–127.4 ppm (PhCH).

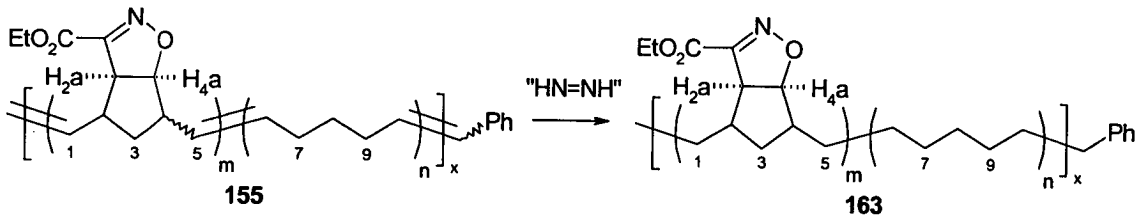
Copolymer	Code	[CPE]:[**114**]:[**2**]	yield / %	$10^{-4}M_w$[a]	$10^{-4}M_w$[b]
160	**JM151**	40:80:1	84.4	6.20	0.11
161	**JM143**	160:80:1	65.8	5.01	0.11
162	**JM150**	640:80:1	61.8	2.82	0.10

[a]M_w of high weight fraction; [b]M_w of low weight fraction.

Table 2.22 – Molecular weight determination of random copolymers **160-162** of *N*-methyl-*C*-phenyl-NBE and cyclopentene

The GPC measurements for the random copolymerisations of **114** and CPE at various ratios produced an unexpected set of results (Table 2.22). Primarily, it was noted that a bimodal distribution resulted for the each copolymer. A similar set of results was obtained from the copolymerisation of isoxazolino NBEs **81** and **82** with CPE as described in Section 2.7.1.2 and 2.7.1.3. It was believed that a backbiting reaction involving the propagating ruthenium alkylidene and a less sterically hindered alkene unit from a poly(1-pentenylene) chain occurred, generating a high molecular weight fraction with the expulsion of a second lower molecular weight product.

2.7.1.4 Reduction of random copolymer 155



155 **163**

Scheme 2.33

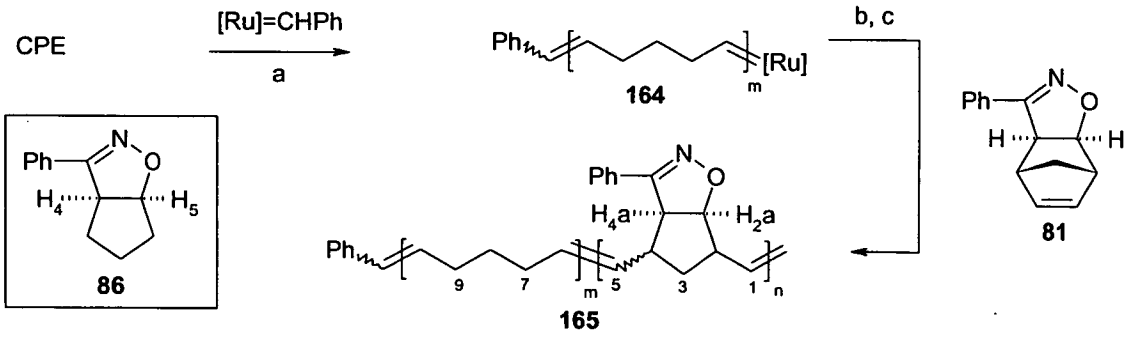
The random copolymer **155** (CPE / ethoxycarbonyl NBE **82**) was dissolved in chlorobenezene and to this was added *p*-toluenesulfonyl hydrazide and the solution refluxed for 2h. Precipitation in methanol yielded a light brown tar (94%) (Scheme 2.33). In the ^{1}H NMR spectrum of the product the absence of olefinic resonances at 5.29-5.52 ppm and the appearance of new peaks at 1.18-1.32 ppm indicated that the reaction had gone to completion. A signal at 0.80-0.82 ppm was assigned as the methyl group of the hydrogenated analogue. In the ^{13}C NMR spectrum of the reduced copolymer the absence of olefinic resonances at 128.0-131.1 and the appearance of new peaks at

33.8-34.8 was further proof that the reaction had gone to completion. The peaks attributable to H-2,4 for the unsaturated polymer are split into two multiplets *cis* 2.59 ppm and *trans* 2.90 ppm from which the *cis* content can be deduced σ_C = 0.77. Upon hydrogenation, these peaks were removed and replaced by a signal at 1.18-1.32 ppm, consistent with the removal of double bonds. Characteristic signals were also present in the ^{13}C NMR spectrum at 160.0 (C=O), 153.1 (C=N), 94.3 (C-4a), 60.7 (OCH_2), 56.3 ppm (C-2a) and in the ^1H NMR spectrum at 4.68-4.74 (C-4a), 4.20-4.30 (OCH_2) and 3.31-3.36 ppm (C-2a) demonstrating that the isoxazoline moiety is stable to the diimide conditions.

2.7.2 Block copolymers

Due to the living nature of the Grubbs initiators,[33] the possibility of preparing diblock copolymers incorporating isoxazoline norbornenes was examined. In a typical example cyclopentene (67 equivs.) was stirred at room temperature with initiator **1** or **2** (1 equiv.) for 24h and then an aliquot of phenylisoxazoline NBE **81** (67 equivs.) was added to the reaction vessel and stirred for a further 24h. The mixture was then heated at 50 °C for 6h before termination with ethyl vinyl ether (Scheme 2.34). A cyclopentene homopolymer was prepared under the same conditions and monomer:initiator ratio in order to make a molecular weight (M_n) comparison between the resulting poly(1-pentylene) homopolymer and the diblock copolymer.

2.7.2.1 Cyclopentene (CPE) / phenyl NBE 81



Reagents: a) [Ru]=CHPh **1** / **2**, 24 h @ r.t.; b) **81**, 24 h @ r.t then 6 h @ 50 °C; c) $EtOCH=CH_2$ for 2 h

Scheme 2.34

Cyclopentene and phenyl isoxazoline **81** were sequentially polymerised in dichloromethane using initiator **1**. The resulting block copolymer **165** had a higher molecular weight (M_n = 0.70 x 10^4) relative to that of the pentenylene homopolymer (M_n = 0.10 x10^4) as determined by GPC (Table 2.23). The PDI of the block copolymer (1.12) was approximately the same as that of the starting

hompolymer (1.14). A block copolymer using the same monomers was prepared with the second generation initiator **2** using the same procedure. M_n increased from 0.15 x10^{-4} (av DP = 21) for pentenylene homopolymer to 2.39 x10^{-4} (av DP = 21/107) for the block copolymer after the addition of *exo*-phenyl isoxazoline **81**. The PDI increased from 1.12 to 1.33. The increase in molecular weight and polydispersity in going from **1** to **2** is as expected attributable to the high propagation rate (k_p) and slow initiation rate (K_i) of the latter case.

monomer[a]	equiv[a]	time (h)[a]	I	10^{-4} M_n[b]	10^{-4} M_n[c]	PDI	yield[d]
CPE / **81**	40/40	24/30	**1**	1.86	0.70	1.12	71
CPE / **81**	40/40	24/30	**2**	1.86	2.39	1.33	75

[a]the order in which monomers were added, the equivalents of each, and the time elapsed at each stage match the orders shown in columns 1-3. [b]Calculated from the monomer/catalyst ratio. [c]Measured by GPC in THF against polystyrene standards (860 – 2.43 million). [d]Isolated yield.

Table 2.23 – Synthesis of diblock copolymers of CPE / **81** using **1** and **2**

Interestingly, the copolymers **165** produced from CPE and monomer **81** using **1** and **2** have narrower PDIs (1.12 and 1.33) than the corresponding homopolymers of **81** initiated using **1** and **2** (M_w/M_n = 1.97 and 2.18). Grubbs *et al.*[134] observed a similar narrowing of PDIs in the preparation of diblock copolymers from a maleimide fused oxa-norbornene and a silyl ether derivatised NBE. Applying Grubbs' postulation[134] to the synthesis of **165**, the ruthenium carbene **164** initiates faster than the original carbenes **1** and **2** resulting in $k_i \sim k_p$ for the subsequent polymerisation of **81**. This results in copolymers with narrower PDI values (Scheme 2.34).

From the ^{1}H NMR spectra of the block copolymers signals for the phenyl group were discernable at 7.32-7.49 ppm and 7.50-7.74 ppm and evidence that copolymerisation had occurred was the presence of signals attributable to the pentyl chain (H-7,8,9) at 1.18-1.98 ppm and also resonances for isoxazoline protons at 3.41-3.65 (H-2a) and 4.65-4.70 ppm (H-4a). The ^{13}C NMR spectrum contained signals at 32.8, 35.0 and 37.2 ppm attributable to carbons of the pentyl chain (C-7,8,9) and peaks for the isoxazoline carbons at 59.2 (C-2a) and 92.7 ppm (C-4a). Resonances for the phenyl group were present at 127.2–128.8 ppm (PhC) and confirmation that the isoxazoline moiety was intact was the presence of a peak at 159.6 ppm (C=N).

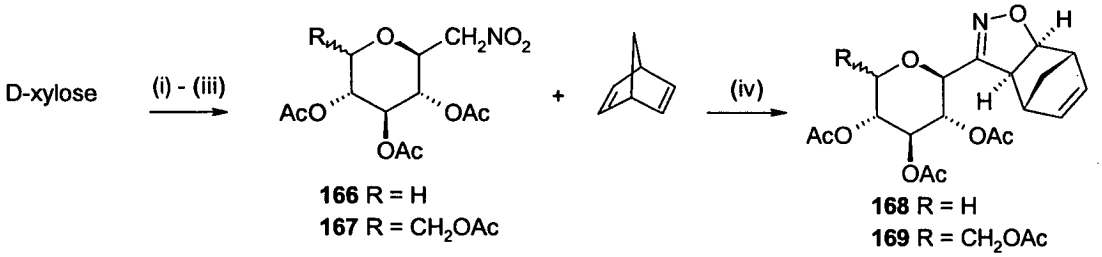
Part 2 – Synthesis of carbohydrate functionalised polymers

2.8 Synthesis of glycosyl isoxazolino norbornenes as monomers for ROMP

2.8.1 Synthesis of glycosyl nitrile oxide precursors

2.8.1.1 Introduction

The synthesis of carbohydrate functionalised polymers via ROMP requires the preparation of monomers in the form of sugar containing norbornenes. Monomers based on this skeleton have been widely used in the preparation of functionalised polymers.[109, 115, 136] The polymer precursors synthesised by the Nitrile Oxide Cycloaddition chemistry (NOC) route require the cycloaddition of pyranosylnitrile oxides to norbornadiene. As the dehydration of pyranosylnitromethanes is known[179] to be an effective method for the generation of pyranosylnitrile oxides, this method was adopted for the present work (Scheme 2.35). D-xylose and D-glucose -derived nitromethyl sugars **166** and **167** were selected due to the commercial availability of the starting materials, the parent monosaccharides, and the common nature of these monosaccharides in biological applications.



166 R = H
167 R = CH_2OAc

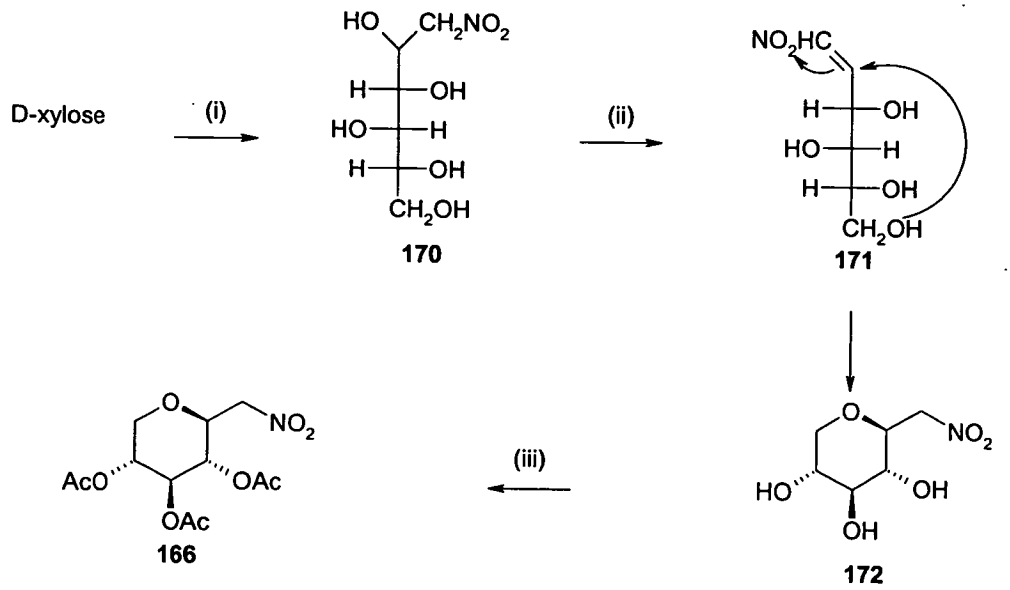
168 R = H
169 R = CH_2OAc

Reagents: (i) $MeNO_2$ / NaOMe, MeOH; (ii) H_2O, reflux; (iii) Ac_2O/CF_3SO_3H; (iv) RNCO, TDI, Et_3N

Scheme 2.35

2.8.1.2 Synthesis of acetylated pyranosylnitromethanes

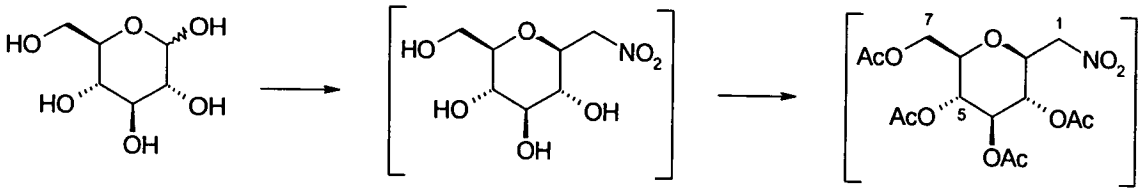
Tri-*O*-acetyl-β-xylopyranosylnitromethane **166** was synthesised in three steps from D-xylose using a modified version of the procedure described by Köll *et al.*[180] (Scheme 2.36). In the first stage, base catalysed addition of nitromethane to D-xylose in its acyclic form proceeds via a nitro aldol (Henry) reaction to give the nitroalditol **170** as described by Fischer and Sowden.[181] The product was not isolated but converted directly to the β-xylopyranosylnitromethane **172** by heating in water. The mechanism is believed to involve dehydration to the α-nitro olefin **171** followed by thermal cyclisation. Acid catalysed acetylation yielded the title compound **166** (40% overall yield from D-xylose).



(i) CH_3NO_2, NaOMe; (ii) H_2O, reflux; (iii) Ac_2O, CF_3SO_3H

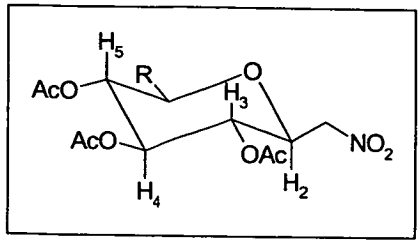
Scheme 2.36

The peracylated glucose derived nitromethyl compound **173** was prepared similarly in three steps, Scheme 2.37, from D-glucose in a 20% overall yield. The 10.1 Hz coupling between H-2 and H-3 supports the assignment of β-configuration at the anomeric position. An equatorial-axial coupling of ~ 2-3 Hz would be expected for the corresponding α-anomer. A summary of the coupling constants for 3,4,5-tri-*O*-acetyl-β-D-xylopyranosylnitromethane **166** and 3,4,5,7-tetra-*O*-acetyl-β-D-glucopyranosylnitromethane **173** is given in Table 2.28.



173

Scheme 2.37



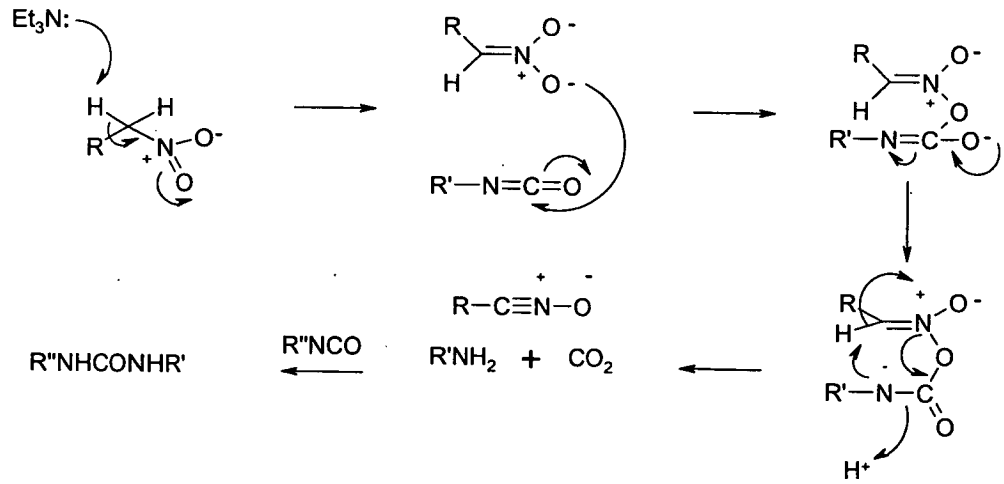
Coupling	D-Xyl (**166**) *J*/Hz	D-Glc (**173**) *J*/Hz
2,3	10.1	10.1
3,4	9.3	9.3
4,5	9.4	9.3
5,6	5.7/10.6[a]	10.0

[a]*J*/Hz 5-6a 5.7; 5-6b 10.6

Table 2.24 – Coupling constants of **166** and **173**

One of the features of nitrile oxides is their short lifetime and tendancy to dimerise to furoxans. Thus, they are generally formed *in situ* from suitable precursors in the presence of the other reactant, in this case the dipolarophile.

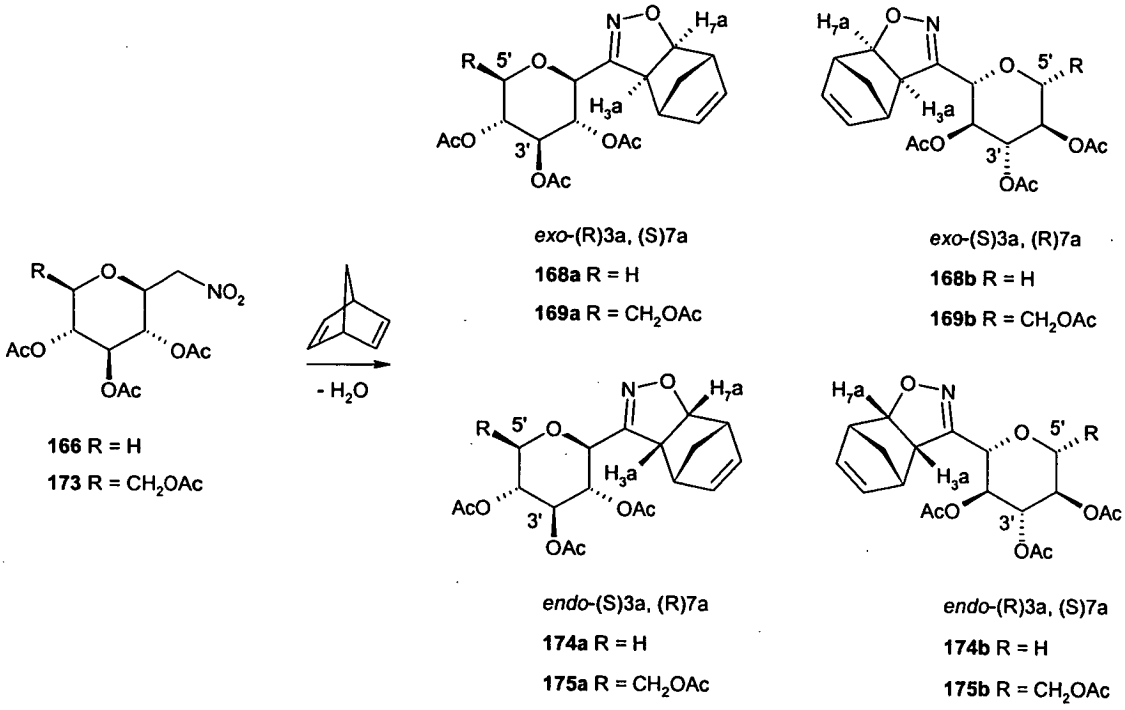
The generation of glycosylnitrile oxides was based on a Mukaiyama-type[179] dehydration of pyranosylnitromethanes. Modification of the Mukaiyama method was made with phenyl isocyanate being replaced by 2,4-tolylene di-isocyanate (TDI) as dehydrating agent and quenching the reaction with 1,2-diaminoethane. Both the aniline by-product and excess TDI are thus converted into polymeric urea which can be removed by filtration. The proposed mechanism for the reaction is shown in Scheme 2.38 below. It involves initial deprotonation of the nitromethyl group to form the nitronate anion, which then reacts with the isocyanate. Collapse of the resulting adduct and loss of CO_2 generates the nitrile oxide along with amine. The latter undergoes further reaction with the isocyanate to form a urea.



Scheme 2.38

2.8.2 Synthesis of glycosyl isoxazolino norbornenes as monomers for ROMP

Although the reaction of pyranosyl nitrile oxides with norbornene has been reported,[182] the corresponding cycloaddition with norbornadiene has yet to be investigated. The addition of nitrile oxides to norbornadiene is known[155, 156] to yield a mixture of *exo* / *endo* adducts, and 2:1 adducts can also be formed by reaction at the second alkene unit (see also Section 2.5.2). In order to minimse the formation of furoxan by-product and 2:1 adducts the reactions were therefore carried out in a large excess of the dipolarophile (Scheme 2.39).

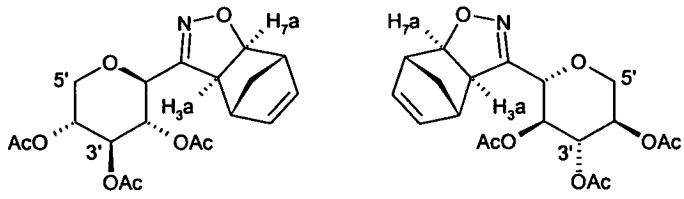


Scheme 2.39

2.8.2.1 *exo*-3-(2',3',4'-Tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole (Xylose NBE) 168 and 174

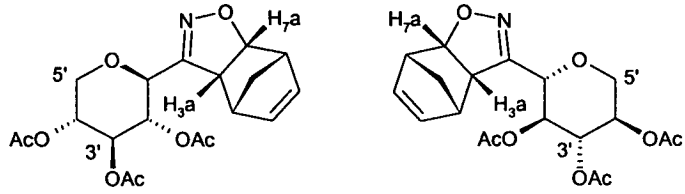
The acetylated xylopyranosylnitromethane **166** and norbornadiene were stirred in toluene and to this was added triethylamine and TDI. The reaction was heated at 75 °C for 7 days after which 1,2-diaminoethane was added. The reaction mixture was stirred for a further one hour and then filtered to remove the polymeric urea. Removal of the solvent afforded an oil which was subjected to dry flash chromatography affording two fractions. The first fraction consisted of a mixture of the *exo* diastereomers **168a** and **168b** (63%) and then a second fraction containing a mixture of the *endo* diastereomers **174a** and **174b** (15%) (Figure 2.18). From the ^{13}C NMR spectrum of the *exo* adducts

168a and **168b** a diastereomeric ratio of 62:38 was measured. For the *exo* products the isoxazoline protons 3a-H (δ_H 3.42) and 7a-H (δ_H 4.94, $J_{3a,7a}$ 9.0 Hz) have small couplings to the adjacent bridgehead protons 4-H and 7-H of 1.9 and 1.5 Hz respectively. The ^{1}H NMR spectrum showed three singlets between 2.04 and 2.06 ppm corresponding to the CH_3 groups of the acetate protecting groups. The β-configuration is confirmed by the the $J_{1',2'}$ value of 9.8 Hz. The ^{13}C NMR spectrum showed three signals between 20.9 and 21.5 ppm (CH_3) and three more at 169.7 – 170.0 ppm (C=O) due to the acetate protection. The presence of the isoxazoline ring was confirmed by diagnostic isoxazoline signals at 58.4, 88.4 and 154.0 ppm corresponding to C-3a, C-7a and C=N. [For ease of use, *exo*-3-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole **168** will now be called xylose NBE **168**].



exo-(R)3a, (S)7a
168a

exo-(S)3a, (R)7a
168b



endo-(S)3a, (R)7a
174a

endo-(R)3a, (S)7a
174b

Figure 2.17

2.8.2.2 *exo*-3-(2',3',4',5'-Tetra-*O*-acetyl-β-D-glucopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole (Glucose NBE) 169/175

Reaction of the glucopyranosylnitromethane **173** with norbornadiene yielded *endo* diastereomers **175a** and **175b** (10%) and *exo* diastereomers **169a** and **169b** (59%) as shown in Figure 2.19. The *exo* adducts **169a** and **169b** were a mixture of diastereomers in a 55:45 ratio which was contaminated with a 15% trace of the *endo* adducts **175a** and **175b** as determined from the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of the *exo* mixture revealed signals at δ_H 1.99-2.06 (4x$COCH_3$), 3.28 ($J_{3a,4}$ 1.9 Hz, $J_{3a,7a}$ 8.3 Hz, 3a-H) and 4.74 ppm ($J_{7a,7}$ 1.6 Hz, $J_{7a,3a}$ 8.3 Hz, 7a-H), The β-configuration is confirmed by the the $J_{1',2'}$ value of 9.9 Hz. The ^{13}C NMR spectrum showed peaks at

20.5-21.3 (4xCOCH_3), 56.7 (C-3a), 89.4 (C-7a), 153.5 (C=N) and 169.2 – 170.4 ppm (4x$COCH_3$). (As with the xylose analogue, *exo*-3-(2',3',4'-tri-*O*-acetyl-β-D-glucopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **169** will now be called glucose NBE **169**).

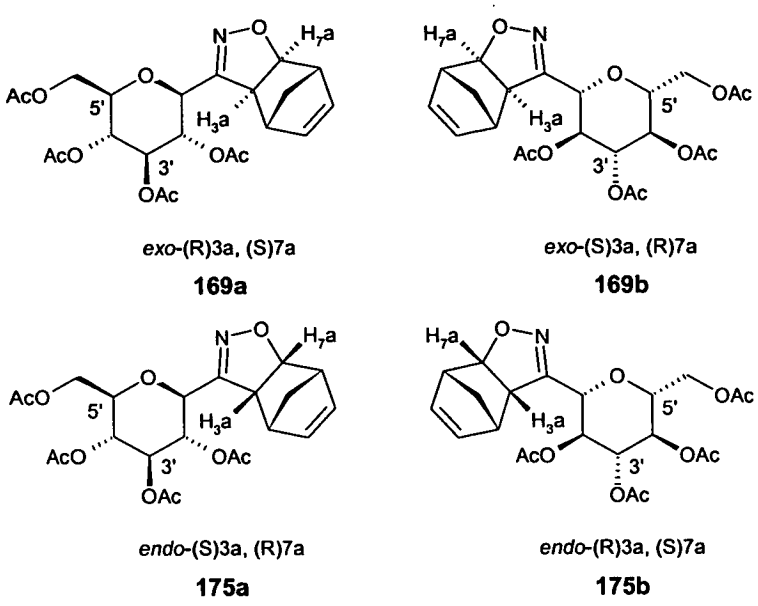
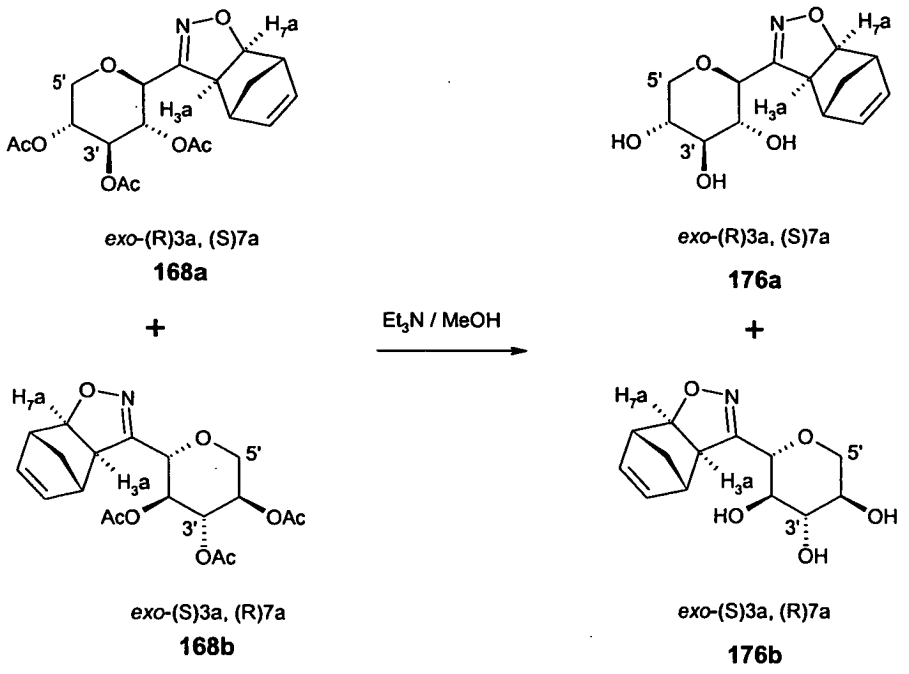


Figure 2.18

2.8.2.3 *exo*-3-(2',3',4'-Tri-hydroxy-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[*d*]isoxazole 176

The biological applications outlined in Section 1.9.4 describe processes which are mediated by multivalent cell surface carbohydrate interactions with proteins. They are implicit for glycopolymers with a deprotected carbohydrate moiety. One of the approaches to be investigated for the preparation of isoxazoline glycopolymers with free sugar residues (Section 2.12) required the polymerisation of *exo*-3-(2',3',4'-tri-hydroxy-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[*d*]isoxazole **176a** and **176b**. Deacetylation of xylose NBE **168** was achieved using the method of Bazin *et al.*[184] Thus **168** in anhydrous methanol containing triethylamine was stirred at room temperature under nitrogen for 36 h. The solvent was removed *in vacuo* and the resulting oil crystallized from ethanol to give a white solid (93%). The ^{1}H NMR spectrum of the deprotected xylose NBE **176** showed the disappearance of the three singlets at 2.04-2.06 ppm. The absence of signals at δ_C 20.6 ppm (3xCOCH_3) and 169.5 ppm (3x$COCH_3$) in the ^{13}C NMR spectrum and its solubility in water was evidence of deacetylation. Peaks at 56.9 (C-3a), 88.7 (C-7a) and 156.4 ppm (C=N) proved that the isoxazoline ring was still intact.

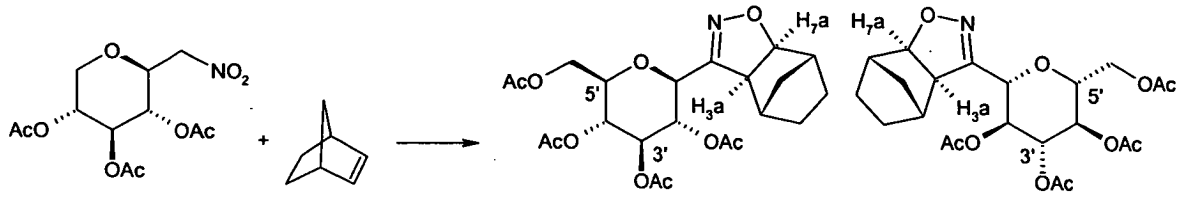


Scheme 2.40

2.9 Homopolymerisation of glycosyl isoxazolino norbornenes

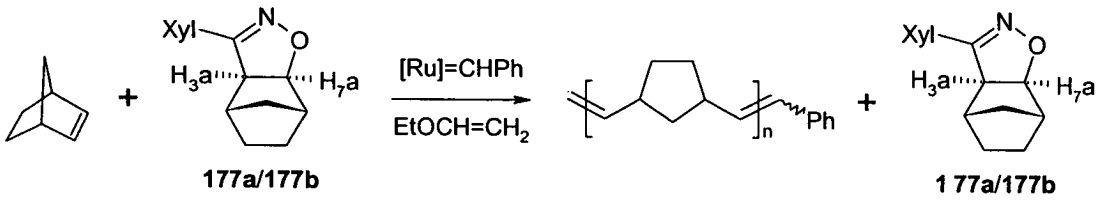
2.9.1 Test reaction – ROMP of NBE in presence of *exo*-3-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[*d*]isoxazole 177a/b

Before attempting polymerisation of the glycosyl isoxazolino norbornenes the compatibility of the isoxazoline ring and the sugar moiety with the ruthenium initiators was tested by subjecting a mixture of *exo*-3-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[*d*]isoxazole **177a/b** (xylose NBA **177**) and norbornene to ROMP conditions using initiator **1**. In order to assess the compatibility of the isoxazoline ring and its sugar substituent with initiator **1**, xylose NBA **177** was prepared as it contains no double bond in the norbornyl framework. Reaction of nitromethyl xylose and norbornene yielded the crude product which was subjected to dry flash chromatography and afforded the *exo* enantiomers **177a** and **177b** as a white crystalline solid (66%) with a diastereomer ratio of 55:45 (Scheme 2.41). It was not possible to measure the coupling constants (*J*) for H-3a/H-7a to provide evidence of *exo*-adduct formation. However, it has been well documented[156] that reaction of norbornene with nitrile oxides affords only *exo*-adducts.



Scheme 2.41

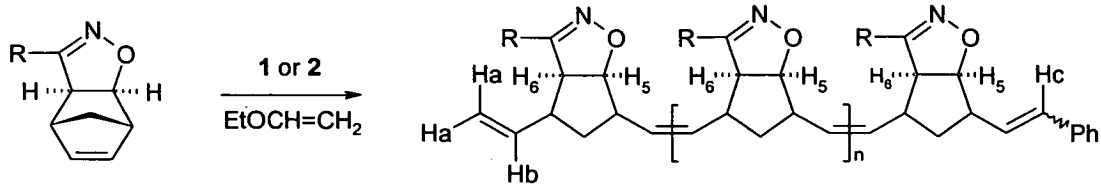
A solution of the Grubbs initiator **1** was added to a solution of norbornene and xylose NBA **177** in dichloromethane. The reaction was then terminated with ethyl vinyl ether and the reaction mixture treated with DMSO overnight. Precipitation in methanol afforded polynorbornene (99%) which was indistinguishable from an authentic sample (Scheme 2.41). Concentration of the filtrate *in vacuo* and column chromatography of the residue afforded recovered xylose NBA **177** (94%). The recovery of **177** and the high yield of polyNBE demonstrated that the isoxazoline was intact after the subsequent ROMP indicating that the Grubbs initiator **1** had no effect on the isoxazoline ring and its sugar substituent, and vice versa



Scheme 2.42

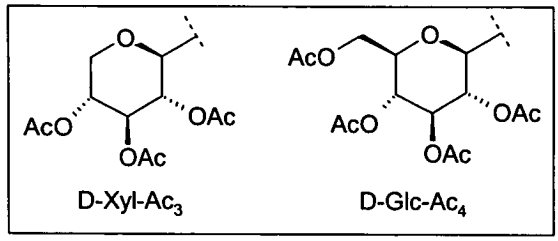
2.9.2 Synthesis of glyco homopolymers

The procedures for the polymerisations of xylose NBE **168** and glucose NBE **169** were similar to those for the phenyl NBE **81** and ethoxycarbonyl NBE **82** as described in Section 2.6. In a typical example, a solution of the Grubbs initiator **1** was added to the xylose NBE **168** in dichloromethane and the reaction stirred for two hours before termination with ethyl vinyl ether. Precipitation in methanol afforded the xylose or glucose isoxazoline functionalised polymers **178** and **179** (Scheme 2.43 and Table 2.25).



168 R = D-Xyl-Ac_3
169 R = D-Glc-Ac_4

178 R = D-Xyl-Ac_3
179 R = D-Glc-Ac_4



Scheme 2.43

2.9.2.1 Synthesis and NMR spectroscopic characterisation of glycopolymers

2.9.2.1.1 Xylose isoxazoline functionalised polymer 178

The ^{1}H NMR spectrum of polymer **178** ([**168**]:[**1**] = 30:1; entry 1, Table 2.29) contained broad signals which are characteristic of these types of polymers. A HETCOR (Heteronuclear correlation) experiment then allowed for full assignment of the ^{1}H NMR spectrum. Broad resonances were observed at 5.32-5.60 ppm which were assigned as the olefinic protons and broad signals between 1.18 and 1.87 ppm and between 2.49 and 2.76 ppm are characteristic of ring-opened polymers of this general type. Signals at 6.10-6.27, 6.41-6.59 and 8.38 ppm are attributable to end group olefinic resonances including vinylic protons H_a, $H_{a'}$ and H_b and the styryl proton H_c (Scheme 2.47). A broad multiplet centred at 7.31 ppm is assigned as the phenyl group. In contrast the ^{13}C NMR spectrum of **178** was much better resolved and allowed for a fuller assignment. The ^{13}C NMR spectra of these polymers showed relatively sharp resonances for the sugar ring carbons at 67.3, 69.4, 69.6, 73.6 and 75.2 ppm (C-1' – C-5') indicating a relatively uniform environment of side chains, including those characteristic of the acetate groups at 20.9-21.6 ppm (3x$COCH_3$) and 169.9-170.6ppm (3x$COCH_3$) and the isoxazoline ring 59.0 (C-6), 92.0 (C-5) and 156.6 ppm (C=N).

2.9.2.1.2 Glucose isoxazoline functionalised polymer 179

The glucose functionalised polymer **179** was prepared using the same method and had broadly speaking similar spectra to the xylose analogue **178** (Scheme 2.38). The ^{1}H NMR spectra revealed broad diagnostic peaks at 3.73 (H-6), 4.23 (H-5), 5.57-5.66 ppm (HC=CH). The ^{13}C NMR spectrum

was equally informative with signals for the isoxazoline ring occurring at 59.5 (C-6), 91.2 (C-5) and 155.3 ppm (C=N). A key difference between the spectra for the xylose **178** and glucose **179** analogues was the presence of the extra methylene on the glucose ring of **179** recorded at δ_H 4.65 (H-6') and δ_C 62.6 ppm (C-6') in the ^1H and ^{13}C NMR spectra.

2.9.2.2 Molecular weight determination

R	I	[M]:[I][a]	Yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI[b]	Propagating species ppm
D-Xyl	**1**	30:1	87	2.39	1.57	40	1.52	19.5
D-Xyl	**2**	30:1	75	47.05	28.67	729	1.64	[c]
D-Glc	**2**	30:1	71	15.44	8.37	180	1.84	[c]

[a] Monomer:initiator ratio; [b]Determined by GPC in THF against polystyrene standards (860 – 2.43 million); [c]not observable by ^1H NMR.

Table 2.25 – Molecular weight of polymers **178** and **179** formed using **1** and **2**

From the above results it is noted that the initiators **1** and **2** give polymers with a very different average degree of polymerisation (av DP). Xylose NBE **168** polymerised with **1** affords a product with av DP = 40, whereas the analogous reaction using **2** generates a polymer with an av DP = 729. Initiator **1** has been reported to polymerise in a living fashion[37] in which the molecular weights of the polymer display a linear dependence on the [initiator]:[monomer] ratio. In contrast the ruthenium complex **2** generates polymers with less control of molecular weight in which significant chain transfer is suggested to occur,[55] thus explaining the deviation from linear dependence on initiator loading with initial monomer concentration. Carbene **2** produced polymers with very different molecular weights for the xylose **178** and the glucose **179** analogues, $M_n = 28.67 \times 10^4$ and 8.37×10^4 respectively. A possible explanation is that the glucose-NBE **169** used in the polymerisation is a mixture of *exo* diastereomers **169a/b** and *endo* diastereomers **175a/b** whereas the xylose analogue **168** consists of only the *exo* diastereomers **168a/b**. As a result, four propagating carbenes are possible with the glucose monomer as opposed to only two with the corresponding xylose based monomer. A difference in reactivity between *exo* and *endo* propagating species might result in the formation of polymers of differing chain length and a large molecular weight distribution.

2.9.2.3 Monitoring the propagating species using ^{1}H NMR spectroscopy

The polymeristion of xylose NBE **168** using the initiator **1** ([M]:[I] = 1.0) in $CDCl_3$ was monitored by ^{1}H NMR spectroscopy. The main propagating species **180** and **181** can be seen as two poorly resolved peaks at *ca.* δ 19.5 ppm along with a sharp singlet at 19.9 ppm attributable to the hydrogen from the initiator. Additionally some broad features are evident at lower frequency (*ca.* 18.8 and 19.1 ppm) which may be attributed to propagating species in which only one phosphine is bound to the ruthenium centre **182** and **183**. These lower frequency signals are more prominent with bulky substituents such as the protected xylose ring of **178** compared to the phenyl group of polymer **83** for which the proton NMR spectrum does not contain these signals (Section 2.6.2.4). This observation is consistent with the metal coordination sphere becoming more crowded and thereby disfavouring binding of a second phosphine ligand.[46] The breadth of these signals can be explained by there being a mixture of regioisomers for both mono- and bis-phoshine ligand bound propagating species (Figure 2.19).

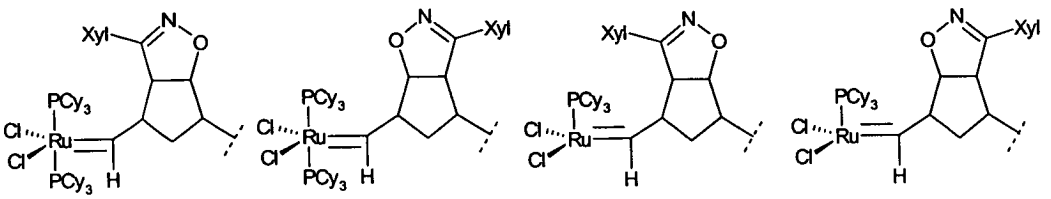
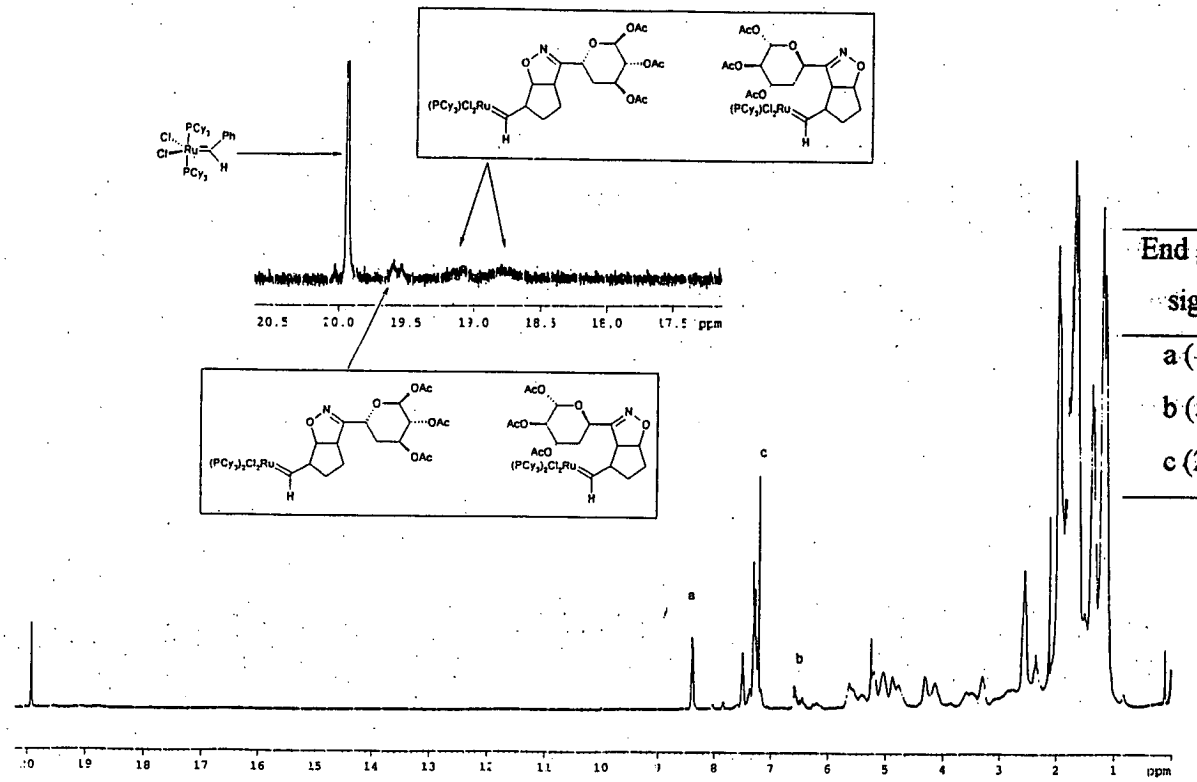


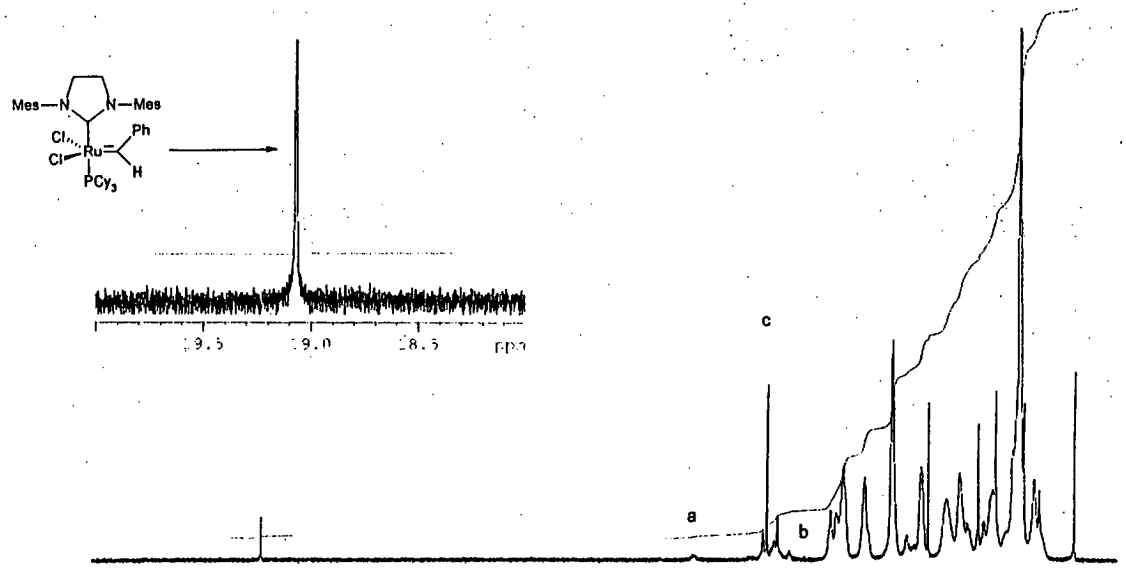
Figure 2.19

The ^{1}H NMR spectrum from the corresponding polymerisation using **2** revealed a signal at 19.08 ppm attributable to the carbene proton of the initiator. As expected no signals were detected for the propagating species as K_p is so much greater than k_i. Another observation from the ^{1}H NMR spectrum of the ROMP product of xylose NBE **168** with **1** [M]:[I] = 1:1 (av DP = 1) is that the end groups are clearly discernable (Table 2.26 and Figure 2.20). The analogous experiment initiated with **2** yielded a polymer of higher molecular weight (av DP = 7) and as a consequence the vinyl and styryl end group signals were at baseline intensity.



End group signal	Structure	δ (ppm)
a (1H)	C*H*=CH_2	8.38
b (5H)	CH=CH*Ph*	7.23-7.31, 7.47-7.51
c (2H)	CH=CH_2	6.10-6.27, 6.41-6.59

ROMP of xylose NBE **168** with **1**



End group signal (nH)	Structure	δ (ppm)
a (1H)	C*H*=CH_2	8.38
b (5H)	CH=CH*Ph*	7.23-7.31, 7.47-7.51
c (2H)	CH=CH_2	6.10-6.27, 6.41-6.59

Table 2.26 – End group signals for the ROMP product of xylose NBE **168** with **1**

2.9.3 Molecular weight control

2.9.3.1 Molecular weight control by varying the monomer-initiator ratio

The effect on polymer molecular weight of varying the monomer / initiator ratio was studied using xylose NBE **168** with the ruthenium carbene **1** as initiator under standard polymerisation conditions. The results are given in Table 2.27. Evidence that the process is a living polymerisation is provided by the linear relationship between [M]:[I] and the average degree of polymerisation (Figure 2.21).

Entry	[M]:[I][a]	Yield / %	$10^{-4}M_{n\ theo.}$[b]	$10^{-4}M_{n\ obs.}$[c]	av DP	PDI
1	3:1	86	0.12	0.12	3	1.15
2	10:1	84	0.39	0.54	14	1.35
3	30:1	87	1.57	2.39	40	1.52
4	50:1	72	1.96	2.43	62	1.34
5	70:1	73	2.75	3.00	76	1.67
6	85:1	85	3.34	3.96	100	1.24

[a]Monomer:Initiator ratio; [b]calculated based on the monomer/catalyst ratio; [c]measured by GPC in THF against polystyrene standards (860-2.43 million)

Table 2.27 – Molecular weight control by varying the [monomer]:[initiator] ratio

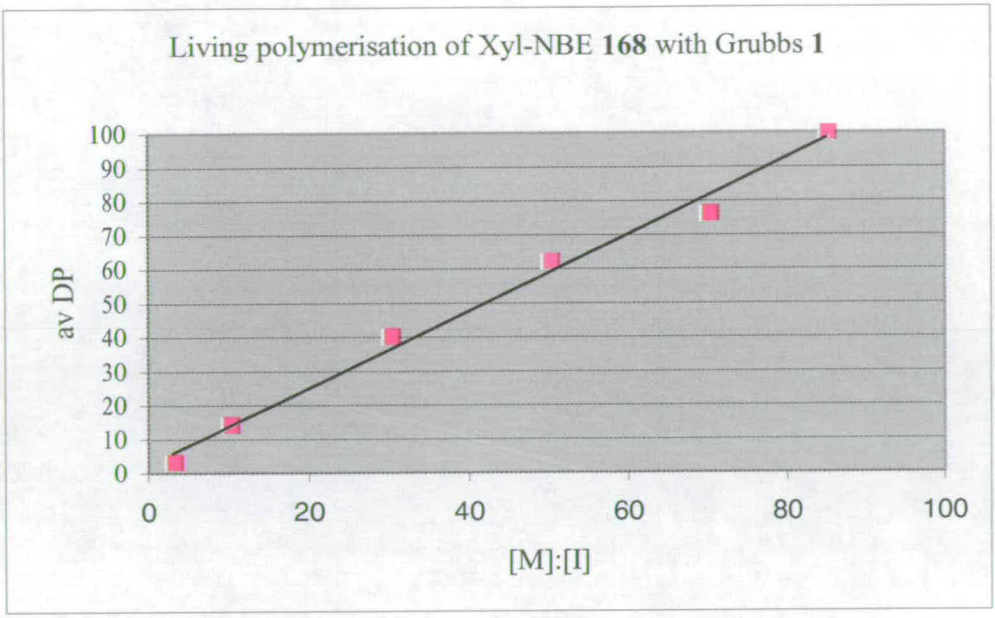


Figure 2.21

There is good correlation between the theoretical molecular weight ($M_{n\ theo.}$) and the observed molecular weight ($M_{n\ obs.}$) as shown in Figure 2.22. This is another indication of a living type polymerisation. Further evidence for the living polymerisation is the facile preparation of block copolymers (Section 2.11) and the ability to follow the polymerisation by ^{1}H NMR and the detection of propagating species (Section 2.9.2.3).

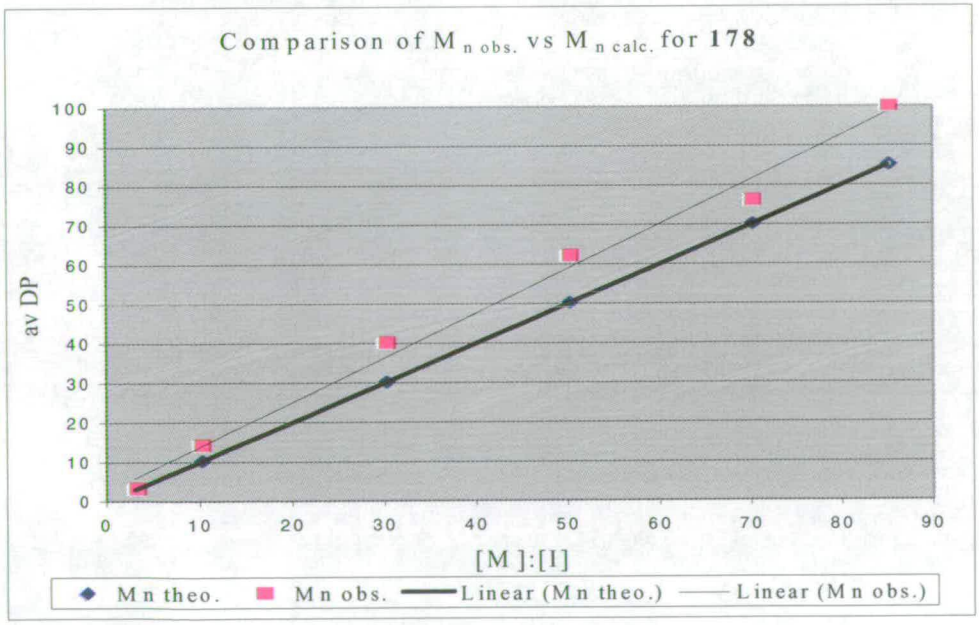
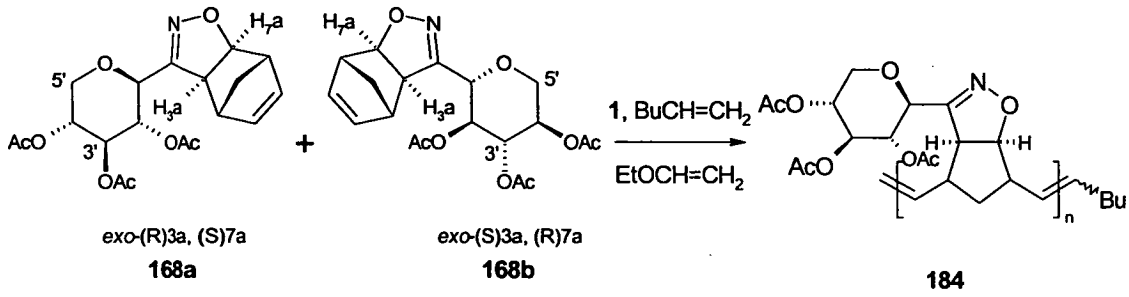


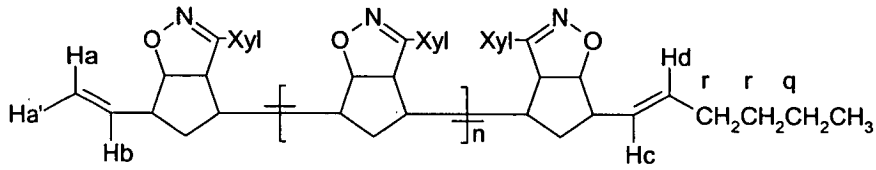
Figure 2.22

2.9.3.2 Molecular weight control using a chain transfer agent (hex-1-ene)



Scheme 2.44

An alternative method of molecular weight control was achieved by polymerising xylose NBE **168** using initiator **1** in the presence of a chain transfer agent, hex-1-ene (10%) under standard conditions, as shown in Scheme 2.44. The reaction was stirred at rt for 2h, and then terminated with ethyl vinyl ether. Precipitation in methanol afforded a brown brittle solid (62%).



184

Stereochemistry not inferred (HH, HT/TH, TT)

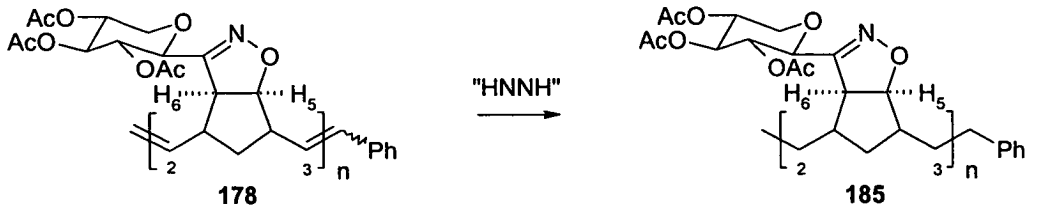
Figure 2.23

In the ^{1}H NMR spectrum of the oligomer **184** (Figure 2.23) the vinyl end group was detected at 5.92 ppm (=CH), 4.89-5.08 ppm ($=CH_2$) and the methyl of the hexenyl end group at 0.85 ppm (the $3xCH_2$ from the butyl group were overlapping with protons from the cyclopentane from the ring opened product). The signals for the vinyl end group in the ^{13}C NMR spectrum appeared at 145.6 (C-b) and 125.2 (C-a,a'), with the butyl signals at 29.5 (2xC-r, C-q) and 20.5 ppm (CH_3).

The average degree of polymerisation for the polymerisation of oligomer **184** using 10% hex-1-ene was calculated as n = 15 (measured by end group analysis). This correlates well to previous polymerisations of isoxazolino norbornenes. For example, the ROMP of ethoxycarbonyl NBE **82** with 10% hex-1-ene afforded an oligomer with an av DP = 16 (Section 2.6.4.2).

2.9.4 Reduction of glyco homopolymers

Glyco homopolymers possess alkene groups that can be functionalised in order to alter the conformational and solubility properties in the scaffold. The hydrogenation of neoglycopolymer **178** using *p*-toluenesulfonyl hydrazide was investigated as this would potentially impart flexibility into the polymer backbone, which may have an improved effect on its biological activity. The neoglycopolymer was dissolved in chlorobenzene and to this was added *p*-toluenesulfonyl hydrazide. The reaction mixture was refluxed at 130 °C with stirring for 4h and then precipitated hot in methanol. The product was then dried *in vacuo* affording the hydrogenated analogue **185** as a grey powder (69%) (Scheme 2.45).



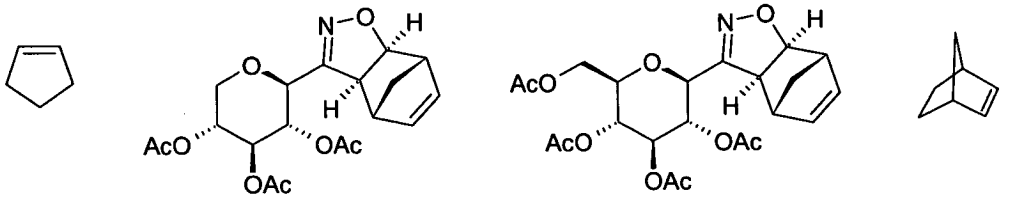
Scheme 2.45

The ^{1}H NMR spectrum of the reduced analogue **185** showed the absence of vinylic protons at 6.91 and 6.78 ppm and also the complete removal of the in chain olefinic protons at 5.32-5.60 ppm. The appearance of a broad multiplet at 0.88 ppm (H-2,3) showed that the reduction had gone to completion. The ^{13}C NMR spectrum revealed the absence of olefinic resonances in the region of 135-138 ppm and the appearance of new peaks at 34.1 and 39.1 ppm (C-2,3) again indicated that the reaction had gone to completion. Characteristic signals were also present at 170.5, 170.0 and 169.6 (3x*C*OCH$_3$), 155.7 (C=N), 92.5 (C-5), 59.4 (C-6) and 20.6 ppm (3xCO*C*H$_3$) demonstrating that the isoxazoline moiety is stable to the diimide reduction conditions.

2.10 Random copolymers of glycosyl isoxazolino NBEs

2.10.1 Introduction

Various sugar-substituted homopolymers have been successfully prepared via ring-opening metathesis polymerisation and exhibit very promising activity in biological assays.[125] Copolymerisation of carbohydrate functionalised monomers by ROMP has, however, been the subject of less investigation,[109, 136, 138] and would provide a new route to tune material properties through combinations of various monomers and reaction stoichiometry. As demonstrated in the Introduction (Section 1.5) it is possible to synthesise random and alternating copolymers by varying the reaction conditions and with living systems block copolymers can be prepared. The present work describes the synthesis of random copolymers with at least one of the comonomers being a glycosyl functionalised norbornene (**168** or **169**). A summary of the reactions and results of their molecular weight measurements is shown in Table 2.28.



CPE **168** **169** **NBE**

[M1]:[M2]:[I][a]	monomer[a]	C/P	I	Yield / %	$10^{-4}M_{n\,calc.}$[b]	$10^{-4}M_{n\,theo.}$[c]	av DP[d]	PDI
[40]:[10]:[1]	CPE/**168**	**186**	**2**	78	0.66	[e]	[e]	[e]
[40]:[10]:[1]	CPE/**169**	**187**	**2**	82	0.74	[e]	[e]	[e]
[10]:[40]:[1]	**168**/NBE	**188**	**1**	64	0.77	2.12	24/120	3.12
[10]:[40]:[1]	**168**/NBE	**189**	**2**	64	0.77	3.62	47/188	1.86
[10]:[40]:[1]	**169**/NBE	**190**	**2**	82	0.84	2.74	36/142	2.07
[67]:[67]:[1]	**168/169**	**191**	**1**	59	5.75	5.43	69/69	1.57

[a]The composition of comonomers and the equivalents of each. [b]Calculated from [monomer]:[catalyst] ratio in feedstock. [c]Measured using GPC in THF against polystyrene standards (860 – 2.43 million). [d][M1]:[M2] in copolymer calculated from ^{1}H NMR. [e]Bimodal distribution occurred.

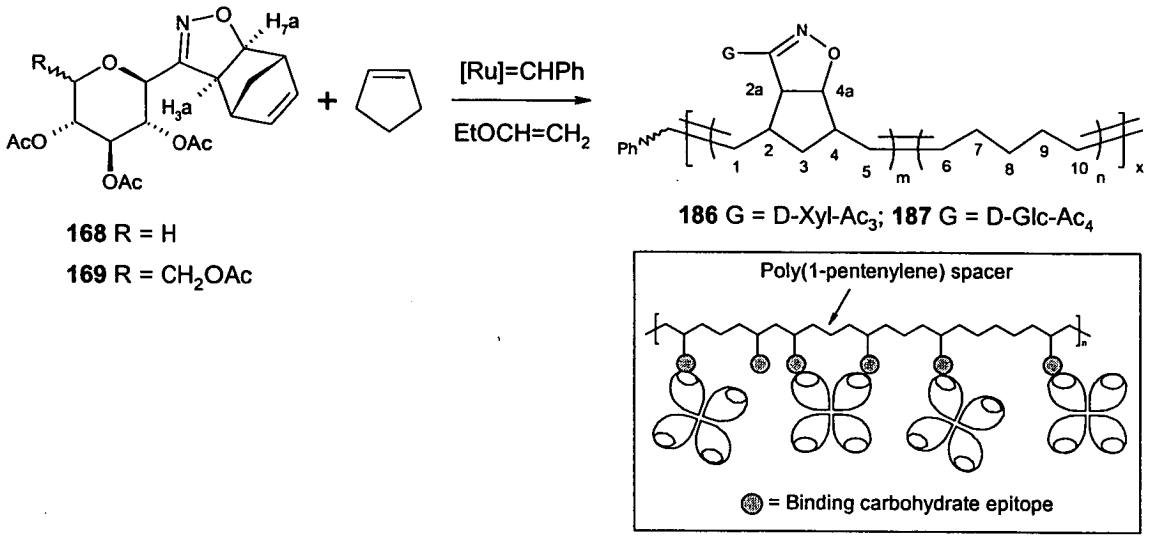
Table 2.28 – Random copolymerisations of isoxazolino norbornenes.

As discussed in the Introduction (Section 1.11.3) the density of the binding epitope of a glyco copolymer can have a profound effect on biological activity. Kiessling *et al.*[138] used the structurally

similar mannose- and galactose-functionalised maleimide norbornenes at varying ratios to give a copolymer with a lower density of the effective Con A mannose-binding epitope, thus allowing for more efficient binding. It was found that this spacing of the biologically active mannose containing blocks with the inert galactose functionalised blocks lead to an increase in binding of the copolymer relative to the homopolymer of mannose.

Based on this rationale, a series of copolymers was prepared using simple alkenes such as CPE and NBE with a carbohydrate functionalised NBE comonomer. It was envisioned that the resulting copolymers would consist of a statistical distribution of the biologically active carbohydrate residues separated by the ring opened products of CPE and NBE. It is visualised that a copolymer of CPE and either xylose NBE **168** or glucose NBE **169** could perform in binding processes as described in the cartoon in Scheme 2.46.

2.10.2 Random copolymers of CPE and glycosyl isoxazolino norbornenes



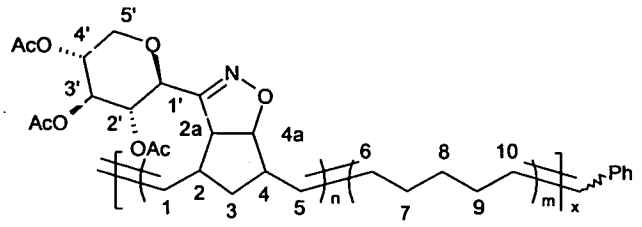
168 R = H
169 R = CH_2OAc

186 G = D-Xyl-Ac_3; **187** G = D-Glc-Ac_4

Scheme 2.46

2.10.2.1 Random copolymer 186 of CPE and xylose NBE (168)

In a typical experiment CPE and xylose NBE **168** were dissolved in dichloromethane (1.5 ml) and to this was added a solution of the Grubbs initiator **2** in dichloromethane (1.0 ml) and the reaction stirred at room temperature for 20h. Precipitation in methanol afforded copolymer **186** (Figure 2.24).



186

Figure 2.24

From the ^{1}H NMR spectrum, signals at 4.21 (H-4a) and 3.40 ppm (H-2a) were assigned to the isoxazoline protons. Resonances for the sugar protons appeared at 5.21 (H-3'), 4.64-4.85 (H-2',4'), 4.06 (H-1') and 3.24 ppm (H-5') and the methyl groups of the acetate groups were at 1.97 ppm. The ^{13}C NMR spectrum revealed isoxazoline carbons at 92.0 (C-4a) and 59.0 (C-2a), along with signals for the sugar carbons 73.7, 72.2, 68.2, 67.9 and 65.7 ppm (C-1' - C-5'). Signals for the pentenylene chain carbons were observed at 31.8, 28.7 and 26.1 (C-7,8,9). Resonances for the acetate protecting groups were also discernable at 19.7 (3xCO*C*H$_3$) and 169.6, 169.2 and 168.8 ppm (3x*C*OCH$_3$). Further evidence of the presence of the isoxazoline ring was the appearance of a signal at 156.6 ppm (C=N).

Due to the reactivity differences between cyclopentene and xylose NBE **168** it was presumed that the more reactive **168** would polymerise first. A segment of random neoglycopolymer / poly(1-pentenylene) polymer would then be formed with a block of predominantly poly(1-pentenylene) at the end of the chain from the residual cyclopentene. The ^{1}H NMR spectrum of the random copolymer **186** contains better-resolved signals than those of the xylose functionalised homopolymer **178**, an effect attributed to the increased flexibility imparted by the presence of poly(1-pentenylene) between the carbohydrate residues. Therefore the structure drawn for **186** should not be taken literally as shown in Figure 2.24. From the GPC measurements it was observed that a bimodal distribution resulted for the copolymers **186** and **187**. This result is consistent with those obtained for phenyl- and ethoxycarbonyl- isoxazoline functionalised copolymers; and is attributed to back biting (see Section 2.7.1.2).

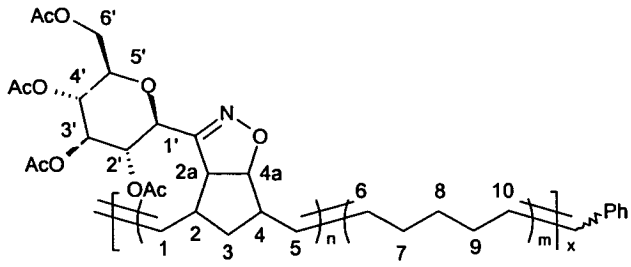
Code	Copolymer	[M1]:[M2]:[I]	yield / %	$10^{-4}M_w$[a]	$10^{-4}M_w$[b]
JM156	**186**	10:40:1	78	0.45	0.09
JM171	**187**	10:40:1	82	1.58	0.13

[a]M_w of high weight fraction measured by GPC in THF against polystyrene standards (860 – 2.43 million); [b]M_w of low weight fraction.

Table 2.29 – Molecular weight distributions of random copolymers

2.10.2.2 Random copolymer 187 of CPE and glucose NBE 169

A random copolymer of glucose NBE **169** and CPE was synthesised by the same method as that used for the xylose analogue. CPE and the glucose norbornene **169** were dissolved in dichloromethane (1.5 ml) and to this was added **2** in dichloromethane (1.0 ml). The reaction was stirred at room temperature for 20h and precipitation in methanol afforded the product **187** (78%) (Figure 2.25).



187

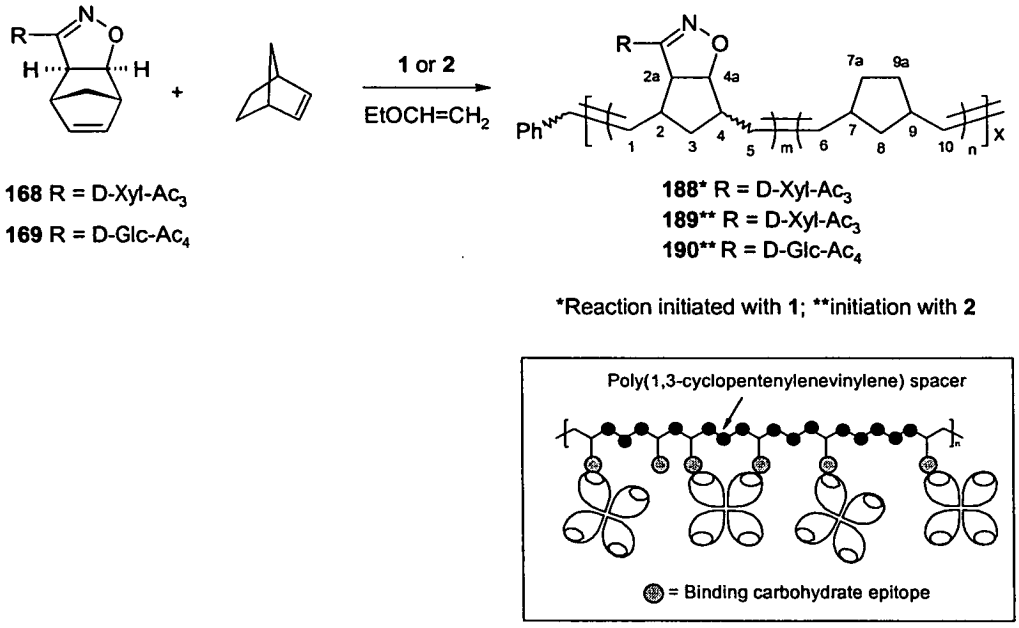
Figure 2.25

In the ^{1}H NMR spectrum of **187** there were signals at 1.99-2.07 ppm ($COCH_3$), 3.49 (H-2a), 4.73 (H-4a). The protons from the xylose ring were observed at 3.73 (H-5'), 4.12, 4.20 (H-6'), 5.08 (H-2',4'), 5.23 (H-3',1'). The ^{13}C NMR spectrum revealed peaks at 20.5 ($4xCOCH_3$) and 170.4, 170.0, 169.9 and 169.2 ppm ($4xCOCH_3$) for the acetate protecting group along with signals for the sugar carbons 62.2 (C-6'), 69.4, 68.0 (C-2',4'), 73.6 (C-3'), 73.8 (C-1'), 75.8 ppm (C-5'). Signals for the pentenylene chain carbons were observed at 26.6, 29.4, and 31.9 (C-7,8,9). Further evidence of the presence of the isoxazoline ring was the appearance of signals at 58.2 (C-2a), 91.9 (C-4a) and 156.0 ppm (C=N).

2.10.3 Random copolymers 188 / 189 / 190 of NBE and glycosyl NBEs 168 / 169

Copolymerisation of CPE and gylcosyl isoxazoline norbornenes **186** and **187** resulted in polymers with a bimodal distribution. In an attempt to produce copolymers with a unimodal distribution norbornene was investigated as the comonomer. NBE is structurally more similar to the glycosyl isoxazolino norbornenes **168** and **169** and it has a greater strain energy compared to that of CPE (100 kJ mol^{-1} relative to 27 kJ mol^{-1}). NBE should therefore polymerise at a similar rate as **168** and **169**, resulting in a copolymer with a unimodal molecular weight distribution. It was believed that the resulting copolymers **188**, **189** and **190** could have the same application as the CPE analogues

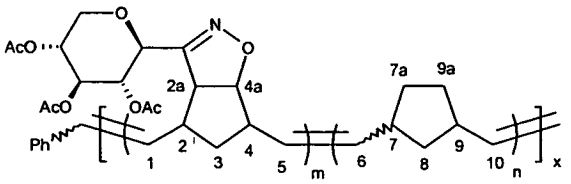
represented by the cartoon in Scheme 2.51. In this case it was envisioned that the resulting copolymers **188**, **189** and **190** would consist of a statistical distribution of the biologically active carbohydrate residues interspersed by poly(1,3-cyclopentenylenevinylene) (ring opened NBE) units. Thus norbornene was polymerised with **168** or **169** with **1** or **2** and the resulting copolymers afforded by precipitation in methanol (Scheme 2.47).



Scheme 2.47

2.10.3.1 Random copolymers 188 / 189 of NBE and xylose NBE 168

Norbornene and xylose NBE **168** were dissolved in dichloromethane and to this was added a solution of the Grubbs initiator **1** or **2** in dichloromethane and the reaction stirred at room temperature for 20h. Precipitation in methanol afforded the copolymer **188/189** (Figure 2.26).



188*
189**

*Reaction initiated with **1**; **initiation with **2**

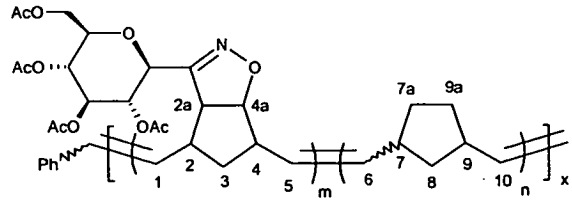
Figure 2.26

From the ^{1}H NMR of **188** and **189** peaks were discernable at 2.03 ($3xCOCH_3$), 3.47 (H-2a) and 4.69 ppm (H-4a). The ^{13}C NMR spectrum showed diagnostic peaks at 20.6 ($3xCOCH_3$), 66.5-74.3 (xylose ring), 58.5 (C-2a), 92.4 (C-4a), 156.2 (C=N) and 169.8 ppm ($3xCOCH_3$). Evidence of copolymerisation was the detection of signals at 32.0, 32.2, 32.7, 32.9 (C-7a, 9a) and 43.0, 43.3 ppm (C-7,9), attributable to the 1,3-cyclopentenylenevinylene units.

The copolymerisation of norbornene and xylose-NBE **168** initiated with **1** resulted in **188** which had a PDI = 3.12, whereas with **2** the analogous copolymer **189** had a PDI = 1.86. Despite the unimodal distribution of the products (measured by GPC), the breadth of the polydispersity index suggests an uncontrolled polymerisation using **1**. Grubbs and coworkers have reported that the polymerisation of norbornene with ruthenium complex **1** results in a product with a broad PDI.[185] In the present work (Section 2.2.1), homopolymers of NBE were prepared using the Grubbs initiators **1** and **2** with a PDI of 2.58 and 2.16 respectively. The xylose-NBE monomer **168** was also homopolymerised with **1** and **2** yielding the corresponding materials with PDIs of 1.15-1.67 and 1.64 respectively. Thus, in the copolymerisation of NBE and **168**, norbornene (which is in a 4 fold excess) is having a greater influence on the copolymerisation resulting in **188** and **189** which have broader PDIs than the corresponding homopolymers **178** and polyNBE. It is interesting to note that **2** yields a norbornene copolymer with a narrower molecular weight distribution than with **1**. This trend is contrary to any found in the literature though at the time of the writing of this thesis, random copolymers of NBE and sugar functionalised NBEs initiated with **2** had not been reported. The polymerisation of a series of comonomer feedstocks using **1** and **2** should be attempted before any further conclusions are made. The copolymer prepared using **1** had a $M_n = 2.11 \times 10^4$, whereas the analogous product achieved using **2** had a higher molecular weight of 3.62×10^4; this is attributable to the difference in initiation and propagation rates of the complexes.

2.10.3.2 Random copolymer 190 of NBE / glucose isoxazoline NBE 169

Norbornene and glucose NBE **169** were copolymerised with initiator **2** using the same procedure as used for the xylose analogue. The copolymer **190** was afforded as a grey polymeric solid (83%) (Figure 2.27).



190

Figure 2.27

The copolymer **190** was analysed by ^{1}H and ^{13}C NMR spectroscopy which revealed signals attributable to the isoxazoline ring δ_H 3.48 (H-2a), 4.69 (H-4a) and δ_C 58.3 (C-2a), 92.9 (C-4a) and 156.2 ppm (C=N). Peaks for the glucose ring were observable at 62.0-75.6 ppm in the ^{13}C NMR spectrum along with those for the cylopentenylenevinylene at 42.0 and 43.3 ppm providing evidence of copolymer formation. Initiator **2** was used in an attempt to prepare a copolymer with the narrowest PDI possible. A comonomer system incorporating NBE polymerised with **2** afforded a copolymer with a narrower molecular weight distribution than the analogous experiment using **1**, as shown with the xylose copolymers **188** and **189**.

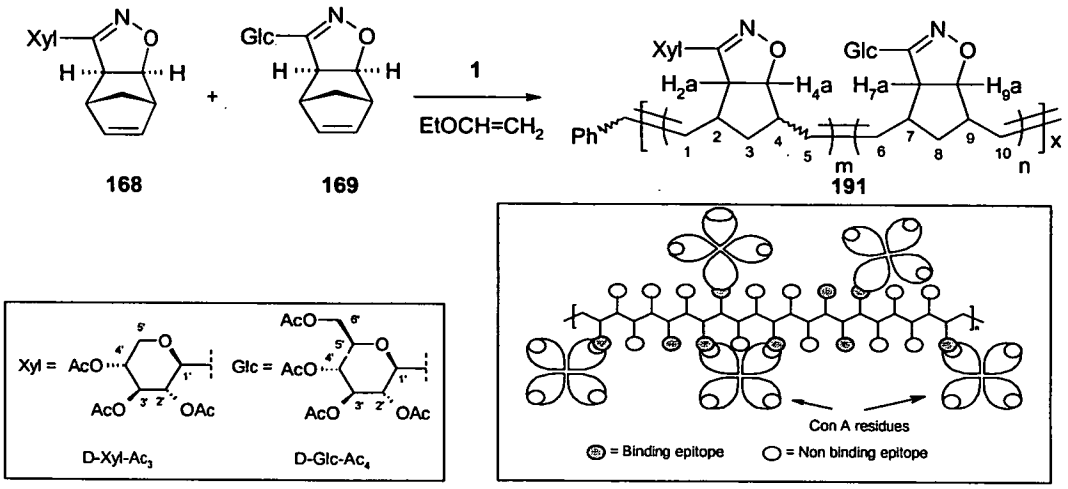
The copolymer **190** a PDI = 2.07. This is comparable to the value recorded for the copolymerisation of NBE and xylose NBE **168** with **2** which resulted in **189** with a PDI = 1.86. The molecular weight of the copolymer **190** (M_n = 2.74 x10^4) was lower than that of copolymer **189** (M_n = 3.64 x10^4). The homopolymers of xylose **178** and glucose **179** homopolymers initiated with **2** resulted in products with M_n = 28.67 x10^4 and 8.37 x10^4 respectively. Thus, a continuation of this trend is observed in the preparation of copolymers.

2.10.4 Random copolymer of glycosyl isoxazolino norbornenes

The last comonomer system investigated for the preparation of random copolymers was based on the two glycosyl isoxazoline norbornenes **168** and **169**. The structurally similar xylose **168** and glucose **169** monomers are expected to have almost identical ring strains and result in similar initiation and propagating rates, and hence a living polymerisation. Initiator **1** was used as this is known to produce living polymers.[37]

2.10.4.1 Random copolymer 191 of xylose NBE 168 and glucose NBE 169

Xylose NBE **168** and glucose NBE **169** were dissolved in dichloromethane and to this was added a solution of the ruthenium complex **1**. The reaction was stirred at room temperature for 20h and terminated with ethyl vinyl ether. Precipitation in methanol afforded the product **191** as a grey polymeric solid (59%) (Scheme 2.48).



Scheme 2.48

From the ^{1}H NMR spectra signals for the acetate protection were discernable at 1.99 ($COCH_3$) and evidence that copolymerisation had occurred was the presence of signals attributable to the isoxazoline protons at 3.54-3.60 (H-2a,7a) and 4.34 ppm (H-4a,9a). The ^{13}C NMR spectrum contained signals for the isoxazoline carbons at 61.9 (C-2a,7a) and 91.5 ppm (C-4a,9a) thus providing further evidence of copolymerisation. Resonances for the acetate groups were present at 20.5, 20.6 ppm ($COCH_3$) and 169.0, 169.6, 170.0 and 170.4 ppm ($COCH_3$). Signals for the sugar resonances were present at 66.6, 68.8, 69.1, 72.8, 73.7, 74.6 ppm (C-1'-6'). Confirmation that the isoxazoline moieties were intact was the presence of peaks at 156.0 (C=N).

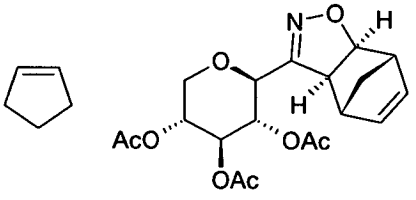
The resulting product had a PDI = 1.57 with a molecular weight $M_n = 5.43 \times 10^4$ (i.e. ~ 63 units of each monomer incorporated into the copolymer chain, calculated from the ^{1}H NMR spectrum), which is within the range of M_w/M_n recorded for the polymerisation of Xyl-NBE with **1** at various ratios (PDI = 1.15-1.67). the similarity between observed molecular weight $M_{n\ obs.} = 5.43 \times 10^4$ and theoretical molecular weight $M_{n\ theo.} = 5.75 \times 10^4$ of copolymer **191** is evidence that the copolymerisation is carried out under controlled conditions.

In conclusion, the above investigation has proven that structurally similar comonomers will lead to better defined products with an increased degree of control than from a feedstock based on structurally different monomers.

2.11 Block glyco copolymers

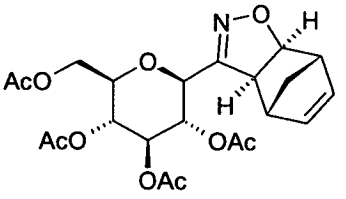
2.11.1 Introduction

Due to the living nature[37] of the ROMP polymers formed using the ruthenium initiator **1**, the preparation of diblock copolymers is possible by sequential addition of the comonomers. This section describes the investigation into the preparation of copolymers based on the structurally different monomers **168**, **169**, **82**, CPE and NBE. In addition the preparation of block copolymers using **2** was also attempted. In each case at least one of the comonomers is a glycosyl isoxazolino norbornene. A summary of the experiments performed and the molecular weight results is shown in Table 2.29.

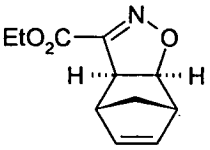


CPE

168



169



82

NBE

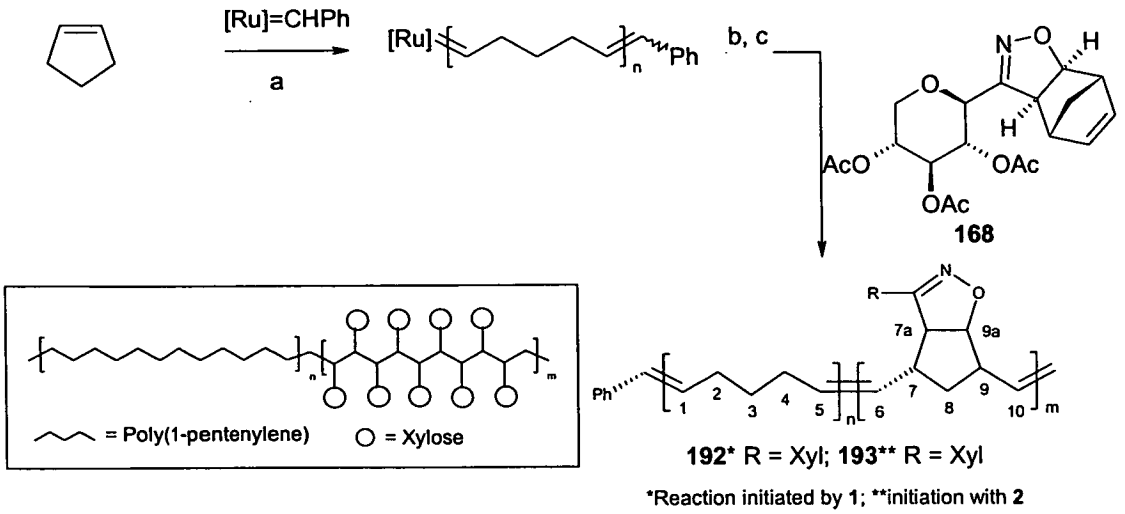
C/P	[M1]:[M2]:[I][a]	M1/M2/I	Yield/%	$10^{-4}M_{n\ calc.}$[b]	$10^{-4}M_{n\ theo.}$[c]	av DP[d]	PDI[a]
192	[67]:[67]:[1]	CPE/**168**/**1**	81	3.09	[e]	[e]	[e]
193	[67]:[67]:[1]	CPE/**168**/**2**	72	3.09	2.84	21/86	2.18
194	[67]:[67]:[1]	NBE/**169**/**1**	76	3.74	19.61	892/223	2.07
195	[40]:[40]:[1]	**168**/**82**/**2**	83	2.40	8.58	211/107	2.13
196	[67]:[67]:[1]	**168**/**169**/**1**	79	5.75	4.01	51/43	1.17

[a]The composition of comonomers and the equivalents of each. [b]Calculated from monomer to catalyst ratio. [c]Measured using GPC in THF against polystyrene standards (860 – 2.43 million). [d][M1]:[M2] in copolymer calculated from ^{1}H NMR. [e]Not determined.

Table 2.29 – Block copolymerisations of isoxazolino norbornenes.

2.11.2 Block copolymers 192, 193 of CPE and xylose NBE 168

A two-step block copolymerisation of cyclopentene (67 equivs.) and xylose NBE **168** (67 equivs.) was carried out using the ruthenium initiators **1** and **2** (1 equiv.) (Scheme 2.49).



Reagents: a) **1** / **2**, 24 h @ r.t.; b) **168**, 24 h @ r.t then 6 h @ 50 °C; c) $EtOCH=CH_2$ for 2 h

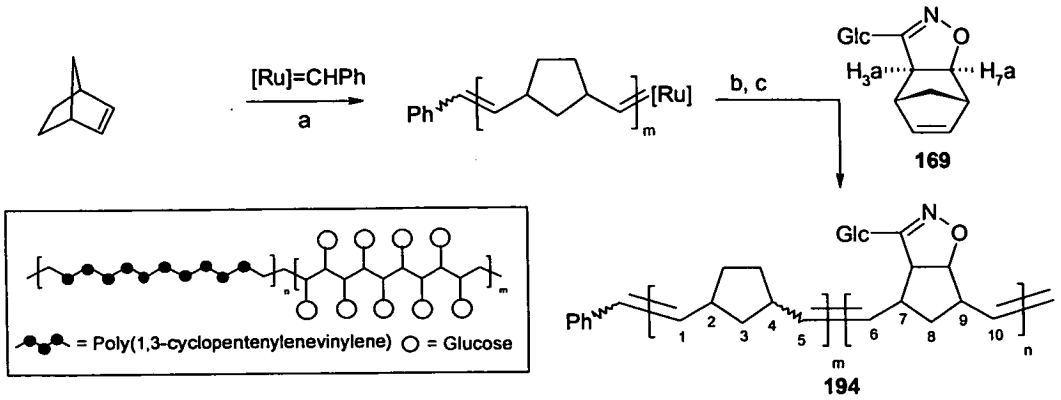
Scheme 2.49

From the ^1H NMR spectrum characteristic resonances for isoxazolino protons were discernible at 3.42 (H-2a) and 4.26 ppm (H-4a). A signal at 1.92 ppm was assigned for the acetate protection ($COCH_3$). The complexity of the olefinic resonances δ_H 5.33-5.51 ppm (H-1,5,6,10) can be attributed to the many variations of monomer sequences for this material. The resonances are broad since the olefinic protons are likely to be sensitive to the stereochemistry of the monomers on both sides of the olefinic bond. The ^{13}C NMR spectrum showed signals at 26.1, 28.7 and 31.8 ppm for the pentylene carbons (C-7,8,9) and proof that the isoxazoline ring was intact was provided by the appearance of signals at 57.0 (C-2a), 91.5 (C-4a) and 155.0 ppm (C=N). The acetate protection showed two resonances at 19.7 ($COCH_3$) and 168.7 ppm ($COCH_3$).

The GPC trace revealed that M_n increased from 0.15 $x10^4$ (av DP = 21) for the homopolymer of cyclopentene to 2.84 $x10^4$ (av DP = 21/86) for the block copolymer after the addition of xylose NBE **168**. The PDI increased from 1.33 to 2.18 on going from the homo- to the co-polymer. This increase in M_n between the first and the second block is evidence of block copolymerisation. The product **193** is a rare example of a carbohydrate functionalised block copolymer prepared using initiator **2**.

2.11.3 Block copolymer 194 of NBE and glucose NBE 169

A two-step block copolymerisation of norbornene (67 equivs.) and glucose NBE **169** (67 equivs.) was carried out using the first generation ruthenium initiator **1** (1 equiv.) (Scheme 2.50).



Reagents: a) **1** for 24 h @ r.t.; b) **169** 24 h @ r.t., then 50 °C for 6 h; c) $EtOCH{=}CH_2$ 2 h @ r.t.

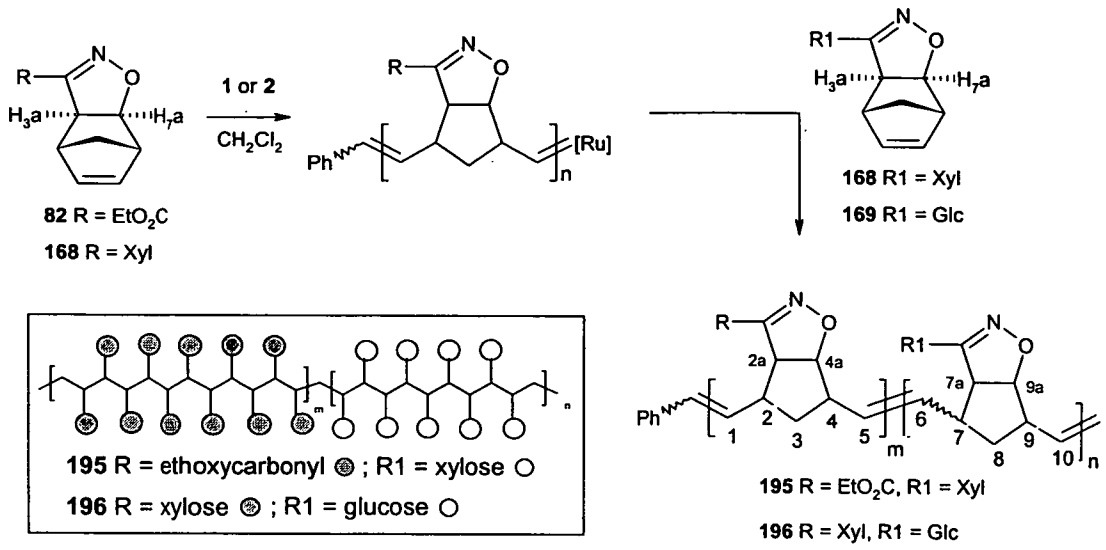
Scheme 2.50

The ^1H NMR spectra contained signals for the isoxazoline protons at 3.48 (H-2a) and 4.71 (H-4a) and the acetate protection at 2.02 ppm ($4xCOCH_3$). The ^{13}C NMR spectrum contained signals for the glucose ring between 62.7-76.5 ppm and evidence of block copolymerisation was the presence of peaks for the cyclopentenylenevinylene at 1.36, 1.43, 1.80 and 1.85 ppm. Signals were observable at 20.5, 20.6 ($4xCOCH_3$), 58.5, 59.6 (C-2a), 91.9, 93.1 (C-4a), 156.0 (C=N) and 169.5, 169.6, 169.9 and 170.0 ppm ($4xCOCH_3$).

An increase in molecular weight was observed on addition of the second monomer from M_n = 8.38 $x10^4$ to 19.61 $x10^4$. The resulting copolymer had an av DP of 892/233 with a PDI = 2.07. Kofinas *et al.*[185] reported the synthesis of block copolymers of norbornene and norbornene dicarboxylic acid (NORCOOH) with narrow PDIs = 1.05–1.51. By polymerising the bulkier NORCOOH monomer first, lower PDIs were observed for the final copolymer in comparison to the copolymers where norbornene was polymerised first. This method of copolymer synthesis could be applied to the Xyl-NBE and NBE comonomer system in an attempt to narrow the polydispersity index.

2.11.4 Block copolymers of (glycosyl) isoxazolino norbornenes

Block copolymers were prepared by the sequential addition of a comonomer feedstock. Thus the polymerisation of two isoxazolino norbornenes was carried out using the first or second generation ruthenium initiator **1** or **2**. The ability to make block copolymers with different functionality on each isoxazoline ring could be of significant interest as a block copolymer could be prepared with one block possessing binding sugar epitopes for recognition and a second block for solubility, drug delivery and other uses.



Reagents: a) **1** for 24 h @ r.t.; b) **168** / **169** 24 h @ r.t., then 50 °C for 6 h; c) $EtOCH{=}CH_2$ 2 h @ r.t.

Scheme 2.51

2.11.4.1 Block copolymer 195 of ethoxycarbonyl NBE 82 and xylose NBE 168

Ethoxycarbonyl NBE **192** was polymerised in dichloromethane until all the monomer had been consumed after which an aliquot of xylose NBE **168** was added to the reaction, resulting in a molecular weight (M_n) increase from 4.38 x10^4 (av DP = 211) for the first block to 8.58 x10^4 (av DP = 211/107) for the final copolymer, as determined by GPC. The PDI of the polymer increased from 1.48 (homopolymer of ethoxy isoxazoline norbornene **84**) to 2.13 (block copolymer).

	Block m				Block n			
Polymer	H-4a	H-2a	C-4a	C-2a	H-9a	H-7a	C-9a	C-7a
Homo	4.89-5.23	3.65	94.6	57.4	4.72	3.56	92.0	59.0
Block	4.26-4.23	[a]	91.5-95.2	57.3	4.26-4.23	[a]	91.5-95.2	57.3

[a]Not determined

Table 2.30 – ^{1}H and ^{13}C NMR shifts in homo- and random co-polymers

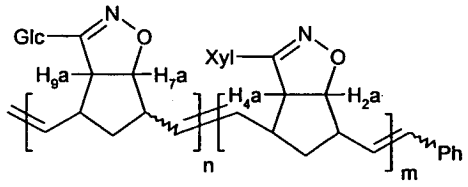
From the ^{1}H NMR spectra of the block copolymers signals for the ester group were discernable at 1.22-1.33 ppm ($COCH_2CH_3$) and evidence that copolymerisation had occurred was the presence of signals attributable to the isoxazoline protons at 3.65 (H-2a,7a) and 4.89-5.23 ppm (H-4a,9a). The ^{13}C NMR spectrum contained signals for the isoxazoline carbons at 57.3 (C-2a,7a) and 91.4-95.2 ppm (C-4a,9a) providing further evidence of copolymerisation. Resonances for the ester group were present at 13.8 ppm ($COCH_2CH_3$), 61.8 ppm ($COCH_2CH_3$) and 160.5 ($COCH_2CH_3$) Signals for the

sugar resonances were present at 74.3 (C-1'), 72.8 (C-3'), 69.0, 68.6 (C-2',4') and 66.3 ppm (C-5'). The acetate protecting group showed resonances at 168.9 ($COCH_3$) and 20.4 ($COCH_3$). Confirmation that the isoxazoline moieties were intact was the presence of peaks at 156.6, 153.6 ppm (C=N).

This preparation of the copolymer **195** is interesting in that it has been prepared using **2**, which has not previously been reported in the synthesis of block carbohydrate containing copolymers to date.[†] Significantly, the development of this copolymer would not have been possible with initiator **1** due to its inability to polymerise ethoxycarbonyl NBE **82**.

2.11.4.2 Block copolymer 196 of xylose NBE 168 and glucose NBE 169

Diblock carbohydrate functionalised copolymers were envisioned to have increased recognition. Thus a model based on xylose-/glucose-isoxazolino norbornenes was prepared. A copolymer of narrow polydisperity was expected as the comonomers were structurally similar with similar ring strain energies which would result in a living type polymerisation. Xylose NBE **168** and glucose NBE **169** were polymerised sequentially using ruthenium complex **1**. The reaction was terminated with ethyl vinyl ether and precipitation in methanol afforded the block copolymer **196** (Figure 2.28).



196

Figure 2.28

From the ^1H NMR spectra of the block copolymer **197** signals for the acetate protection were discernable at 1.98 ($COCH_3$) and evidence that copolymerisation had occurred was the presence of signals attributable to the isoxazoline protons at 3.45-3.64 (H-2a,7a) and 4.35 ppm (H-4a,9a). The ^{13}C NMR spectrum contained signals for the isoxazoline carbons at 57.1 (C-2a,7a) and 91.8 ppm (C-4a,9a) providing further evidence of copolymerisation. There was good correlation of chemical shift for the isoxazoline carbons in the xylose/glucose containing blocks in the copolymer and their corresponding homopolymers (Table 2.37). Resonances for the acetate groups were present at 20.5,

[†] At the time of writing this thesis, Nomura *et al.* reported the synthesis of glucose and maltose derived norbornenes and their block copolymerisation with NBE using **2**; (K. Nomura, I. Sakai, Y. Imanishi, M. Fujiki, Y. Miyamoto, *Macromol. Rapid. Commun.*, 2004, **25**, 571).

20.6 ppm ($COCH_3$) and 169.6, 170.1 and 170.4 ppm ($COCH_3$). Signals for the sugar resonances were present at 61.9, 66.6, 68.8, 69.1, 72.8, 74.5 ppm (C-1'-6'). Confirmation of the isoxazoline moieties was the presence of a peak at 156.0 ppm (C=N).

	Block m				Block n			
Polymer	H-4a	H-2a	C-4a	C-2a	H-9a	H-7a	C-9a	C-7a
Homo	3.56	4.72	59.0	92.0	3.73	4.23	59.5	91.2
Block	3.64	4.35	57.1	91.8	3.64	4.35	57.1	91.8

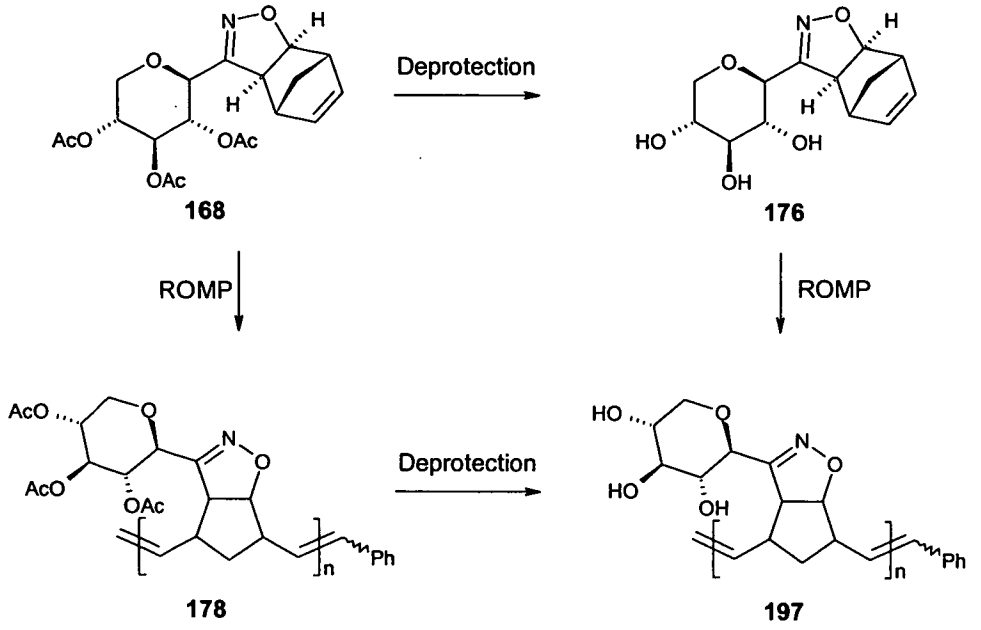
Table 2.31 – ^1H and ^{13}C NMR shifts in homo- and random co-polymers

The molecular weight increased from M_n = 2.00 x10^4 (av DP = 51) to 4.01 x10^4 (av DP = 51/43) on addition of the second monomer, as determined by GPC, with a PDI of 1.17 for the copolymer. This value is within the range of polydispersities measured for the homopolymerisation of Xyl-NBE with **1** at various ratios PDI = 1.15 - 1.67 (Section 2.9.3). This result proves that copolymers prepared from structurally similar comonomers with comparable ring strain energies will result in materials with a more monodisperse molecular weight distribution.

2.12 Deacetylated carbohydrate functionalised polymers

2.12.1 Introduction

In order to participate in recognition events such as binding with cell surface proteins the glycopolymers must have the sugar hydroxyl groups free (Section 1.9.2). Two approaches were investigated for the preparation of deacetylated carbohydrate functionalised polymers using D-xylose as a representative example. The first route was via the preparation of a deprotected monomer **176** and its subsequent ROMP with **1** or **2**. The second approach involved the synthesis of a protected glycopolymer **178** and its deprotection (Scheme 2.52).



Scheme 2.52

2.12.2 Aqueous ROMP of deprotected monomers

2.12.2.1 Ruthenium trichloride hydrate in water

Using the procedure described by Grubbs *et al.*[186] deprotected xylose NBE **176** and $RuCl_3$ were added to a round bottomed flask, dissolved in degassed water, and the mixture heated at 55-60 °C for 18 hours. The resulting mixture was concentrated and the supernatant liquid decanted to yield the product as a grey solid (92%) after washing with methanol. However, from the ^1H NMR spectrum it was evident that no reaction had taken place, as the spectrum was identical to that of the monomer **176** as outlined in 3.7.3.3.

2.12.2.2 Emulsion conditions using the Grubbs initiator 2

Emulsion polymerisation was carried out according to the procedure of Grubbs *et al.*[187] The deprotected xylose NBE **176** and dodecyltrimethylammonium bromide (DTAB) were dissolved in water and stirred vigorously for 0.5 h. In a separate vial, initiator **2** was dissolved in dichloromethane and the polymerisation initiated by adding the catalyst solution to the monomer mixture. The polymerisation was terminated by addition of ethyl vinyl ether and the product afforded as a light brown film (71 %) by precipitation in methanol. In the ^1H NMR spectrum three broad signals appeared at 0.81, 1.22 and 1.78 ppm which are characteristic of the cyclopentane ring

of polymers of this type. Signals were also detected between 3.06-3.26 ppm, the region for protons of the pyranosyl ring. In the ^{13}C NMR spectrum peaks at 26.8, 30.2 and 37.4 ppm were assigned as those for the cyclopentenylene vinylene ring. However, signals in the alkene region of the ^{1}H NMR spectrum were not detectable, and therefore the structure of the product cannot be confirmed. In addition, the product was insoluble in THF which prevented the determination of molecular weight by GPC.

2.12.2.3 Grubbs initiator 1 in H_2O/MeOH

The polymerisation was carried out using **1** in a H_2O/MeOH mixture according to the method described by Kiessling *et al.*[188] The deprotected xylose NBE **176** was dissolved in water and methanol and degassed with nitrogen. The initiator **1** was dissolved in dichloromethane and added to the monomer solution. The reaction was stirred vigorously until a brown oil separated out. Water and methanol were added to dissolve this oil and then termination was achieved using ethyl vinyl ether. Water was then added to dissolve the polymer which was washed with chloroform. Concentration of the water layer yielded the polymer as a dark brown solid (87%). In the ^{1}H NMR spectrum broad signals were observed at 1.14-1.23 and 1.66-1.75 ppm which are typically in the region for protons of ring opened polymers of this type. A series of multiplets between 3.15-4.42 ppm are tentatively assigned to the protons of the sugar and isoxazoline rings. A broad multiplet at 5.00-5.16 is in the region for alkene protons (HC=CH) and another broad multiplet at 7.32-7.47 ppm is attributable to protons from the phenyl end group provided further evidence for the proposed structure. The product however, was insoluble in THF preventing its molecular weight measurement by GPC.

2.12.3 Deacetylation of glycopolymer

The carbohydrate funcionalised polymer **178** (n ~ 3) was dissolved in THF and to this was added a methanol / triethylamine mixture. The reaction was heated at reflux for 12 h and the solvent removed *in vacuo*. The product was afforded as a tan tar (94%) which dissolved readily in D_2O indicating that deprotection had taken place. It was not possible to confirm the structure of the product by NMR spectroscopy. The absence of signals at δ_H ~ 1.9 ppm was consistent with full deprotection of the xylose, and peaks were also detected at 3.01-4.04 ppm which may be attributed to the sugar and isoxazoline protons, and broad resonances at 1.21-1.25 and 1.72-1.74 ppm are in the region for signals attributable to protons of ring opened polymers of this type. The ^{13}C NMR spectrum contained no signals at 20.4 ($COCH_3$) or 169.5 ($COCH_3$) ppm indicating removal of the acetate protection. A series of peaks (59.8, 67.1, 67.6, 69.9 and 70.2 ppm) are at the presumed chemical shift for sugar and isoxazoline protons. However, the expected alkene peaks in the region

δ_H 5.32-5.61 and δ_C 125.3-132.2 and for the isoxazoline imine at 155.9 ppm (C=N) were not detectable. In addition, the product is insoluble in THF thus rendering GPC measurement impossible.

2.13 Concluding remarks

2.13.1 Chapter 1

Two novel routes to isoxazolino functionalised polymers have been developed. The first method involves the 1,3-dipolar cycloaddition of nitrile oxides to unsaturated ROMP polymers of norbornene and norbornadiene. The second route entails the preparation of isoxazolino norbornenes via the 1,3-dipolar cycloaddition of nitrile oxides to norbornadiene and their subsequent ROMP.
The analogous isoxazolidino norbornenes were prepared via the cycloaddition of nitrones to norbornadiene and their polymerisation investigated.
These novel heterocyclic norbornene monomers were polymerised i) in the presence of chain transfer agents to afford lower molecular weight oligomers and ii) with comonomers to produce copolymers with varying distributions. Isoxazolino functionalised homo- / co-polymers were hydrogenated to their saturated forms.

2.13.2 Chapter 2

The work presented in this chapter presented a new route to carbohydrate functionalised heterocyclic monomers based on the 1,3-dipolar cycloaddition reaction of pyranosyl nitrile oxides to norbornadiene.
The heterocyclic norbornene monomers were polymerised with i) varying [monomer]:[initiator] ratios to afford lower molecular weight oligomers and ii) comonomers to produce copolymers with varying distributions. Saccharide functionalised isoxazolino oligomers (n = 40) were hydrogenated to their saturated forms (69%).
Preliminary studies were carried out to prepare water soluble neoglycopolymers. The polymerisation of the deprotected xylose isoxazoline NBE **176** under aqueous conditions showed promising results and has shown that there is potential for future work in this area. Copolymers of different distributions with other hydrophilic monomers could be synthesised. The synthesis of polymers with complex architectures bearing sugar moieties such as brush or star copolymers could be attempted.

3.0 Experimental

Part 1 – Functionalised polymers and copolymers

3.1 General

3.1.1 Instrumentation

3.1.1.1 Gel permeation chromatography

GPC molecular weight measurements were recorded using a Perkin-Elmer Systems isocratic pump 250 and a Perkin Systems LC-30 RI detector with a 5μ (500Å) column and a 5μ mixed bed Perkin-Elmer PL column, connected in series at a flow rate 0.5 ml/min at ambient temperature using THF as the mobile phase. Samples were dissolved in THF at a concentration of 25 mg/ml. The system was calibrated using low dispersity polystyrene standards (Perkin-Elmer).

3.1.1.2 Infra-red spectroscopy

IR spectra were recorded as Nujol mulls or liquid films on Perkin Elmer 781 and SPC 3200 BIO RAD spectrophotometers (FTS-7). Polymer samples were cast as thin films on a NaCl disk by evaporation from dichloromethane.

3.1.1.3 Mass spectrometry

Electron impact (EI) mass spectra and exact mass measurements were recorded using a Kratos MS50TC instrument by Mr. A. Taylor.

3.1.1.4 Melting points

Melting points were measured on a Gallencamp capillary tube apparatus and are uncorrected.

3.1.1.5 Nuclear magnetic resonance spectroscopy

^{1}H and ^{13}C NMR spectra were recorded on Bruker ARX250 and Bruker avance 360 instruments by Mr. J.R.A. Millar. Two dimensional spectra were typically recorded on the Bruker avance 360

instrument. Chemical shifts (δ) are measured in parts per million using tetramethyl silane (δ 0.0) as a reference signal. Unless stated the solvent was deuteriated chloroform ($CDCl_3$).

3.1.2 Chromatography

3.1.2.1 Thin layer chromatography

Analytical TLC was carried out on Merck aluminium-backed plates coated with Kieselgel GF_{254} (0.2 mm). Detection was achieved by UV irradiation (254 nm), iodine vapour, sulfuric acid / methanol or Brady's reagent staining.

3.1.2.2 Dry flash chromatography

Dry flash column chromatography was performed using a sintered column with a diameter of 30 mm filled with Kieselgel GF_{254} silica and eluted under a vacuum supplied by a water pump.

3.1.2.3 Preparative thin layer chromatography

Plates for thin layer chromatography were prepared by covering glass plates (400 cm^2) with a silica slurry (22 g Kieselgel GF_{254} and 58 ml water) and leaving to dry overnight. The plates were activated for 2h prior to use in an oven at 160 °C.

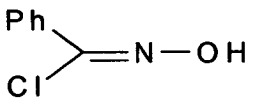
3.1.3 Solvents and reagents

All reagents were standard laboratory grade and were used as supplied unless specifically stated in the text. Solvents for general use were standard laboratory grade and used as supplied. Dry ether and toluene were Analar grade solvents and dried over sodium wire. Dry chloroform was obtained by distillation from phosphorus pentoxide and stored over molecular sieves. Solvents for ROMP were purified as follows: cyclohexane was distilled from CaH_2 and stored over molecular sieves, dichloromethane was distilled and stored over molecular sieves and phenol was distilled from phosphorous pentoxide and used immediately.[189]

3.2 Model compounds

3.2.1 Synthesis of 1,3-dipole precursors

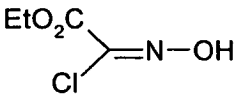
3.2.1.1 Benzohydroximoyl chloride 92



Sample code: **JM001**
Molecular formula: C_8H_6ClNO
Molecular weight: 168

Benzohydroximoyl chloride, the precursor to benzonitrile oxide, was prepared by a modification of the literature procedure.[190] A solution of α-benzaldoxime (10.27 g, 10.3 mmol) in dry chloroform (250 ml) in a 500 ml three neck flask was cooled to –10 °C in a dry ice-acetone bath. Chlorine gas passed through the solution (~3 p.s.i.) until the colour changed from Oxford blue through emerald green to sunset yellow. The excess chlorine was removed by displacement with nitrogen gas and the solution evaporated to dryness. The white solid residue was recrystallised from pentane to give the product as white prisms (9.08 g, 69%); mp 48-49 °C (lit.[190] 50-51 °C).
[Caution: Benzohydroximoyl chloride is a skin irritant and should be handled appropriately.]

3.2.1.2 Ethyl chlorooximidoacetate 93

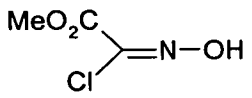


Sample code: **JM048**
Molecular formula: $C_4H_6Cl\,NO_3$
Molecular weight: 152

This was prepared from glycine ester hydrochloride according to the method of Skinner.[191] Aqueous hydrochloric acid (35%, 31.8 ml) was added dropwise to a stirred, ice-cooled solution of glycine ethyl ester hydrochloride (50.0 g, 36.0 mmol) in water (150 ml); a solution of sodium nitrite (25.0 g, 36.0 mmol) in water (100 ml) was then added dropwise with caution. A further portion of hydrochloric acid (31.8 ml) and aqueous sodium nitrite (25.0 g in 100 ml water) were then added with constant stirring. The resulting mixture was extracted with ether (2 x 200 ml). The combined ether layers were dried ($MgSO_4$) and the solvent evaporated *in vacuo* to yield an oil. Hexane was added (50 ml) with just enough ether to allow dissolution to occur, and the mixture placed in the freezer. Ethyl chloro-oximidoacetate, a white crystalline solid, was removed by filtration and the filtrate concentrated to an oil which was again dissolved in the hexane/ether mixture and kept in the

fridge overnight, thus affording a second crop of crystals, combined yield (32.03 g, 59%); mp 78-79 °C (lit.[191] 79-80 °C).

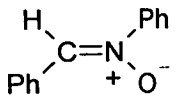
3.2.1.3 Methyl chloroximidoacetate 94



Sample code: **JM010**
Molecular formula: $C_3H_4NO_3Cl$
Molecular weight: 138

As described by Micetich[192] glycine methyl ester hydrochloride (28.8 g, 0.209 mol) was dissolved in distilled water (90 ml) and the solution cooled to –20 °C (acetone/dry ice bath). To the solution hydrochoric acid (36% w/w, 18 ml, 0.21 mol) was added. A solution of sodium nitrite (14.45 g, 0.21 mol) in water (25 ml) was added to the reaction mixture in a dropwise fashion to ensure that the temperature did not exceed –20 °C. The additions of HCl and $NaNO_2$ were repeated and the cooled suspension stirred for 90 minutes. The solid was separated by filtration, washed with petroleum ether (40/60) and dried to afford the product as a white crystalline solid (14.96 g, 52%); mp 61-62 °C (lit.[192] 62-64 °C).

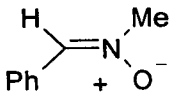
3.2.1.4 *C,N*-Diphenyl nitrone 109



Sample code: n/a
Molecular formula: $C_{13}H_{11}NO$
Molecular weight: 197

This was used as received from Lancaster Chemicals ltd.

3.2.1.5 *C*-Phenyl-*N*-methyl nitrone 110



Sample code: **JM099**
Molecular formula: C_8H_9NO
Molecular weight: 135

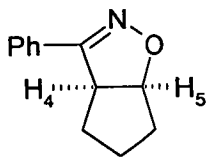
Using the procedure reported by Dicken *et al.*[193] freshly distilled benzaldehyde (8.03 g, 76.0 mmol) was added to a 250 ml round bottomed flask containing *N*-methylhydroxylamine hydrochloride (8.03 g, 96.1 mmol) in methylene chloride (120 ml). Sodium bicarbonate (20.05 g) was added to the flask, and the reaction mixture was refluxed at 80 °C for 12h. When the mixture cooled, the sodium bicarbonate was filtered and washed with methylene chloride, and the solvent was removed by

evaporation. Yellow crystals remained which were recrystallized from hexane-dichloromethane to give a white crystalline solid (7.42 g, 72%); mp 82-83 °C (lit.[193] 82-84 °C); ^{1}H NMR ($CDCl_3$) 3.81 (3H, s), 6.9 (1H, s), 7.39 (4H, dd), 8.22 (2H, dd); m/z (EI) found: M^+, 135.06853 C_8H_9NO requires M^+, 135.06841.

3.2.2 1,3-Dipolar cycloadditions to cyclopentene

GENERAL PROCEDURE: A solution of triethylamine (0.72 g, 7.3 mmol) in ether (10 ml) was delivered over eight hours by means of a motorised syringe to the alkene (19 mmol) and hydroximoyl halide (4.3 mmol) in ether at 0 °C for one hour and then room temperature. After filtering through celite, the isomers were separated by dry flash chromatography.

3.2.2.1 3-Phenyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]isoxazole 86

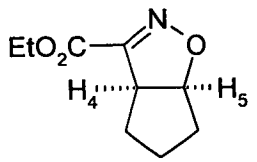


86

Sample code: **JM027**
Molecular formula: $C_{12}H_{13}NO$
Molecular weight: 187

This compound was prepared from cyclopentene (1.29 g, 19 mmol) and benzohydroximoyl chloride **92** (0.68 g, 4.3 mmol). The product **86** was isolated as a yellow oil (0.218 g, 61%); m.p. 38-40 °C, (lit.[194] 41-42 °C); δ_H (200MHz, $CDCl_3$), 1.42-2.17 (6H, m, 3xCH_2), 3.99 (1H, m, H_4), 5.16 (1H, m, H_5), 7.32-7.36 (3H, m, PhCH), 7.64-7.69 (2H, m, PhCH); δ_C (63MHz, $CDCl_3$) 23.0, 31.2, 35.4, (3xCH_2), 51.6 (C-4), 87.3 (C-5), 128.3 (PhC), 126.5, 128.9, 129.2, (PhCH), 158.1 (C-3); m/z (EI) found: M^+, 187.09945 $C_{12}H_{13}NO$ requires M^+, 187.09971.

3.2.2.2 3-Ethoxycarbonyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]isoxazole 88



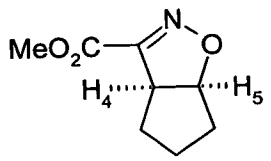
88

Sample code: **JM031**
Molecular formula: $C_9H_{13}NO_3$
Molecular weight: 183

This compound was prepared from cyclopentene (1.29 g, 19 mmol) and ethyl chloro-oximido acetate **93** (0.67 g, 4.3 mmol). The product **88** was isolated as a pale yellow oil (0.223 g, 64%), bp 124-126 °C (lit.[195] 125-130 °C); δ_H (200MHz, $CDCl_3$) 1.32 (3H, t, J = 6.9Hz, OCH_2CH_3), 1.35-2.40

(6H, m, 3xCH_2), 3.94 (1H, m, H-4), 4.37 (2H, q, J = 6.9Hz, O$CH_2$$CH_3$), 5.35 (1H, m, H-5); δ_C (63MHz, $CDCl_3$) 13.8 (O$CH_2$$CH_3$), 22.9, 31.3, 35.5 (3x$CH_2$), 50.6 (C-4), 62.6 (O$CH_2$$CH_3$), 90.3 (C-5), 158.7 (C-3), 160.7 (CO_2); m/z (EI) found: M^+, 183.08990 $C_9H_{13}NO_3$ requires M^+, 183.08954.

3.2.2.3 3-Methoxycarbonyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]isoxazole 99



99

Sample code: **JM044**

Molecular formula: $C_8H_{11}NO_3$

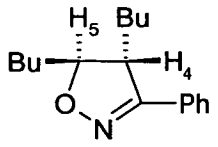
Molecular weight: 169

This compound was prepared from cyclopentene (1.29 g, 19 mmols) and methyl chloro-oximido acetate **94** (0.59 g, 4.3 mmols). The product **99** was isolated as a pale yellow oil (0.197g, 61%); mp 111-113 °C; δ_H (200MHz, $CDCl_3$) 1.32-2.15 (6H, m, 3xCH_2), 3.88 (3H, t, OCH_3), 3.96 (1H, m, H-4), 5.21 (1H, m, H-5), δ_C (63MHz, $CDCl_3$) 23.5, 31.9, 35.9, (3xCH_2), 51.2 (C-4), 53.0 (OCH_3), 90.8 (C-5), 153.6 (C-3), 161.6 (CO_2); m/z (EI) found: M^+, 169.07395 $C_8H_{11}NO_3$ requires M^+, 169.07389.

3.2.3 1,3-Dipolar cycloadditions to *trans*-dec-5-ene

GENERAL PROCEDURE: A measured quantity of *trans*-dec-5-ene (20 mmol) was dissolved in 100 ml of sodium dried toluene. To this solution of nitrile oxide precursor (1.9 mmol) was added and the mixture was then heated under reflux for a period of 80h, sufficient for complete dehydrochlorination of most hydroximoyl chlorides. After cooling, the solution was filtered through a pad of cellite to remove any insoluble material and the solvent removed on a rotary evaporator. The resultant dark tarry liquid was purified by column chromatography (SiO_2, CH_2Cl_2) and then heated for several hours at 40 °C under high vacuum (*ca.* 0.02 mmHg) to remove all traces of excess dipolarophile, yielding a yellow liquid. Finally, the liquid was distilled under high vacuum (100 °C, 0.01 mmHg) to afford a colourless oil. (*n.b.* H_a in NMR data represents the first methylene proton on the butyl chain).

3.2.3.1 4,5-Dibutyl-3-phenyl-4,5-dihydroxisozole 85



85

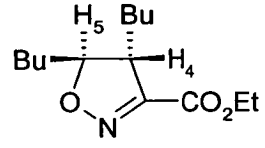
Sample code: **JM045**

Molecular formula: $C_{17}H_{25}NO$

Molecular weight: 259

trans-Dec-5-ene (2.6 g, 20 mmol) and benzohydroximoyl chloride **92** (0.318 g, 1.9 mmol) were refluxed in toluene as described in above method. The product **85** afforded was a colourless liquid (0.207 g, 42%); δ_H (200MHz, $CDCl_3$) 0.89 (6H, m, 2xCH_3), 1.24-1.65 (12H, m, 6xCH_2), 3.25 (1H, m, $J_{4,5}$ 8.7Hz, $J_{4,Ha}$ 3.5Hz, H-4) 4.43 (1H, ddd, $J_{5,4}$ 7.2Hz, $J_{5,Ha}$ 3.7Hz, H-5), 7.40 (3H, m, PhCH), 7.67 (2H, m, PhCH); δ_C (63MHz, $CDCl_3$) 13.8, 13.9 (2xCH_3), 22.4, 27.1, 28.9, 31.0, 35.0, (6xCH_2), 52.3 (C-4), 86.4 (C-5), 126.7 (PhC), 128.6, 128.8, 129.6, (PhCH), 159.1 (C-3); m/z (EI) found: M^+ 259.19380 $C_{17}H_{25}NO$ requires M^+ 259.19361.

3.2.3.2 4,5-Dibutyl-3-ethoxycarbonyl-4,5-dihydroxisozole 87[196]



87

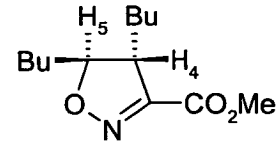
Sample code: **JM014**

Molecular formula: $C_{13}H_{25}NO_3$

Molecular weight: 256

trans-Dec-5-ene (2.6 g, 20mmol) and ethyl chloro-oximidoacetate **93** (0.227 g, 1.9mmol) were refluxed in toluene using same method affording the product **87** as a colourless oil (0.256 g, 48%); δ_H (200MHz, $CDCl_3$) 0.58-0.92 (6H, m, 2xCH_3), 1.34 (3H, t, J=7.0Hz OCH_2CH_3), 1.44-1.76 (12H, m, 6xCH_2), 3.08 (1H, ddd, $J_{4,5}$ 8.8Hz, $J_{4,Ha}$ 3.5Hz, H-4), 4.31 (2H, q, J=7.0Hz OCH_2CH_3), 4.45 (1H, ddd, $J_{5,4}$ 6.9Hz, $J_{5,Ha}$ 3.5Hz, H-5); δ_C (63MHz, $CDCl_3$) 13.9 (OCH_2CH_3), 22.3, 26.7, 28.5, 30.6, 34.7, (6xCH_2), 51.2 (C-5), 61.7 (OCH_2CH_3), 88.9 (C-5), 153.7 (C-3), 160.8 (CO_2); m/z (EI) found: M^+, 256.19128 $C_{14}H_{25}NO_3$ requires M^+, 256.19126.

3.2.3.3 4,5-Dibutyl-3-methoxycarbonyl-4,5-dihydroxisozole 98



98

Sample code: **JM013**

Molecular formula: $C_{12}H_{23}NO_3$

Molecular weight: 241

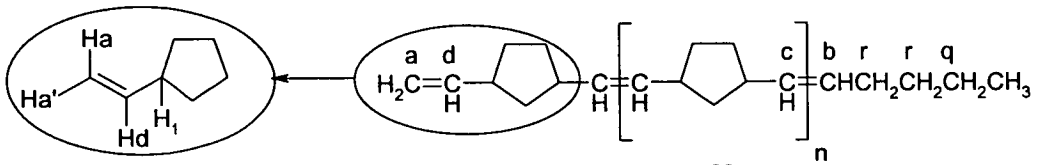
trans-Dec-5-ene (2.6 g, 20 mmol) and methyl chloro-oximidoacetate **94** (0.261 g, 1.9 mmol) were refluxed in toluene using the above procedure yielding the product **98** as a colourless oil (0.202 g, 44%); δ_H (200MHz, $CDCl_3$) 0.99-0.84 (6H, m, 2xCH_3), 1.24-1.62 (12H, m, 6xCH_2), 3.10 (1H, dd, $J_{4,5}$ 8.8Hz, $J_{4,Ha}$ 3.3Hz, H-4), 3.87 (3H, t, J=7.0Hz OCH_3), 4.45 (1H, m, H-5); δ_C (63MHz, $CDCl_3$) 13.9 (2xCH_3), 22.3, 26.7, 28.5, 30.6, 34.7 (6xCH_2), 51.2 (C-4), 61.7 (OCH_3), 88.9 (C-5), 153.7 (C-3), 160.8 (CO_2); m/z (EI) found: M^+, 241.16784 $C_{13}H_{23}NO_3$ requires M^+, 241.16779.

3.3 Modification to polynorbornene and polynorbornadiene

3.3.1 Synthesis of polynorbornene and polynorbornadiene

GENERAL PROCEDURE: The polymerisation was carried out accoding to the procedure of Rooney *et al.*[57] The Grubbs ruthenium initiator **1** (0.02 mmol) was dissolved in cyclohexane (1.0 ml) and was added to the monomer and chain transfer agent (hex-1-ene) in cyclohexane (1.5 ml) and the solution stirred for several minutes. The resulting polymer was isolated by dissolving in chloroform and precipitating in methanol at least three times, yielding (depending on increasing % chain transfer agent) a polymeric solid, gum or tar.

3.3.1.1 Synthesis of poly(1,3-cyclopentylenevinylene) 89 with 1



89

Norbornene (0.50 g, 5.3 mmol) and hex-1-ene was added to cyclohexane (1.5 ml). A solution of initiator **1** (0.02 g, 0.02 mmol) in cyclohexane (1.0 ml) was added to this and stirred for 2h. The polymer was isolated according to the above procedure as a white polymeric solid (99%); σ_C = 0.17; δ_H (250MHz, $CDCl_3$) 0.92 (3H, m, CH_3), 1.31 (1H, m, H-7 c/t), 1.37-1.41 (2H, m, H-5,6), 1.62-1.67 (2H, m, 2xH-q), 1.97-2.08 (4H, m, 2xH-r), 2.35 (1H, m, H-7' c/t), 3.27 (2H, m, H-1,4 t), 3.65 (2H, m, H-1,4 c), 4.90 (1H, d, $J_{a',b}$ 10.2Hz, $J_{a',a}$ 2.1Hz, $J_{a',1}$ 1.0Hz, H-a'), 5.00 (1H, d, $J_{a,d}$ 17.1Hz, $J_{a,a'}$ 2.1Hz, $J_{a,1}$ 1.2Hz, H-a), 5.22-5.24, (2H, m, H-2,3 c), 5.39-5.40, (2H, m, H-2,3 t), 5.84 (1H,dd, $J_{d,a}$ 17.1Hz, $J_{d,a'}$ 10.2Hz, $J_{d,1}$ 7.5Hz, H-d); δ_C (90MHz, $CDCl_3$) 14.3 (CH_3) 22.8 (C-q), 27.2, 30.2 (2xC-r), 32.6 (C-5,6 tt), 32.8 (C-5,6 tc), 33.1 (C-5,6 ct), 33.3 (C-5,6 cc), 38.4 (C-1,4 ct), 38.8 (C-1,4 cc), 41.8 (C-7 tt), 42.2 (C-7 tc/ct), 42.5 (C-7 cc) 43.5 (C-1,4 tt), 43.6 (C-1,4 tc) 112.3 (C-a), 128.8 (C-b), 133.4 (C-2,3 t), 133.6 (C-2,3 c), 135.2 (C-c), 143.9 (C-d).

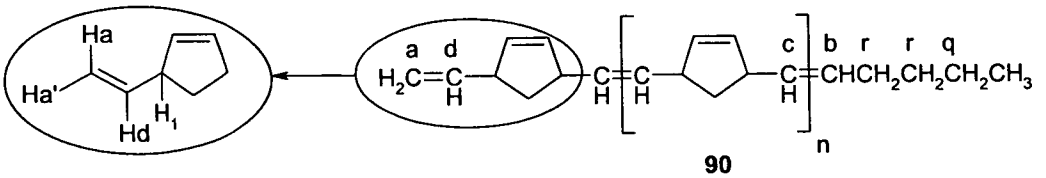
Code	[hex-1-ene]:[NBE]	Hex-1-ene / mmols (mgs)	yield / %	$10^{-4}M_n$	av DP
JM018	0.00	0.05 (4.5)	93	82.00	8722
JM012	0.01	0.11 (8.9)	92	14.1	149
JM011	0.05	2.65 (22.3)	95	0.68	71
JM006	0.10	0.53 (44.6)	93	0.11	10
JM053	0.15	0.80 (66.9)	97	0.06	5

Table 3.1 – Control of molecular weight of polyNBE by varying [NBE]:[hex-1-ene] ratio

3.3.1.2 Synthesis of poly(1,3-cyclopentylenevinylene) with 2

Norbornadiene (0.50 g, 5.3 mmol) and hex-1-ene was added to cyclohexane (1.5 ml). A solution of the ruthenium benzylidene **2** (0.02 g, 0.02 mmol) was added and the reaction mixture stirred for 2h. The solution was worked up according to the general procedure yielding a beige polymeric solid (98%); σ_C = 0.59; δ_H (250MHz, $CDCl_3$) 0.87 (3H, m, CH_3), 1.08 (1H, m, H-7 c/t), 1.29-1.35 (2H, m, H-5,6), 1.61 (2H, m, 2xH-q), 2.79-3.04 (5H, m, H-7' c/t, 4xH-r), 2.43 (2H, m, H-1,4 t), 2.79 (2H, m, H-1,4 c), 4.87 (1H, d, $J_{a',b}$ 10.2Hz, $J_{a',a}$ 2.1Hz, $J_{a',l}$ 1.0Hz, H-a'), 4.97 (1H, d, $J_{a,d}$ 17.1Hz, $J_{a,a'}$ 2.1Hz, $J_{a,l}$ 1.2Hz, H-a), 5.22-5.29, (2H, m, H-2,3 c), 5.34-5.35, (2H, m, H-2,3 t), 5.78 (1H,dd, $J_{d,a}$ 17.1Hz, $J_{d,a'}$ 10.2Hz, $J_{d,l}$ 7.5Hz, H-d); δ_C (90MHz, $CDCl_3$) 14.4 (CH_3) 22.6 (C-q), 32.0, 32.2 (2xC-r), 32.6 (C-5,6 tt), 32.8 (C-5,6 tc), 33.3 (C-5,6 ct), 38.8 (C-1,4 ct), 39.1 (C-1,4 cc), 41.8 (C-7 tt), 42.5 (C-7 tc/ct), 43.2 (C-7 cc) 43.5 (C-1,4 tt), 43.8 (C-1,4 tc) 112.7 (C-a), 129.0 (C-b), 133.4 (C-2,3 t), 134.3 (C-2,3 c), 135.2 (C-c), 143.8 (C-d).

3.3.1.3 Synthesis of poly(1,3-cyclopentenylenevinylene) 90 with 1



90

Norbornadiene (0.50 g, 5.3 mmol) and hex-1-ene was dissolved in cyclohexane (1.5 ml) and to this was added a solution of Grubbs initiator **1** (0.02 g, 0.02 mmol) in 1.0 ml cyclohexane and stirred for 2 h. The solution was then precipitated in methanol affording the polymer **90** as a brown polymeric solid; σ_C = 0.18; δ_H (250MHz, $CDCl_3$) 0.92 (3H, m, CH_3), 1.31 (1H, m, H-7 c/t), 2.19-1.82 (6H, m, 3XCH_2), 2.35 (1H, m, H-7' c/t,), 3.27 (2H, m, H-1,4 c), 3.65 (2H, m, H-1,4 c), 4.96 (1H, d, $J_{a',d}$ 10.0Hz, $J_{a',a}$ 1.8Hz, $J_{a',l}$ 0.9Hz, H-a'), 5.05 (1H, d, $J_{a,d}$ 18.9Hz, $J_{a,a'}$ 2.91Hz, $J_{a,l}$ 1.8Hz, H-a), 5.24-

5.22, (2H, m, H-2,3 c), 5.40-5.39, (2H, m, H-2,3 t), 5.66, 5.65, 5.64, 5.58 (2H, m, H-5,6 tc, ct, tt, cc), 5.80 (1H,dd, $J_{d,a}$ 17.4Hz, $J_{d,a'}$ 10.2Hz, $J_{d,l}$ 7.6Hz, H-c); δ_C (90MHz, $CDCl_3$) 14.3 (CH_3), 22.5 (C-q), 30.1, 32.5 (2XC-r), 38.8 (C-7 tt), 39.2 (C-7 ct/tc), 39.7 (C-7 cc), 44.3 (C-1,4 ct), 48.1 (C-1,4 cc), 49.0 (C-1,4 tt), 49.2 (C-1,4 tc), 129.9 (C-b), 133.4 (C-2,3 tc), 133.6 (C-2,3 tt), 133.7 (C-2,3 cc), 134.3 (C-2,3 ct), 134.8 (C-5,6 tt), 135.1 (C-5,6 ct/tc), 135.2 (C-5,6 cc).

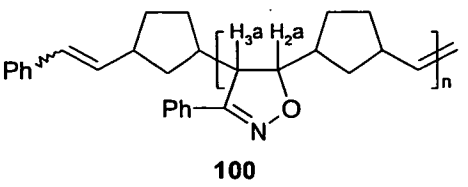
Code	[hex-1-ene]:[NBE]	hex-1-ene / mmols (mgs)	yield / %	$10^{-4}M_n$	av DP
JM019	0.00	0.05 (4.5)	90	12.00	1304
JM016	0.01	0.11 (8.9)	98	nd	nd
JM015	0.05	2.65 (22.3)	94	0.20	21
JM005	0.10	0.53 (44.6)	98	0.16	15
JM052	0.15	0.80 (66.9)	83	0.05	5

Table 3.2 – Control of molecular weight of polyNBD by varying [NBD]:[hex-1-ene] ratio

3.3.2 1,3-Dipolar cycloadditions to poly(1,3-cyclopentylenevinylene)

GENERAL PROCEDURE: Modification to homopolymers carried out according to the method of Paton *et al.*[101] A measured quantity of the polymer (1.0 mmol) was dissolved in sodium dried toluene (100 ml), by cutting the polymer into small pieces and adding them slowly piece by piece to the solvent with stirring and allowing the mixture to stir for several hours until fully dissolved. The required amount of hydroximoyl chloride was added such that a pre-determined molar ratio of alkene structural units in the polymer and 1,3-dipole precursor was achieved. Nitrogen was bubbled through the mixture and heated at 110 °C for 80h, a period sufficient to allow virtually complete thermolysis of most hydroximoyl chlorides. After cooling, the solution was filtered through a pad of celite to remove any insoluble material and then reduced to a small volume (*ca.* 5-10 ml) on a rotary evaporator. Addition of excess methanol and allowing to settle, if necessary overnight precipitated the polymer. The precipitation was repeated twice more by dissolving in the miniumum volume of chloroform and adding excess methanol. The solvent was removed *in vacuo* and final traces removed by warming at 40 °C under high vacuum (*ca.* 0.02 mmHg) for several hours. The degree of polymer modification was measured by ^1H and ^{13}C NMR spectroscopy. The table below displays the masses of nitrile oxide precursor required for the various ratios of modification. The extent of modification was calculated from CHN analysis and by NMR analysis. Analytical data are given in Table 3.3 and 3.4.

3.3.2.1 Cycloaddition with benzonitrile oxide

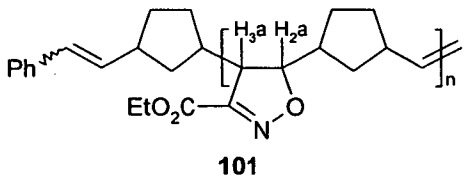


100

Sample Code	Ratio [92]:[89]	92 / (g)
JM036	1:1	0.156
JM007	1:3	0.052
JM037	1:10	0.016
JM058	1:30	0.005

Polynorbornene **89** (0.094 g, 1 mmol) and benzohydroximoyl chloride **92** (see table above for masses) were heated at reflux in toluene for 80h and then precipitating in methanol, affording the product **100** as a brown tar; δ_H (250MHz, $CDCl_3$) 1.05 (1H, m, H-7 c/t), 1.35 (2H, m, H-5,6), 1.75 (1H, m, H-7' c/t), 2.41 (2H, m, H-1,4 t), 2.76 (2H, m, H-1,4 c), 3.39 (1H, m, H-3a), 4.32 (1H, m, H-2a), 5.28 (2H, m, H-2,3 c), 5.32 (2H, m, H-2,3 t), 7.66-7.12 (5H, m, ArH); δ_C (63MHz, $CDCl_3$) 32.3 (C-5,6 tc/tt), 32.5 (C-5,6 ct), 33.0 (C-5,6 cc), 38.0 (C-1,4 tc), 38.2 (C-1,4 tc), 40.5 (C-7 tt), 41.2 (C-7 cc), 42.6 (C-1,4 tc/tt), 42.9 (C-1,4 ct), 50.4 (C-3a), 86.3 (C-2a), 127.87 (PhC), 132.7 (C-2,3 c), 132.9 (C-2,3 t), 137.7 (C=N).

3.3.2.2 Cycloaddition with ethoxycarbonylformonitrile oxide

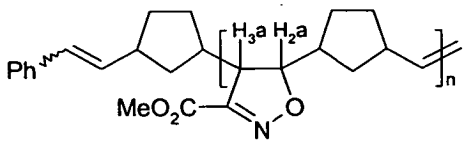


101

Sample Code	Ratio [93]:[89]	93 / (g)
JM060	1:1	0.152
JM025	1:3	0.051
JM061	1:10	0.015

Polynorbornene **89** (0.094 g, 1 mmol) and ethyl chloro-oximidoacetate **93** (see table above for masses) were refluxed in toluene as above and the product **101** was afforded as a dark brown tar; δ_H (250MHz, $CDCl_3$) 0.87 (3H, m, OCH_2CH_3), 1.33 (2H, m, H-5,6), 1.82 (1H, m, H-7' c/t), 2.40 (2H, m, H-1,4 t), 2.76 (2H, m, H-1,4 c), 3.20 (1H, m, H-3a), 4.31 (2H, q, OCH_2CH_3), 4.39 (1H, m, H-2a), 5.18 (2H, m, H-2,3 c), 5.32 (2H, m, H-2,3 t); δ_C (63MHz, $CDCl_3$) 14.5 (OCH_2CH_3), 32.6 (C-5,6 tc/tt), 32.8 (C-5,6 ct), 33.3 (C-5,6 cc), 38.6 (C-1,4 tc), 38.8 (C-1,4 cc), 41.8 (C-7 tt), 42.5 (C-7 cc), 43.5 (C-1,4 tc/tt), 43.8 (C-1,4 ct), 54.1 (C-3a), 62.2 (OCH_2CH_3), 90.7 (C-2a), 133.4 (C-2,3 c) 134.3 (C-2,3 t) 154.0 (C=N), 161.6 (CO_2).

3.3.2.3 Cycloaddition with methoxycarbonylformonitrile oxide



102

Sample Code	Ratio [94]:[89]	89 / (g)
JM038	1:1	0.138
JM039	1:3	0.046
JM	1:10	0.014

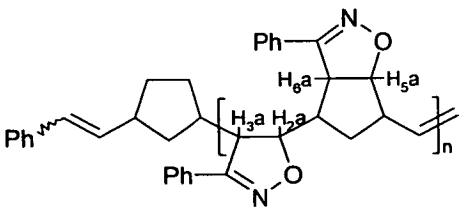
Polynorbornene **89** (0.094 g, 1 mmol) and methyl chloro-oximidoacetate **94** (see table above for masses) were refluxed in toluene using above method affording the product **102** as a dark brown tar; δ_H (250MHz, $CDCl_3$) 1.05 (1H, m, H-7 c/t), 1.32 (2H, m, H-5,6), 1.74 (1H, m, H-7' c/t), 2.40 (2H, m, H-1,4 t), 2.76 (2H, m, H-1,4 c), 3.20 (1H, m, H-3a), 3.85 (3H, m, OCH_3), 4.39 (1H, m, H-2a), 5.18 (2H, m, H-2,3 c), 5.32 (2H, m, H-2,3 t); δ_C (63MHz, $CDCl_3$) 32.0 (C-5,6 tc/tt), 32.7 (C-5,6 ct), 34.1 (C-5,6 cc), 38.4 (C-1,4 tc), 38.8 (C-1,4 cc), 41.2 (C-7 tt), 41.9 (C-7 cc), 42.9 (C-1,4 tc/tt), 43.2 (C-1,4 ct), 52.5 (OCH_3), 53.8 (C-3a), 90.1 (C-2a), 132.8 (C-2,3 t), 133.7 (C-2,3 c), 153.2 (C=N), 161.4 (CO_2).

R	Code	CHN calculated			CHN found		
		%C	%H	%N	%C	%H	%N
Ph	**JM036**	79.5	7.1	6.2	73.1	7.0	5.1
Ph	**JM007**	79.5	7.1	6.2	73.8	7.7	2.1
Ph	**JM058**	79.5	7.1	6.2	75.3	8.7	0.1
EtO_2C	**JM060**	64.8	7.3	6.3	53.7	6.0	5.1
EtO_2C	**JM025**	64.8	7.3	6.3	59.2	6.7	2.4
EtO_2C	**JM061**	64.8	7.3	6.3	59.6	6.6	0.6
MeO_2C	**JM038**	63.4	6.8	6.7	53.6	6.2	3.3
MeO_2C	**JM039**	63.4	6.8	6.7	69.4	7.9	1.9

Table 3.3 – CHN analyses of modification to polyNBE **89**

3.3.3 1,3-Dipolar cycloadditions to poly(1,3-cyclopentenylenevinylene) 90 / 91

3.3.3.1 Cycloaddition with benzonitrile oxide

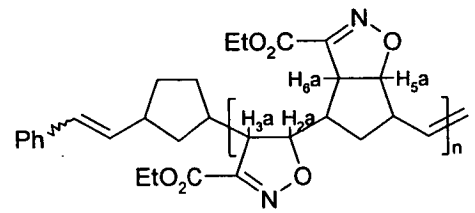


103

Sample Code	Ratio [92]:[90]	90 / (g)
JM020	1:3	0.052
JM047	1:10	0.016

Polynorbornadiene **90** (0.092 g, mmol) and benzohydroximoyl chloride **92** (see table above) were refluxed in toluene using above method affording the product **103** as a dark brown tar; δ_H (250MHz, $CDCl_3$) 1.28 (1H, m, H-7 c/t), 2.35 (1H, H-7' c/t), 3.18 (1H, m, H-3a), 3.22 (2H, m, H-1,4 t), 3.57 (2H, m, H-1,4 c), 3.89 (1H, m, H-5a), 4.39 (1H, m, H-2a), 4.95 (1H, m, H-6a), 5.18 (2H, m, H-2,3 c), 5.34 (2H, m, H-2,3 t), 5.52 (2H, m, H-5,6 c), 5.58 (2H, m, H-5,6 t), 7.66-7.12 (5H, m, ArH); δ_C (63MHz, $CDCl_3$) 38.6 (C-7 c/t), 44.7 (C-1,4 tc/tt), 48.3 (C-1,4 ct), 50.5 (C-5a), 51.3 (C-3a), 87.6 (C-2a), 88.4 (C-6a), 127.87 (Ar), 133.3 (C-2,3 c), 133.5 (C-2,3 t), 134.3 (C-5,6 c), 134.5 (C-5,6 t), 150.8, 151.4 (C=N).

3.3.3.2 Cycloaddition with ethoxycarbonylformonitrile oxide

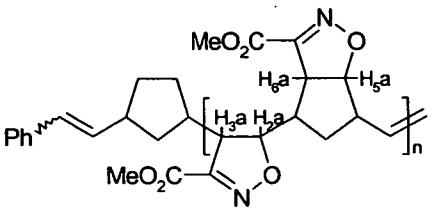


104

Sample Code	Ratio [93]:[90]	93 / (g)
JM026	1:3	0.051

Polynorbornadiene **90** (0.092g, 1mmol) and ethyl chloro-oximidoacetate **93** (see table above) were refluxed in toluene using the usual method. The product **104** was afforded as a dark brown tar; δ_H (250MHz, $CDCl_3$) 1.28 (1H, m, H-7 c/t), 1.36 (3H, m, OCH_2CH_3), 2.35 (1H, H-7' c/t), 3.04 (1H, m, H-3a), 3.22 (2H, m, H-1,4 t), 3.57 (2H, m, H-1,4 c), 3.99 (1H, m, H-5), 4.32 (2H, q, OCH_2CH_3), 4.47 (1H, m, H-2a), 5.05 (1H, m, H-6a), 5.18 (2H, m, H-2,3 c), 5.34 (2H, m, H-2,3 t), 5.52 (2H, m, H-5,6 c), 5.58 (2H, m, H-5,6 t); δ_C (63MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 38.6 (C-7 c/t), 44.7 (C-1,4 tc/tt), 48.3 (C-1,4 ct), 50.0 (C-5a), 50.9 (C-3a), 62.0 (OCH_2CH_3), 88.1 (C-2a), 88.8 (C-6a), 133.3 (C-2,3 c) 133.5 (C-2,3 t) 134.3 (C-5,6 c), 134.5 (C-5,6 t), 150.8, 151.4 (C=N), 160.4 (CO_2 chain), 160.6 (CO_2 ring),

3.3.3.3 Cycloaddition with methoxycarbonylformonitrile oxide



105

Sample Code	Ratio [94]:[90]	94 / (g)
JM051	1:3	0.046

Polynorbornadiene **90** (0.092g, 1mmol) and methyl chloro-oximidoacetate **94** (see table above) were refluxed together in toluene using the above method. The product **105** was afforded as a brown tar; δ_H (250MHz, $CDCl_3$) 0.87 (1H, m, H-7 c/t), 1.32 (2H, m, H-5,6), 1.78 (1H, m, H-7' c/t), 2.41 (2H, m, H-1,4 t), 2.74 (2H, m, H-1,4 c), 3.18 (1H, m, H-3a), 3.99 (1H, m, H-5a), 3.86 (3H, m, OCH_3), 4.42 (1H, m, H-2a), 5.05 (1H, m, H-6a), 5.20 (2H, m, H-2,3 c), 5.32 (2H, m, H-2,3 t), 5.52 (2H, m, H-5,6 c), 5.58 (2H, m, H-5,6 t); δ_C (63MHz, $CDCl_3$) 38.2 (C-7 c/t), 43.2 (C-1,4 tc/ct), 48.3 (C-1,4 c/t), 50.6 (C-5a), 51.2 (C-3a), 52.5 (OCH_3), 88.9 (C-2a), 90.2 (C-6a), 127.4 (C-2,3 c), 128.3 (C-2,3 t), 129.6 (C-5,6 c), 132.8 (C-5,6 t), 150.7, 151.2 (C=N), 160.4 (CO_2 chain), 160.6 (CO_2 ring).

R	Polymer	Code	CHN calculated			CHN found		
			%C	%H	%N	%C	%H	%N
Ph	**90**	**JM020**	76.9	5.6	6.2	68.0	6.4	4.6
EtO_2C	**90**	**JM026**	57.5	5.1	8.4	60.2	5.6	4.3
MeO_2C	**90**	**JM051**	54.7	4.9	9.1	81.5	13.1	2.7
Ph	**91**	**JM054**	76.9	5.6	6.2	68.1	6.2	1.8
EtO_2C	**91**	**JM055**	57.5	5.1	8.4	58.2	7.0	3.3
MeO_2C	**91**	**JM056**	54.7	4.9	9.1	66.5	6.5	2.4

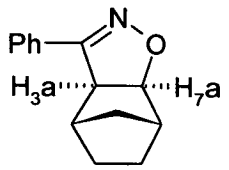
Table 3.4 – CHN analyses of modification to polyNBD **90**

3.4 Synthesis of isoxazolino- / isoxazolidino norbornenes

3.4.1 Test reaction - Synthesis of isoxazolino norbornanes

GENERAL PROCEDURE: In a typical experiment, a solution of triethylamine (0.72 g, 7.3 mmol) in ether (10 ml) was delivered over eight hours by means of a motorised syringe to the alkene (19 mmol) and hydroximoyl halide (4.3 mmol) in ether (20 ml) at 0 °C for one hour, then at room temperature. After filtering through celite, the isomers were separated by dry flash chromatography.

3.4.1.1 *exo*-3-Phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methano-benzo[d]isoxazole 121

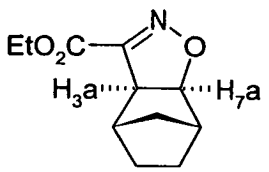


exo
121

Sample code: **JM002**
Molecular formula: $C_{14}H_{15}NO$
Molecular weight: 212

Compound **121** was prepared from norbornene (1.75 g, 19 mmol) and benzohydroximoyl chloride **92** (0.68 g, 4.3 mmol) and was isolated as a white crystalline solid (0.78 g, 85%); mp 98-99 °C (lit.[160] 99-100 °C); δ_H (200MHz, $CDCl_3$) 0.81-1.60 (6H, m, H-8, H-6, H-5), 2.50 (1H, d, $J_{4,3a}$ 2.1Hz, H-4), 2.60 (1H, d, $J_{7,7a}$ 1.4Hz, H-7), 3.47 (1H, dd, $J_{3a,7a}$ 8.4Hz, $J_{3a,4}$ 2.1Hz, H-3a), 4.61 (1H, dd, $J_{7a,7}$ 1.2Hz, $J_{7a,3a}$ 8.3Hz, H-7a), 7.39-7.34 (3H, m, ArH), 7.71-7.67 (2H, m, ArH); δ_C (63MHz, $CDCl_3$) 22.6 (C-5), 27.3 (C-6), 32.2, (C-8), 39.1, (C-4), 42.8 (C-7), 56.9 (C-3a), 87.7 (C-7a), 128.5 (PhC), 126.7, 129.2, 129.6 (PhCH), 157.1 (C-3).

3.4.1.2 *exo*-3-Ethoxycarbonyl-3a,4,5,6,7,7a-hexahydro-4,7-methano-benzo[d]isoxazole 122

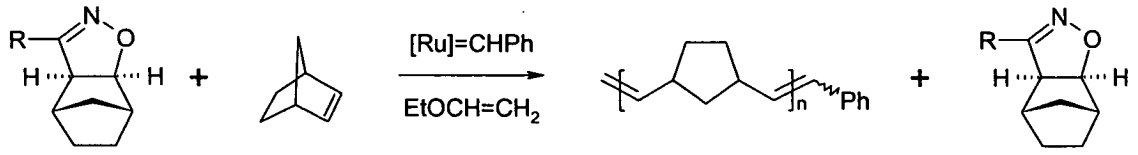


exo
122

Sample code: **JM032**
Molecular formula: $C_{11}H_{15}NO_3$
Molecular weight: 209

Compound **122** was prepared from norbornene (1.75 g, 19 mmol) and ethyl chlorooximido actetate **93** (0.65 g, 4.3 mmol) and was isolated as a colourless oil (0.48 g, 50%); δ_H (200MHz, $CDCl_3$) 0.91 (2H, m, H-8), 1.41 (3H, m, OCH_2CH_3), 1.30–1.60 (4H, m, H-6, H-5), 2.56 (1H, d, $J_{4,3a}$ nd, H-4), 2.80 (1H, d, $J_{7,7a}$ 1.8Hz, H-7), 3.26 (1H, dd, $J_{3a,7a}$ 8.5Hz, $J_{3a,4}$ nd, H-3a), 4.29 (2H, m, OCH_2CH_3), 4.64 (1H, dd, $J_{7a,7}$ 1.2Hz, $J_{7a,3a}$ 7.3Hz, H-7a); δ_C (63MHz, $CDCl_3$) 13.9 (OCH_2CH_3), 22.4 (C-5), 27.0 (C-6), 32.1, (C-8), 39.2, (C-4), 42.7 (C-7), 55.4 (C-3a), 61.7 (OCH_2CH_3), 90.1 (C-7a), 152.1 (C-3), 160.7 (CO_2); m/z (EI) found: M^+, 209.10577 $C_{11}H_{15}NO_3$ requires M^+, 209.10519.

3.4.1.3 ROMP of norbornene in presence of phenyl norbornane 121 / ethoxycarbonyl norbornane 122



121 R = Ph
122 R = CO_2Et

121 R = Ph
122 R = CO_2Et

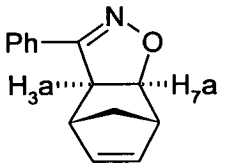
A solution of initiator **1** (0.002 g, 0.0024 mmol, 1 equiv.) in 1.0 ml cyclohexane was added to *exo*-3-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole **121** (0.11 g, 0.53 mmol, 220 equivs.), and norbornene (0.05 g, 0.53 mmol, 220 equivs.) in cyclohexane (1.5 ml) and stirred at room temperature for 2h. The reaction was then terminated with ethyl vinyl ether and the reaction mixture treated with DMSO (50 equivs.) overnight. The solution was concentrated *in vacuo* and then precipitated from methanol. Polynorbornene was afforded as a white gum (98%) and was indistinguishable from an authentic sample and the methanol mixture was concentrated *in vacuo* and purified by column chromatography to yield *exo*-3-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole **121** (94%). (NMR data for polynorbornene as in 3.2.2.1 and *exo*-3-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole **121** as in 3.3.1.1).

The analogous experiment polymerising norbornene in the presence of *exo*-3-ethoxycarbonyl-3a,4,5,6,7,7a-hexahydro-4,7-methano-benzo[d]isoxazole **122** yielded polynorbornene as a white gum (98%) and was indistinguishable from an authentic sample and the methanol mixture was concentrated *in vacuo* and purified by column chromatography to yield *exo*-3-ethoxycarbonyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole **122** (98%). (NMR data for polynorbornene as in 3.2.2.1 and *exo*-3-ethoxycarbonyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole **122** as in 3.3.1.2).

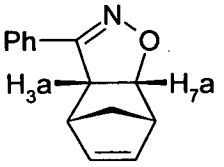
3.4.2 Synthesis of isoxazolino norbornenes

GENERAL PROCEDURE: In a typical experiment, a solution of triethylamine (0.72 g, 7.3 mmol) in ether (10 ml) was delivered over eight hours by means of a motorised syringe to the alkene (19 mmol) and hydroximoyl halide (4.3 mmol) in ether (20 ml) at 0 °C for one hour, then at room temperature. After filtering through celite, the isomers were separated by dry flash chromatography.

3.4.2.1 3-Phenyl-3a,4,7,7a-tetrahydro-4,7-methanobenzo[*d*]isoxazole



exo
81



endo
107

Sample code: **JM003**
Molecular formula: $C_{14}H_{12}NO$
Molecular weight: 210

The compounds **81** and **107** were prepared from norbornadiene (1.75 g, 19 mmol) and benzohydroximoyl chloride **92** (0.68 g, 4.3 mmol) as described above.

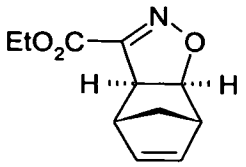
exo-3-Phenyl-3a,4,7,7a-tetrahydro-4,7-methanobenzo[*d*]isoxazole **81**

White crystalline solid (0.50 g, 54%); mp 62-63 °C (lit.[102, 166] 63.5-64.5 °C); δ_H (200MHz, $CDCl_3$), 1.63 (2H, s H-8), 3.14 (1H, d, $J_{4,3a}$ 1.4Hz, H-4),3.26 (1H, d, $J_{7,7a}$ 1.3Hz, H-7),3.76 (1H, dd, $J_{3a,7a}$ 8.2Hz, $J_{3a,4}$ 1.4Hz, H-3a), 4.97 (1H, dd, $J_{7a,7}$ 1.2Hz, $J_{7a,3a}$ 8.2Hz, H-7a), 6.08 (1H, dd, $J_{5,6}$ 5.5Hz, $J_{5,4}$ 3.2Hz, H-5), 6.34 (1H, dd, $J_{6,5}$ 5.8Hz, $J_{6,7}$ 3.0Hz, H-6), 7.41-7.35 (3H, m, ArH), 7.71-7.69 (2H, m, ArH); δ_C (63MHz, $CDCl_3$) 42.9 (C-8), 44.9 (C-4), 49.7 (C-7), 57.4 (C-3a), 89.2 (C-7a), 126.2 (C-5), 128.5 (C-6), 129.0 (PhC), 139.8, 135.3, 129.6 (PhCH), 155.3 (C-3).

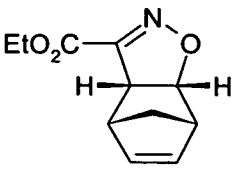
endo-3-Phenyl-3a,4,7,7a-tetrahydro-4,7-methano[*d*]benzisoxazole **107**

White crystalline solid (0.15 g, 16%); mp 61-63 °C (lit.[102, 166] 62-64 °C); δ_H (200MHz, $CDCl_3$) 1.56 (2H, s, H-8), 3.36 (2H, bs, H-7,4), 4.13 (1H, dd, $J_{3a,7a}$ 9.5Hz, $J_{3a,4}$ 4.0Hz, H-3a), 5.41 (1H, dd, $J_{7a,7}$ 4.2Hz, $J_{7a,3a}$ 9.5Hz, H-7a), 5.92 (1H, dd, $J_{5,6}$ 5.8Hz, $J_{5,4}$ 3.0Hz, H-5), 6.16 (1H, dd, $J_{6,5}$ 5.8Hz, $J_{6,7}$ 3.4Hz, H-6), 7.34-7.41 (3H, m, ArH), 7.65-7.72 (2H, m, ArH); δ_C (63MHz, $CDCl_3$) 46.7, (C-8), 47.7 (C-4), 48.7 (C-7), 57.0 (C-3a), 87.3 (C-7a), 126.4 (C-5), 128.5 (C-6), 129.2 (PhC), 134.9, 133.9, 129.6 (PhCH), 156.4 (C-3).

3.4.2.2 Ethyl-3-oxa-4-aza-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-diene-5-carboxylate



exo
82



endo
108

Sample code: **JM029**
Molecular formula: $C_{11}H_{13}NO_3$
Molecular weight: 207

The title compound was prepared from norbornadiene (1.75 g, 19 mmol) ethyl chloro-oximidoacetate **93** (0.67 g, 4.3 mmol) using the above method.

exo- Ethyl-3-oxa-4-aza-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-diene-5-carboxylate **82**

Product was afforded as white crystalline prisms (0.60 g, 67%); mp 62-63 °C; δ_H (200MHz, $CDCl_3$) 1.30-1.36 (3H, m, OCH_2CH_3), 1.60 (2H, s, H-8), 3.20 (1H, d, $J_{4,3a}$ 0.6Hz, H-4), 3.25 (1H, d, $J_{7,7a}$ 1.3Hz, H-7), 3.53 (1H, dd, $J_{3a,7a}$ 8.3Hz, $J_{3a,4}$ 0.6Hz, H-3a), 4.21-4.36 (2H, m, OCH_2CH_3), 4.97 (1H, dd, $J_{7a,7}$ 1.3Hz, $J_{7a,3a}$ 8.4Hz, H-7a), 6.00 (1H, dd, $J_{5,6}$ 5.7Hz, $J_{5,4}$ 3.2Hz, H-5), 6.28 (1H, dd, $J_{6,5}$ 5.8Hz, $J_{6,7}$ 3.0Hz, H-6), δ_C (63MHz, $CDCl_3$) 13.9 (OCH_2CH_3), 42.7, (C-8), 45.0, (C-4), 49.7 (C-7), 56.0 (C-3a), 61.7 (OCH_2CH_3), 91.7 (C-7a), 134.6 (C-5), 140.3 (C-6), 150.9 (C-3), 160.5 (CO_2); m/z (EI) found: M^+, 207.09719 $C_{11}H_{13}NO_3$ requires M^+, 207.09737.

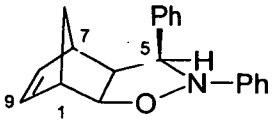
endo- Ethyl-3-oxa-4-aza-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-diene-5-carboxylate **108**

Product was afforded as white crystalline prisms (0.13 g, 15%); m.p. 61-62 °C; δ_H (200MHz, $CDCl_3$), 1.30-1.36 (3H, m, OCH_2CH_3), 1.60 (2H, s H-8), 3.29 (1H, d, J_{43a} 4.2Hz, H-4), 3.34 (1H, d, J_{77a} 4.1Hz, H-7), 4.02 (1H, dd, J_{3a7a} 9.3Hz, J_{3a4} 4.2Hz, H-3a), 4.21-4.36 (2H, m, OCH_2CH_3), 5.39 (1H, dd, J_{7a7} 4.1Hz, J_{7a3a} 9.4Hz, H-7a), 5.82 (1H, dd, $J_{5,6}$ 5.7Hz, $J_{5,4}$ 3.2Hz, H-5), 6.09 (1H, dd, $J_{6,5}$ 5.8Hz, $J_{6,7}$ 3.0Hz, H-6); δ_C (63MHz, $CDCl_3$) 13.9 (OCH_2CH_3), 42.7, (C-8), 45.0, (C-4), 49.7 (C-7), 56.0 (C-3a), 61.7 (OCH_2CH_3), 90.7 (C-7a), 134.9 (C-5), 138.3 (C-6), 150.7 (C-3), 156.4 (CO_2); m/z (EI) found: M^+, 207.08959 $C_{11}H_{13}NO_3$ requires M^+, 207.08954.

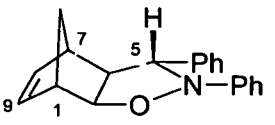
3.4.3 Synthesis of isoxazolidino norbornenes

GENERAL PROCEDURE: In a typical experiment a solution of the nitrone (5.00 mmol, 1 equiv.) and norbornadiene (20.0 mmol, 4 equivs.) in toluene was heated at reflux for 3 days, and then a second aliquot of norbornadiene (4 equivs.) was added to the reaction. The resulting dark brown solution was evaporated to dryness and the residue extracted repeatedly with ether, filtered, and washed with water to remove any residual traces of nitrone.

3.4.3.1 4,5-Diphenyl-3-oxa-4azatricyclo[5.2.1.0]dec-8-ene[13]



111 exo, endo



112 exo, exo

Sample code: **JM081**
Molecular formula: $C_{20}H19NO$
Molecular weight: 289

A mixture of norbornadiene and *C,N*-diphenyl nitrone **109** (0.98 mg, 5.00 mmol) was dissolved in dry toluene (5 ml) and heated at reflux for 3 days and then a further aliquot of norbornadiene (1.84 g, 20.0 mmol) was added to the reaction mixture. Chromatography gave a mixture of the *exo* diastereomers **111** and **112** (combined yield 56%) in a 61:39 ratio. Preparative TLC afforded the major, *exo, endo* isomer **111** and then the minor *exo, exo* **112** which was contaminated with traces of the major isomer **111**.

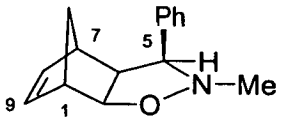
4,5^{endo}-Diphenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene **111**

Product was recrystallised from methanol as colourless needles; mp 110-111 °C (MeOH) (lit.[159] 111 °C); δ_H (200 MHz, $CDCl_3$) 1.68 (2H, m, 10-H), 2.26 (1H, d, $J_{1,9}$ nd, $J_{1,2}$ 1.2Hz, 1-H), 2.90 (1H, ddd, $J_{6,5}$ 8.8Hz, $J_{6,2}$ 5.6Hz, $J_{6,7}$ 2.1Hz, 6-H), 3.06 (1H, d, $J_{5,6}$ 8.8Hz, 5-H), 4.57 (1H, dd, $J_{2,1}$ 1.2Hz, $J_{2,6}$ 5.6Hz, 2-H), 4.67 (1H, d, $J_{5,6}$ 8.8Hz, 5-H), 6.05, (1H, dd, $J_{8,9}$ 5.5Hz, $J_{8,7}$ 3.0Hz, 8-H), 6.15 (1H, dd, $J_{9,8}$ 5.4Hz, $J_{9,1}$ 3.2Hz, 9-H); δ_C (63 MHz, $CDCl_3$) 42.7 (C-7), 43.9 (C-10), 46.7 (C-1), 56.4 (C-6), 70.6 (C-5), 84.8 (C-2), 127.0-128.5 (Ar), 136.3 (C-8), 139.2 (PhC), 141.4 (C-9), 150.8 (PhN); *m/z* (EI) found M^+, 289.14626, $C_{20}H_{19}NO$ requires: M^+, 289.14666.

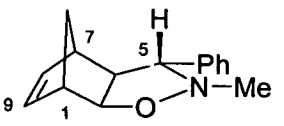
4,5^{exo}-Diphenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene **112**

This diastereomer contained traces of the higher isomer **111**, which could not be separated using chromatography. The mixture of **111** and **112** was afforded as a white solid; δ_H (200 MHz, $CDCl_3$) 1.68 (2H, m, 10-H), 2.64 (1H, ddd, $J_{6,5}$ nd, $J_{6,2}$ nd, $J_{6,7}$ nd, 6-H), 3.00 (1H, d, $J_{1,9}$ nd J $_{1,2}$ nd, 1-H), 3.84 (1H, d, $J_{5,6}$ nd, 5-H), 4.55 (1H, dd, $J_{2,1}$ nd, $J_{2,6}$ nd, 2-H), 6.09, (1H, dd, $J_{8,9}$ nd, $J_{8,7}$ nd, 8-H), 6.13 (1H, dd, $J_{9,8}$ nd, $J_{9,1}$ nd, 9-H); δ_C (63 MHz, $CDCl_3$) 29.6 (C-10), 38.9 (C-7), 52.2 (C-1), 59.3 (C-6), 74.2 (C-5), 84.4 (C-2), 127.1-128.9 (Ar), 138.0 (C-8), 140.5 (PhC), 140.5 (C-9), 150.8 (PhN).

3.4.3.2 4-Methyl-5-phenyl-3-oxa-4-azatricyclo[5.2.1.0]dec-8-ene



113 exo, endo



114 exo, exo

Sample code: **JM098**

Molecular formula: $C_{15}H_{17}NO$

Molecular weight: 227

C-phenyl-*N*-methyl nitrone **110** (1.35 g, 4.66 mmol) in toluene (10ml) and norbornadiene (2.8 g, 30.4 mmol) was heated at reflux with the exclusion of moisture. After 3 days a second portion of norbornadiene (2.8 g, 30.4 mmol) was added and heating was continued for a further 3 days. The product was afforded according to the general preocedure. The ^{1}H NMR spectrum of a sample showed from the N-Me region that two *exo* diastereomers **113** and **114** were present in the ratio 7:1. The crude product was chromatographed to give a minor *exo, endo* **113** isomer contaminated with traces of the major isomer **114** and then a pure sample of the major *exo, exo* diastereomer **114**.

exo-4-Methyl-5^{exo}-phenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene **114**

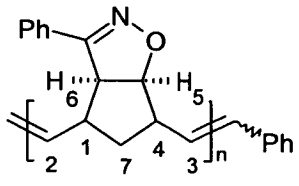
The major isomer was recrystallized from ethanol as yellow needles 0.627 g, 70% (lit.[157] 0.670 g, 74%); mp 66-67 °C (lit.[157] 67-68 °C); δ_H (500 MHz, $CDCl_3$) 2.15 (2H, s, 10-H), 2.53 (1H, d, $J_{7,6}$ 1.2Hz, $J_{7,8}$ 3.3Hz H-7), 2.60 (3H, s, N-CH_3), 2.76 (1H, d, $J_{1,2}$ 1.1Hz, $J_{1,9}$ 3.1Hz, 1-H), 2.87 (1H, d, $J_{7,6}$ 1.9Hz, $J_{7,8}$ 3.1Hz, 6-H), 3.06 (1H, d, $J_{5,6}$ 7.2Hz, 5-H), 4.32 (1H, dd, $J_{2,6}$ 6.4Hz, $J_{2,1}$ 1.1Hz, 2-H), 6.02 (1H, dd, $J_{8,9}$ 5.7Hz, $J_{8,7}$ 3.3Hz, 8-H), 6.17 (1H, dd, $J_{9,1}$ 3.1Hz, $J_{9,8}$ 5.7Hz, 9-H), 7.38-7.29 (5H, m, ArH); δ_C (62.9 MHz, $CDCl_3$) 42.8 (C-7), 43.1 (C-10), 43.3 (N-Me), 45.0 (C-1), 61.0 (C-6), 78.2 (C-5), 83.2 (C-2), 128.5-127.8 (Ar), 134.5 (C-8), 139.6 (PhC), 140.5 (C-9); m/z (EI) found M^+, 227.13010, $C_{15}H_{17}NO$ requires: M^+, 227.13053.

3.5 Homopolymersiations

3.5.1 ROMP of isoxazolino norbornenes

GENERAL PROCEDURE: A typical polymerisation reaction was conducted as follows. A solution of the ruthenium initiator **1** or **2** in dry degassed dichloromethane (1.0 ml) was added by syringe to a solution of the monomer in dichloromethane (1.0 ml). After 24 hours the reaction was terminated by the addition of ethyl vinyl ether, and the mixture added dropwise to methanol containing 2,6-di-tert-butyl-4-methylphenol (5 mg) to afford a precipitate, which was filtered, washed with methanol and dried.

3.5.1.1 ROMP of *exo*-3-phenyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[*d*]isoxazole 81



83

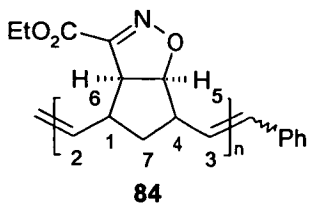
Sample code: **JM021***

Sample code: **JM088****

*Initiated using **1**, **initiated using **2**

Phenyl NBE **81** (0.05 g, 0.24 mmol, 80 equivs.) was dissolved in dichloromethane and to this was added a solution of **1*** or **2**** (0.002 g, 0.003 mmol, 1equiv.) in dichloromethane. The reaction was worked up in usual manner to afford **83** as a dark brown solid; δ_H (500MHz, $CDCl_3$) 1.22, 1.92 (2H, m, 7-H), 2.66, 2.89 (2H, bd, 1,4-H), 3.77 (1H, bs, 6-H), 4.89 (1H, m, 5-H), 5.44 (2H, m, H-2,3), 7.28, 7.63 (5H, bd, Ph); δ_C (63 MHz, $CDCl_3$) 26.6, 27.3 (C-7), 43.6, 48.2, 50.1 (C-1,4), 58.5 (C-6), 92.0 (C-5), 127.9, 128.4, 129.0, (PhCH, PhC), 130.3-134.5 (C-2,3), 159.5 (C=N).

3.5.1.2 ROMP of *exo*-3-ethoxycarbonyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[*d*]isoxazole 82



84

Sample code: **JM030***

Sample code: **JM105****

*Initiated using **1**, **initiated using **2**

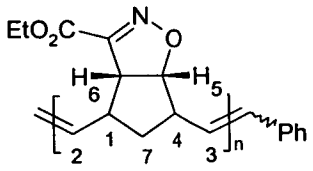
Ethoxycarbonyl NBE (**82**), (0.1 g, 0.48 mmol, 80 equivs.) was dissolved in dichloromethane and to this was added a solution of **2** (0.005 g, 0.006 mmol, 1equiv.) in dichloromethane. The reaction was worked up in usual manner to afford the product **84** as a brown polymeric solid; δ_H (500MHz, $CDCl_3$) 1.43 (3H, m, $CO_2CH_2CH_3$) 1.62-1.98 (2H, m, H-7), 3.05 (2H, m, H-1,4(t)), 3.23 (2H, m, H-1,4(c)), 3.65 (1H, m, H-6), 4.33 (2H, m, $CO_2CH_2CH_3$) 4.89-5.23 (1H, m, H-5), 5.42-5.77 (2H, m, H-2,3); δ_C (90 MHz, $CDCl_3$) 14.2 ($CO_2CH_2CH_3$), 39.2 (C-7), 43.6, 46.5, 50.7 (C-1,4), 57.4 (C-6), 62.0 ($CO_2CH_2CH_3$), 94.6 (C-5), 130.0-134.3 (C-2,3), 153.6 (C-3a), 160.5 ($CO_2CH_2CH_3$).

Isoxazoline	I	[M]:[I]	Yield / %	σ_C	$10^{-4}M_n$	av DP	PDI[a]	Propagating species ppm
81	**1**	80:1	63	[d]	1.79	85	1.97	19.4-19.5
81	**2**	80:1	62	62	3.27	155	2.18	[b]
82	**1**	80:1	[c]	[c]	[c]	[c]	[c]	[c]
82	**2**	80:1	75	63	13.84	668	1.65	[b]

[a]measured by GPC against polystyrene standards; [b]not observable; [c]did not polymerise; [d]doublet used to calculate σ_C became a broad multiplet.

Table 3.5 – Selected physical data for ROMP of isoxazoline norbornenes with **1** and **2**

3.5.1.3 ROMP of *endo*-3-ethoxycarbonyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[*d*]isoxazole 107



132

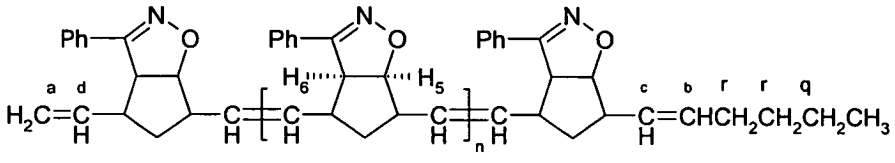
Sample code: **JM186** (Initiated using **2**)

endo-EthoxycarbonylNBE **107**, (0.02 g, 0.097 mmol, 80 equivs.) was dissolved in dichloromethane and to this was added a solution of **2** (0.001 g, 0.001 mmol, 1 equiv.) in dichloromethane. The reaction was worked up in usual manner to afford the product **132** as a brown polymeric solid; δ_H (500MHz, $CDCl_3$) 1.27, (3H, m, $CO_2CH_2CH_3$) 1.36-1.76 (2H, m, H-7), 2.57-3.02 (2H, m, H-1,4), 3.91-3.93 (1H, m, H-6), 4.20-4.32 (2H, m, $CO_2CH_2CH_3$) 4.97-5.14 (1H, m, H-5), 5.39-5.65 (2H, m, H-2,3).

3.5.2 Control of molecular weight (M_n) using a chain transfer agent

GENERAL PROCEDURE: A typical chain transfer reaction was conducted as follows. A solution of the ruthenium initiator **1** or **2** in dry degassed dichloromethane (1.0 ml) was added by syringe to a solution of the monomer and chain transfer agent (hex-1-ene) in dichloromethane (1.0 ml). After 24 hours the reaction was terminated by the addition of ethyl vinyl ether, and the mixture added dropwise to methanol containing 2,6-di-tert-butyl-4-methylphenol (5 mg) to afford a precipitate, which was filtered, washed with methanol and dried.

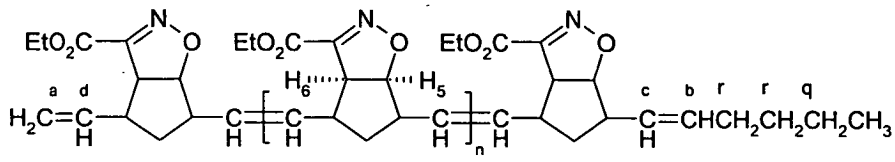
3.5.2.1 ROMP of phenyl NBE 81 in presence of hex-1-ene



147

exo-3-Phenyl-3a,4,5,6-tetrahydro-4,7-methano-benzo[*d*]isoxazole **81**, (80 mg, 0.38 mmol, 100 equivs.) and hex-1-ene (3.20 mg, 0.038 mmol, 10 equivs.) was dissolved in dichloromethane and to this was added a solution of **1** or **2** (3.23 mg, 0.0038 mmol, 1 equiv.) in dichloromethane. The product **147** was afforded using general procedure as a brown tar; σ_C = 0.62; δ_H (500 MHz, $CDCl_3$) 0.80-0.85 (3H, m, CH_3), 1.14-1.31, 1.92-2.10 (8H, m, H-7, 3xCH_2), 2.22-2.65 (2H, m, H-1,4), 3.77-3.80 (1H, m, H-6), 4.84-5.06 (1H, m, H-5), 5.35-5.49 (2H, m, H-2,3), 5.75-5.94 (2H, m, =CH_2), 7.28-7.31, 7.60-7.75 (5H, m, PhCH); δ_C (90 MHz, $CDCl_3$) 13.8 (CH_3), 22.1 (C-q), 26.9, 32.0 (2xC-r), 39.1 (C-7), 45.9, 47.7, 48.3, 50.2 (C-1,4), 57.5 (C-6), 91.8 (C-5), 115.5 (C-a), 127.2-127.6 (PhCH, PhC), 128.3-132.2 (C=C, C-c, C-b), 141.0 (C-d), 159.0 (C=N).

3.5.2.2 ROMP of ethoxycarbonyl NBE in presence of hex-1-ene



148

Ethoxycarbonyl NBE **82**, (80 mg, 0.38 mmol, 100 equivs.) and hex-1-ene (3.20 mg, 0.038 mmol, 10 equivs.) was dissolved in dichloromethane and to this was added a solution of initiator **2** (3.23 mg, 0.0038 mmol, 1 equiv.) in dichloromethane. The reaction was stirred at room temperature for

24h and then worked up in usual manner to afford **148** as a brown tar; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, m, CH_3), 1.25 (3H, m, $CO_2CH_2CH_3$), 1.25, 1.94-2.07 (8H, m, H-7, 3xCH_2), 2.72, 3.02 (2H, bd, H-1,4), 3.64 (1H, m, H-6), 4.34 (2H, m, $CO_2CH_2CH_3$), 4.96 (1H, m, H-5), 5.12 (2H, bd, HC=CH_2), 5.47-5.77 (2H, m, H-2,3) 5.99 (2H, m, H-end group); δ_C (90 MHz, $CDCl_3$) 12.9 (CH_3), 13.1 ($CO_2CH_2CH_3$), 21.2, 21.3, 26.3, 26.4 (C-q) 30.4, 30.5, 30.8, 31.1 (2xC-r), 37.5 (C-7), 42.4, 45.3, 46.3, 49.5 (C-1,4), 56.1 (C-6), 61.0 ($CO_2CH_2CH_3$), 93.7 (C-5), 113.9 (C-a), 128.4 (C-b), 130.1-132.3 (C=C), 133.2 (C-c), 138.9 (C-d), 152.5 (C=N), 159.7 ($CO_2CH_2CH_3$).

Code	[hex-1-ene] / [**82**]	yield / %	σ_C	$10^{-4}M_n$	PDI	av DP[a/b]
JM105	0.00	75	0.63	13.84	1.65	554[a]
JM110	0.05	96	0.64	3.29	1.45	159[a]/157[b]
JM119	0.10	99	0.60	0.34	[c]	[c]/16[b]
JM132	0.15	93	0.59	0.20	1.55	9[a]/8[b]
JM136	0.25	92	0.55	0.09	[c]	[c]/4[b]

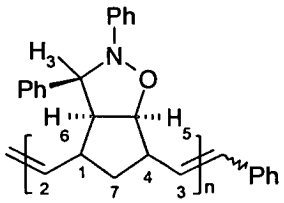
[a]Determined by GPC analysis in THF against polystyrene standards (860-2.43 million); [b]determined by NMR end group analysis; [c]not determined

Table 3.6 – Molecular weight control of polymerisation of **82** using (hex-1-ene)

3.5.3 ROMP of isoxazolidino norbornenes

GENERAL PROCEDURE: Homopolymerisation of isoxazolidino norbornenes was carried out in the same manner as with isoxazolino norbornenes in Section 3.5.1.

3.5.3.1 ROMP of *exo*-4,5^{endo}-diphenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene 111



133

Sample code: **JM084***

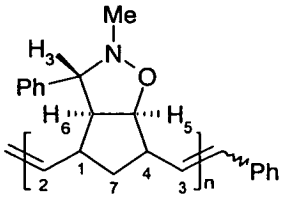
Sample code: **JM101****

*Initiated using **1**, **initiated using **2**

The product **133** was afforded as a grey polymeric solid; δ_H (500 MHz, $CDCl_3$) 1.60-1.97 (2H, m, H-7), 2.58-2.89 (2H, m, H-1,4) 4.51-4.70 (2H, m, H-3,6), 4.87-5.00 (1H, m, H-5), 5.37-5.70 (2H,

m, H-2,3), 6.96-7.11, 7.21-7.46 (5H, m, ArH); δ_C (90 MHz, $CDCl_3$) 28.8, 29.6, 32.2 (C-7), 42.5, 42.9, 46.8 (C-1,4), 60.8 (C-6), 71.6 (C-3), 88.9 (C-5), 127.1, 127.8, 128.1, 128.5 (PhCH), 131.0, 131.6, 132.3 (C-2,3), 138.0 (PhC), 150.3 (PhC-N).

3.5.3.2 ROMP of *exo*-4-methyl-5^{exo}-phenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene 114



134

Sample code: **JM107** (Initiation using **1**)

Sample code: **JM157** (Initiation using **2**)

*Initiated using **1**, **initiated using **2**

The product **134** was afforded as a grey polymeric solid; δ_H (500 MHz, $CDCl_3$) 1.10-1.36 (2H, m, H-7), 1.81-2.10 (2H, m, H-1,4), 2.50 (3H, m, NCH_3), 2.99-3.60 (2H, m, H-3,6), 4.17-4.40 (1H, m, H-5), 5.08-5.52 (2H, m, H-2,3), 7.11-7.34 (5H, m, PhCH); δ_C (90 MHz, $CDCl_3$) 28.8, 29.6, 32.2 (C-7), 41.6 (N-CH_3), 42.5, 42.9, 46.8 (C-1,4), 60.0 (C-6), 80.0 (C-3), 87.6 (C-5), 126.8-127.4 (PhCH), 130.6 (C-2,3), 138.2 (PhC).

Isoxazolidine	I	[M]:[I]	yield / %	σ_C	$10^{-4}M_n$	av DP[a]	PDI[a]	propagating species ppm
111	**1**	80:1	95	36	5.70	363	1.84	18.6
111	**2**	80:1	73	61	11.14	903	2.37	[b]
114	**1**	80:1	75	[c]	6.76	458	1.54	19.1
114	**2**	80:1	76	[c]	20.04	1853	2.09	[b]

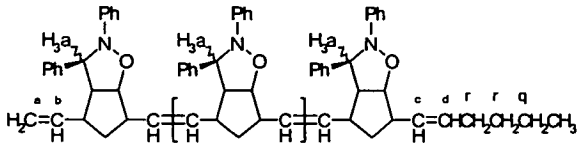
[a]Measured by GPC in THF against Polystyrene standards (860 – 2.43 million); [b]not observable; [c]doublet used to calculate σ_C became a broad multiplet.

Table 3.7 – Selected physical data for isoxazolidino functionalised polymers

3.5.4 Control of Molecular weight (M_n) using a chain transfer agent

GENERAL PROCEDURE: Same procedure used as that for the molecular weight control of isoxazolino norbornenes with hex-1-ene (Section 3.5.2).

3.5.4.1 ROMP of *exo*-4,5^{endo}-diphenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene 111 with chain transfer agent (hex-1-ene)



149

Sample Code	[CTA]:[111]
JM108	1:50
JM123	1:10
JM096	1:2

C,N-diphenyl-isoxazolidino norbornene **111** (100 mg, 0.34 mmol) and hex-1-ene was dissolved in dichloromethane and to this was added a solution of the Grubbs initiator **1** or **2** (2 mg, 0.002mmol) stirred at room temperature for 24 h and then terminated with ethyl vinyl ether. Precipitation in methanol afforded the product **149** as a grey polymeric solid; δ_H (500 MHz, $CDCl_3$) 0.79 (3H, m, CH_3), 0.93-1.32 (6H, m, 3xCH_2), 1.89-1.95 (2H, m, H-7), 2.46 (1H, m, H-1,4), 2.68 (1H, m, H-6), 2.81 (1H, m, H-1,4), 2.97 (1H, m, H-6), 4.07, 4.55 (1H, m, H-5), 4.62 (H-3a), 4.89 (5H, m, H-a,b,c,d), 5.12-5.61 (2H, m, H-2,3), 6.88-7.31 (5H, bd, Ar); δ_C (90 MHz, $CDCl_3$) 12.9 (CH_3), 21.3 (C-q), 30.8, 25.8 (2xC-r), 39.2 (C-7), 45.8, 42.5 (C-1,4), 57.5 (C-6), 70.0 (C-3a), 87.9 (C-5), 112.5 (C-a), 116.1 (C-d), 121.4 (C-c), 127.3 (PhCH), 131.5-129.5 (C-2,3), 137.1 (PhC), 139.2 (C-b), 149.3 (PhC-N).

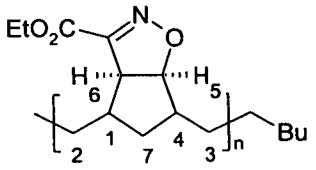
Initiator	[CTA]:[111]	Yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP [a/b]	PDI
2	1:50	76	1.35	1.25	43[a]	1.08
1	1:10	84	0.22	0.18	6[a]/8[b]	1.23
2	1:2	89	[c]	0.07	2[b]	[c]

[a]Determined by GPC in THF using polystyrene standards (860-2.43 million); [b]determined by end group analysis; [c]not determined

Table 3.8 - Selected physical data for isoxazolidino functionalised oligomers

3.5.5 Reduction of ethoxycarbonyl isoxazoline functionalised oligomers 148

GENERAL PROCEDURE: As reported by Rooney *et al.*[177] a sample of the polymer **148** (100 mg, 0.48 mmol, 1 equiv.) was dissolved in chlorobenzene (10 ml) and to this was added *p*-toluenesulfonyl hydrazide (2g, 10.5 mmol, 22equivs.). The mixture was heated at 120 °C with stirring for 2.5 h. The polymer dissolved and the reaction mixture became effervescent as the reaction proceeded. The mixture was then added to methanol (250 ml) and the precipitated polymer collected by filtration, washed twice with methanol, and dried *in vacuo*.



151 / 152

Oligomer	av DP	yield/%
151*	4	85
152**	16	92

Sample code: **JM121***

Sample code: **JM136****

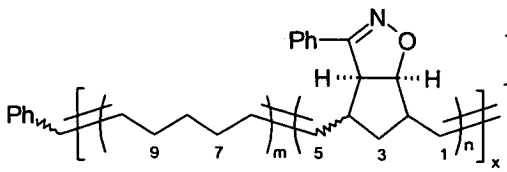
The product was afforded as a pale grey solid; δ_H (500 MHz, $CDCl_3$) 0.81 (3H, bs, CH_3), 1.18-1.30 (5H, m, H-7, $CH_3CH_2O_2C$), 1.50 (4H, m, H-2,3), 1.95 (8H, m, 3xCH_2, H-7), 2.72 (2H, m, H-1,4), 3.41 (1H, m, H-6), 4.26 (2H, m, $CH_3CH_2O_2C$), 4.71 (1H, m, H-5); δ_C (90 MHz, $CDCl_3$) 11.2 (CH_3), 13.2 ($CO_2CH_2CH_3$), 20.4, 20.6, 28.0, 28.3 (CH_2), 30.8, 32.7 (C-2,3), 37.4 (C-7), 44.1, 47.2 (C-1,4), 56.3 (C-6), 60.9 ($CO_2CH_2CH_3$), 93.9 (C-5), 152.9 (C=N), 160.0 ($CO_2CH_2CH_3$).

3.6 Copolymerisations

3.6.1 Random copolymerisations

GENERAL PROCEDURE: The co-monomers were dissolved in dry degassed dichloromethane (1.0 ml) and to this was added a solution of initiator **2** in dichloromethane (1.0 ml). The reaction was stirred at room temperature for 24h and was then terminated by addition of ethyl vinyl ether (50 mg) followed by stirring at room temperature for >2h. The polymer was purified by precipitation in methanol containing 5 mg of 2,6-di-tert-butyl-4-methylphenol and washing with MeOH (2x). The product was dried *in vacuo* prior to characterisation.

3.6.1.1 Random copolymer of CPE and phenyl NBE 81

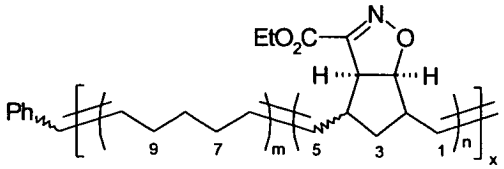


153

Sample code	[CPE]:[81]:[1]	Yield / %
JM162	80:80:1	95

Cyclopentene (16.2 mg, 0.24 mmol, 80 equivs.) and phenyl NBE **81** (50 mg, 0.24 mmol, 80 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **2** (2.52 mg, 0.003 mmol, 1 equiv.) and the reaction stirred at rt for 24h. Precipitation in methanol afforded the product **153** as a brown tar; δ_H (500 MHz, $CDCl_3$) 1.02-1.96 (8H, m, H-3,7,8,9), 2.59, 2.92 (2H, bs, H-2,4), 3.77 (1H, bs, H-2a), 4.82 (1H, m, H-4a), 5.19-5.54 (4H, m, HC=CH), 7.39, 7.61 (5H, bd, PhCH); δ_C (90 MHz, $CDCl_3$) 26.7, 29.2, 31.9 (C-7,8,9), 39.4 (C-3), 50.3, 47.6, 42.6 (C-2,4), 57.9 (C-2a), 92.5 (C-4a), 127.3-128.8 (Ph), 129.6-132.8 (C=C), 159.2 (C=N).

3.6.1.2 Random copolymerisation of CPE and ethoxycarbonyl NBE 82



154-159

Sample Code	[CPE]:[82]:[2]
JM155	20:80:1
JM152	40:80:1
JM145	80:80:1
JM137	160:80:1
JM144	320:80:1
JM148	640:80:1

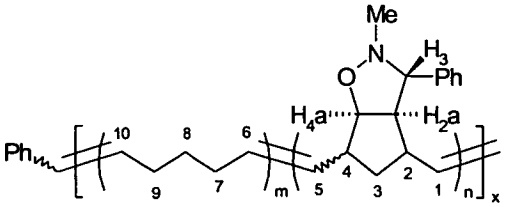
Cyclopentene (M_1) (16.5 mg, 0.242 mmol, 80 equivs.) and ethoxycarbonyl NBE **82** (M_2) (50 mg, 0.242 mmol, 80 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added the Grubbs initiator **2** (2.57 mg, 0.003 mmol, 1 equiv.). The reaction stirred at rt for 24h and then terminated with ethyl vinyl ether. Precipitation in methanol afforded the product as a brown tar; δ_H (500 MHz, $CDCl_3$) 1.27 (3H, m, $CO_2CH_2CH_3$), 1.32-1.95 (8H, m, H-3,7,8,9), 2.59, 2.90 (2H, m, H-2,4), 3.49 (1H, m, H-2a), 4.26 (2H, m, $CO_2CH_2CH_3$) 4.84 (1H, m, H-4a), 5.29-5.52 (4H, m, HC=CH), 6.91 (1H, s, $CH=CH_2$), 7.19, 7.21 (5H, bd, PhCH end group); δ_C (90 MHz, $CDCl_3$) 13.2 ($CO_2CH_2CH_3$), 25.8, 27.9, 31.0 (C-7,8,9), 37.6 (C-3), 46.4, 49.7 (C-2,4), 56.6 (C-2a), 60.9 ($CO_2CH_2CH_3$), 93.7 (C-4a), 124.3 (CHPh), 128.0-131.1 (olefinics), 152.8 (C=N), 159.5 ($CO_2CH_2CH_3$).

Code	[CPE]:[82]:[2]	yield / %	$10^{-4}M_w$[a]	$10^{-4}M_w$[b]	$10^{-4}M_n$	PDI
JM155	20:80:1	95	9.33	-	4.83[c]	1.93
JM152	40:80:1	91	7.08	0.18	[d]	[d]
JM145	80:80:1	83	2.82	0.12	[d]	[d]
JM137	160:80:1	81	[e]	[e]	[d]	[d]
JM144	320:80:1	69	1.78	0.11	[d]	[d]
JM148	640:80:1	36	0.12	-	0.07[c]	1.60

[a]M_w of high weight fraction; [b]M_w of low weight fraction; [c]copolymers with unimodal distribution allow for measurement of M_n; [d]unable to calculate PDI of copolymers with bimodal distribution; [e]not determined.

Table 3.9 – Molecular weight determination of random copolymers **154-159** of **82** and CPE.

3.6.1.3 Random copolymers 160 / 161/ 162 of CPE and 114



160 -162

Sample Code	[CPE]:[114]:[2]
JM151	40:80:1
JM143	160:80:1
JM150	640:80:1

Cyclopentene (n equivs.) and *exo*-4-methyl-5^{exo}-phenyl-3-oxa-4-azatricyclo[5.2.1.0^{2,6exo}]dec-8-ene **114** (80 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **2** (1 equiv.) and the reaction stirred at rt for 24h. Precipitation from methanol afforded the product as a dark brown tar; δ_H (250 MHz, $CDCl_3$) 1.18-1.31 (2H, bd, CH_2), 1.36 (3H, s, N-CH_3), 1.78-1.92 (4H, bd, 2xCH_2), 2.49-2.77 (1H, m, H-2a), 3.21, 3.41 (1H, bd, H-3), 4.37 (1H, bs, H-4a), 4.95-5.42 (4H, bd, H-1,5,6,10), 6.91 (1H, s, CH=CH_2), 7.19-7.50 (5H, bs, PhCH); δ_C (90 MHz, $CDCl_3$) 25.9, 28.3 (2xCH_2), 29.3 (N-CH_3), 30.9 (CH_2), 42.2 (C-3), 46.5, 47.6 (C-1,4), 63.1 (C-2a), 80.1 (C-3a), 87.8 (C-4a), 126.6-127.4 (PhCH), 129.2-131.1 (C=C), 138.5 (PhC).

Code	[CPE]:[114]:[2]	yield / %	$10^{-4}M_w$[a]	$10^{-4}M_w$[b]
JM151	40:80:1	84.4	6.20	0.11
JM143	160:80:1	65.8	5.01	0.11
JM150	640:80:1	61.8	2.82	0.10

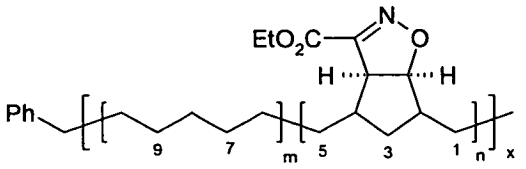
[a]M_w of high weight fraction; [b]M_w of low weight fraction.

Table 3.10 – Molecular weight determination of random copolymers of *N*-methyl-*C*-phenyl-NBE and cyclopentene

3.6.2 Reduction of random copolymers

GENERAL PROCEDURE: Procedure as that of reduction of homopolymers in Section 3.5.5.

3.6.2.1. Reduction of random copolymer 155 of CPE and 82



163

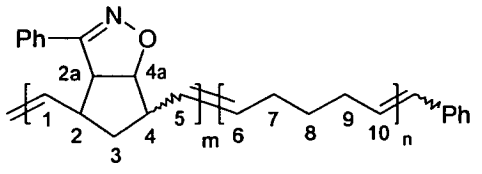
Sample code: **JM140** (Reduction of **JM137**)

Product was afforded as a light brown tar (94%); δ_H (300 MHz, $CDCl_3$) 0.83-0.91 (3H, m, CH_3), 1.18-1.32 (13H, m, 5xCH_2, C$H_3$$CH_2CO_2$), 1.92-1.94 (6H, m, C-3, 2xCH_2), 3.31-3.36 (1H, m, H-2a), 4.20-4.30 (2H, m, $CH_3CH_2CO_2$), 4.68-4.74 (1H, m, H-4a); δ_C (90 MHz, $CDCl_3$) 13.1 ($CO_2CH_2CH_3$, CH_3), 26.9, 27.2, 28.7 (C-7,8,9), 33.8, 34.8 (C-1,5,6,10) 37.6 (C-3), 44.3, 47.1 (C-2,4), 56.3 (C-2a), 60.7 ($CO_2CH_2CH_3$), 94.3 (C-4a), 153.1 (C=N), 160.0 ($CO_2CH_2CH_3$).

3.6.3 Block copolymerisation

GENERAL PROCEDURE: As reported by Schrock *et al.*[133] monomer one (67 equivs.) was dissoloved in dichloromethane and to this was added a solution of **1** or **2** (1 equiv.) and the reaction stirred for 24 h at room temperature. A solution of the second monomer (67 equivs.) in dichloromethane was added to the mixture and stirred for a further 24h at room temperature. The reaction was then stirred at 50 °C for 6 hours before termination with ethyl vinyl ether and precipitated from methanol containing 2,6-di-tert-butyl-4-methylphenol (5 mg) to afford a precipitate, which was filtered, washed with methanol and dried. as before.

3.6.3.1 Block copolymerisation of CPE / phenyl NBE 81



165a* / 165b**

Sample code: **JM246** *

Sample code: **JM247** **

*Initiation using **1**, **initiation using **2**

Product was afforded as a brown tar (71 mgs, 75%); δ_H (250 MHz, $CDCl_3$) 1.18-1.98 (8H, m, H-3,7,8,9), 2.48-2.70 (2H, m, H-2,4), 3.41-3.65 (1H, m, H-2a), 4.65-4.70 (1H, m, H-4a), 5.35-5.51

(4H, m, H-1,5,6,10), 7.32-7.41 (3H, m, PhCH), 7.50-7.74 (2H, m, PhCH); δ_C (63 MHz, $CDCl_3$) 32.8, 35.0, 37.2 (C-7,8,9), 43.4 (C-3), 44.8, 47.3 (C-2,4), 59.2 (C-2a), 92.7 (C-4a), 127.2, 128.6, 128.8 (PhCH, PhC), 129.2-129.7 (C=C), 159.6 (C=N).

	BLOCK n			BLOCK m			COPOLYMER	
I	$10^{-4}M_n$	PDI	av DP	$10^{-4}M_n$	PDI	av DP	$10^{-4}M_n$	PDI
1	0.01	1.14	13	0.60	1.12	29	0.70	1.12
2	0.15	1.20	21	2.24	1.33	107	2.39	1.33

Table 3.11 – Molecular weight data for block copolymer **165a** and **165b** of CPE / **81**

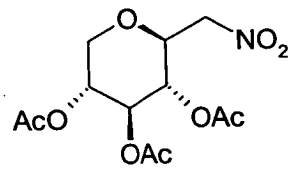
Part 2 – Synthesis of carbohydrate functionalised polymers

3.7 Synthesis of glycosyl isoxazolino functionalised polymers

3.7.1 Synthesis of pyranosyl nitromethanes

GENERAL PROCEDURE: Using the procedure reported by Köll *et al.*[180] solid sodium (2.5 g, 108 mmol) was dissolved in methanol (90 ml) under an atmosphere of N_2. Sodium methoxide (90 ml in methanol) was added to a stirred solution of D-(+)-xylose (13.5 g, 83 mmol), nitromethane (45 ml, 0.83 mmol) and dry methanol (30 ml). The solution was stirred for 24h. The resultant brown solid was filtered, washed with ice cold methanol, and dissolved in ice-cold deionised water (200 ml). The solution was rapidly forced through an amberlite 120 (H^+) ion-exchange column*. Excess nitromethane was removed *in vacuo*, and the residual liquid was heated at reflux for 48h. Charcoal (5 g) was added to the sugar solution and the mixture was heated at reflux for 2h. The charcoal was filtered over celite and the filtrate concentrated *in vacuo* to yield an orange oil. The oil was dissolved in dry acetic anhydride (140 ml) (under an atmosphere of N_2), cooled to 0 °C, triflic acid (0.1 ml) was added and the solution stirred for 14h. The resultant solution was added to ice-water (100 ml), extracted with chloroform (3 x 40 ml), washed with $NaHCO_3$ (3 x 40 ml) and the combined extracts dried over $MgSO_4$.

3.7.1.1 3,4,5-Tri-*O*-acetyl-β-D-xylopyranosylnitromethane 166



166

Sample code: **JM067**

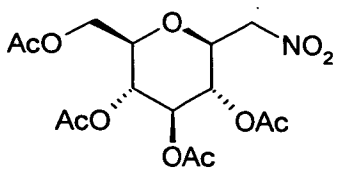
Molecular formula: $C_{12}H_{17}NO_9$

Molecular weight: 319

The dried extract was concentrated *in vacuo* and the resultant orange oil crystallised from ethanol to yield the product as white needles (10.48 g, 40%); mp 164-166 °C (lit.[180] 164-165 °C); δ_H (250 MHz, $CDCl_3$), 2.30, 2.33 (9H, 3 x s, 3x$COCH_3$), 3.61 (1H, dd, 6b-H), 4.40 (1H, dd, 6a-H), 4.44 (1H, m, 2-H), 4.67 (1H, dd, 1a-H), 4.76 (1H, dd, 1b-H), 5.15 (1H, dd, 3-H), 5.26 (1H, dd, 5-H), 5.52 (1H, t, 4-H); *J*(x-y)/Hz 1a-1b 13.4, 1a-2 3.0, 1b-2 8.9, 2-3 10.1, 3-4 9.3, 4-5 9.4, 5-6a 5.7, 5-6b 10.6, 6a-6b 11.3; δ_C (63 MHz, $CDCl_3$) 21.1, 21.2, 21.4, (3x$COCH_3$), 67.1, 69.0, 69.9, 73.5, 75.4, 76.4 (C-1, C-2, C-3, C-4, C-5, C-6), 170.1, 170.2, 170.6 (3x$COCH_3$).

* The column was prepared by washing through with water until any colourisation disappeared. The amberlite was then acidified by addition of 1M HCl. Water was then passed through until pH 4 was reached.

3.7.1.2 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-nitromethane 173



173

Sample code: **JM163**

Molecular formula: $C_{15}H_{21}NO_{11}$

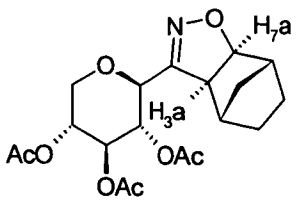
Molecular weight: 391

The product **173** was crystallised from ethanol to give a white solid (0.70 g, 80%); mp 143-145°C (lit.[180] 144-145 °C); $[\alpha]_D^{18}$ = +15.0 (c = 0.4, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.95, 1.97, 2.00, 2.01 (12H, 4 x s, 4x$COCH_3$), 3.70 (1H, ddd, 6-H), 3.99 (1H, dd, 7a-H), 4.21 (1H, dd, 7b-H), 4.24 (1H, dd, 2-H), 4.58 (1H, dd, 1a-H), 4.85 (1H, dd, 1b-H), 4.48 (1H, dd, 3-H), 5.01 (1H, dd, 5-H), 5.21 (1H, dd, 4-H); *J*(x-y)/Hz 1a-1b 13.7, 1a-2 2.9, 1b-2 8.8, 2-3 10.1, 3-4 9.3, 4-5 9.3, 5-6 10.0, 6-7a 2.3, 6-7b 4.9, 7a-7b 12.5; δ_C (90 MHz, $CDCl_3$) 20.3, 20.4 (4x$COCH_3$), 61.4 (C-7), 67.7, 69.0, 73.3, 74.1, 75.5, (C-2, C-3, C-4, C-5, C-1), 75.7 (C-6), 169.1, 169.5, 169.8, 170.3 ($4_x COCH_3$); m/z (FAB) M^++1 Found: M^++1 392.11964 $C_{15}H_{22}NO_{11}$ requires M^++1 392.11929.

3.7.2 Test reaction – synthesis of isoxazolino norbornanes (NBA)

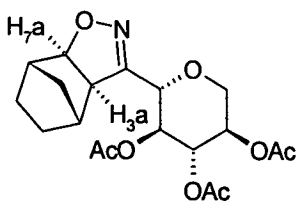
GENERAL PROCEDURE: As described by Mukaiyama *et al.*[179] the acetylated pyranosylnitromethane (1 equiv.) in toluene (50 cm^3) was stirred protected from the atmosphere (N_2 atmosphere) and the alkene (2-5 equivs.) added. Triethylamine (0.1 cm^3) catalytic, and tolylene diisocyanate (3 equivs.) were added and the reaction heated at 80 °C for 7 days over which period polymeric urea formed. The reaction was cooled to 0 °C and diaminoethane (3 equivs.) was slowly added dropwise with vigorous stirring. After 1 hour, the reaction was filtered through a celite pad to remove the polymeric urea present. The pad was washed with chloroform (2 x 50 ml) and the combined organics evaporated. The crude oil obtained, was purified by dry flash chromatography (ether / hexane).

3.7.2.1 *exo*-3-(2',3',4'-Tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isoxazole 177



exo-(R)3a, (S)7a

177a



exo-(S)3a, (R)7a

177b

Sample code: **JM072**

Molecular formula: $C_{19}H_{25}NO_8$

Molecular weight: 395

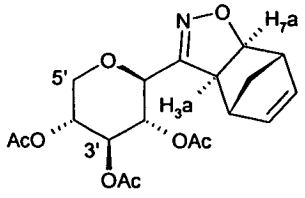
Reaction of nitromethyl xylose **166** (100 mg, 0.27 mmol, 1 equiv.) with norbornene (125 mg, 1.33 mmol, 5 equivs.) was carried out according to the general procedure. The crude product was chromatographed to afford a mixture of the *exo* diastereomers as a white solid 0.081 g, (76%) in a 55:45 ratio; mp = 169.5-170.0 °C (from hexane-ether); δ_H (250 MHz, $CDCl_3$) 1.19-1.57 (6H, m, H-5,6,8), 2.03, 2.05, 2.06, (9H, 3 x s, 3x$COCH_3$), 2.51 (1H, bs, H-7), 2.57 (1H, bs, H-7), 3.15 (1H, d, H-3a), 3.32 (2H, t, H-5ax', H-5eq'), 4.24 (1H, d, H-1'), 4.46 (1H, dd, H-7a), 5.03-5.12 (2H, m, H-2', H-4'), 5.28 (1H, t, H-3'), J(x-y, Hz) 1'-2' 9.9, 2'-3' 9.4, 3'-4' nd, 4'-5ax' nd, 4'-5eq' 5.7, 5ax'-5eq' 10.8, 3a-4 nd, 3a-7a 8.1, 4-5 nd, 5-6 6.1, 6-7 nd, 7-7a nd; δ_C (63 MHz, $CDCl_3$) 20.6 (3x$COCH_3$), 22.6 (C-8), 27.1, 27.2 (C-6), 31.5, 32.1 (C-5), 39.2, 39.3 (C-4), 42.2, 42.4 (C-7), 55.9, 56.6 (C-3a), 66.7 (C-5'), 68.7, 68.9 (C-4'), 69.1, 69.6 (C-2'), 72.8, 73.6 (C-3'), 74.4, 75.0 (C-1'), 87.5, 88.0 (C-7a), 154.6, 154.7 (C-3), 169.4, 169.8, 170.1 (3x$COCH_3$); m/z (EI) Found: M^++H 396.16653 $C_{19}H_{25}NO_8$ requires M^++H 396.16584.

3.7.3 Synthesis of carbohydrate functionalised monomers

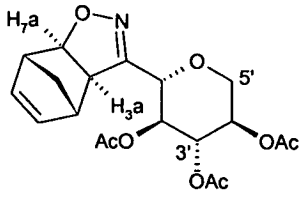
GENERAL PROCEDURE: Method as that described in 3.7.2 for preparation of *exo*-3-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,5,6,7,7a-hexahydro-4,7-methano-benzo[d]isoxazole **177**

3.7.3.1 *exo*-3-(2',3',4'-Tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole (xylose NBE) 168

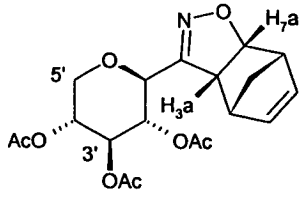
Sample code: **JM077**, Molecular formula: $C_{19}H_{23}NO_8$, Molecular weight: 393



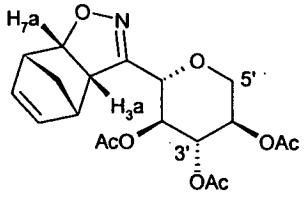
exo-(R)3a, (S)7a
168a



exo-(S)3a, (R)7a
168b



endo-(S)3a, (R)7a
174a

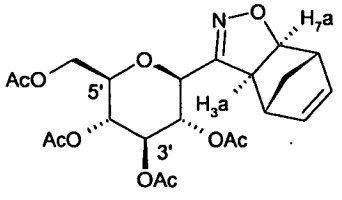


endo-(R)3a, (S)7a
174b

Reaction of nitromethyl xylose **166** (100mg, 0.27 mmol, 1 equiv.) with norbornadiene (125 mg, 1.35mmol, 5 equivs.) was carried out according to the general procedure. The crude product (0.083 g, 78%) was chromatographed to afford a mixture of the *exo* diastereomers **168a** and **168b** as a white solid (0.067 g, 63%) in a 62:38 ratio; (mp 127-128 °C) (from hexane-ether); [α] = (c=0.29, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 1.54-1.55 (2H, bs, H-8), 2.04, 2.05, 2.06, (9H, 3 x s, 3x$COCH_3$), 3.00 (1H, bs, H-4), 3.14 (1H, bs, H-7), 3.42 (1H, d, H-3a), 3.86, 3.90 (2H, m, H-5ax', H-5eq'), 4.59 (1H, d, H-1'), 4.71-4.75 (2H, m, H-2', H-4'), 4.94 (1H, dd, H-7a), 5.24 (1H, t, H-3'), 5.96 (1H, dd, H-5), 6.19 (1H, dd, H-6); J(x-y, Hz) 1'-2' 9.8, 2'-3' 8.8, 3'-4' nd, 4'-5ax' nd, 4'-5eq' 5.7, 5ax'-5eq' 11.4, 3a-4 1.9, 3a-7a 9.0, 4-5 3.2, 5-6 5.7, 6-7 3.0, 7-7a 1.5; δ_C (63 MHz, $CDCl_3$) 20.9 – 21.5 (3x$COCH_3$) 42.8 (C-8), 44.5 (C-4), 49.6 (C-7), 58.4 (C-3a), 65.3 (C-5'), 66.5 (C-2'), 66.9 (C-4'), 68.3 (C-3'), 70.0 (C-1'), 88.4 (C-7a), 135.2 (C-5), 139.9 (C-6), 154.0 (C-3), 169.7, 169.8, 170.0 (3x$COCH_3$); m/z (EI) Found: M^+ 393.142 $C_{19}H_{23}NO_8$ requires M^+ 393.142.

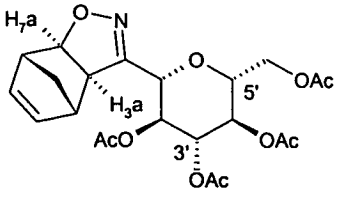
3.7.3.2 *exo*-3-(2',3',4',5'-Tetra-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole (glucose NBE) 169

Sample code: **JM160**, Molecular formula: $C_{22}H_{27}NO_{10}$, Molecular weight: 465



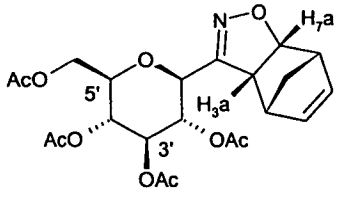
exo-(R)3a, (S)7a

169a



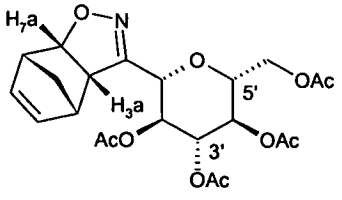
exo-(S)3a, (R)7a

169b



endo-(S)3a, (R)7a

175a



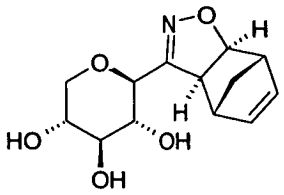
endo-(R)3a, (S)7a

175b

Reaction of nitromethyl glucose **173** (100mg, 0.27 mmol, 1 equiv.) with norbornadiene (125 mg, 1.35mmol, 5 equivs.) was carried out according to the general procedure. The crude product (90 mg, 76%) was chromatographed to afford a mixture of the *exo* diastereomers **169a** and **169b** in a 45:55 ratio, contaminated with a 15% trace of a mixture of the *endo* adducts **175a** and **175b** as a white solid (70 mg, 59%); (mp 156-157 °C); δ_H (250 MHz, $CDCl_3$) 1.49-1.54 (2H, m, H-8), 1.99,

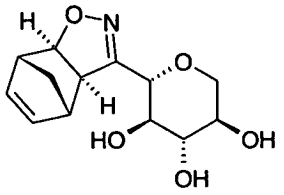
2.00, 2.03, 2.06, (12H, 4 x s, 4xCOCH_3), 3.11 (2H, bs, H-4,7), 3.28 (1H, d, H-3a), 3.67 (1H, ddd, H-5'), 4.13 (1H, dd, H-6a'), 4.24 (1H, dd, H-6b'), 4.39 (1H, d, H-1'), 4.74 (1H, d, H-7a), 5.02-5.21 (2H, m, H-2',4'), 5.63 (1H, dd, H-3'), 5.96 (1H, dd, 5-H), 6.16 (1H, dd, 6-H); J(x-y, Hz) 1'-2' 9.9, 2'-3' nd, 3'-4' nd, 4'-5' 9.8, 5'-6a' 2.9, 5'-6b' 6.9, 6a'-6b' 12.2, 3a-4 2.9, 3a-7a 8.3, 4-5 3.8, 5-6 7.2, 6-7 3.8, 7-7a 1.6; δ_C (63 MHz, $CDCl_3$) 20.5-21.3 (4xCOCH_3), 42.8 (C-8), 45.1, 46.8 (C-4), 49.0, 49.3 (C-7), 56.3, 57.1 (C-7a), 61.8, 62.0 (C-6'), 68.0, 68.2, 68.7, 69.2 (C-2',4'), 73.2, 73.7 (C-3'), 74.2, 74.3 (C-1'), 75.7, 75.9 (C-5'), 89.3, 89.6 (C-3a), 135.2, 135.0, (C-6), 140.0, 140.1 (C-5), 153.4, 153.6 (C=N), 169.2, 169.3, 169.4, 169.7, 169.9, 170.1, 170.4 (4xCOCH$_3$); m/z (EI) Found: M^++H 465.16317 $C_{19}H_{23}NO_8$ requires M^++H 465.16350.

3.7.3.3 *exo*-3-(2',3',4'-Tri-*O*-hydroxy-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[d]isoxazole 176



exo-(R)3a,(S)7a

176a



exo-(S)3a,(R)7a

176b

Sample code: JM220

Molecular formula: $C_{13}H_{17}NO_5$

Molecular weight: 267

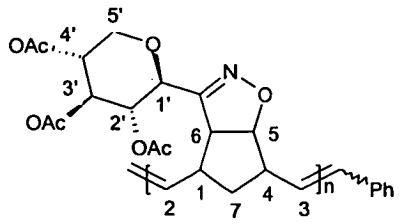
exo-3-(2',3',4'-tri-*O*-acetyl-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **168** was deprotected according to the method of Bazin *et al.*[184] A solution of **168** (0.1 g, 0.25 mmol, 1.6 equivs.) in anhydrous methanol (5 ml) containing triethylamine (0.016 g, 0.16 mmol, 1 equiv.) was stirred at room temperature under nitrogen for 36h. The solvent was removed *in vacuo* to give **176** as a white amorphous solid (0.07 g, 93%); (mp 133-134 °C) (EtOH); δ_H (250MHz, D_2O) 1.53 (2H, bs, H-8), 3.09 (1H, bs, H-4,7), 3.22 (1H, t, H-3a) 3.37-3.68, 3.89-3.95(6H, m, H-1',2',3', 4', H-5ax, H-5eq) 4.73 (1H, d, H-7a), 5.94 (1H, dd, H-5), 6.19 (1H, dd, H-6); J(x-y, Hz) 1'-2' nd, 2'-3' nd, 3'-4' nd, 4'-5ax' nd, 4'-5eq' nd, 5ax'-5eq' nd, 3a-4 1.9, 3a-7a 8.2, 4-5 3.2, 5-6 5.6, 6-7 2.8, 7-7a nd; δ_C (63 MHz, $CDCl_3$) 42.9 (C-8), 44.7 (C-4), 49.5 (C-7), 56.9 (C-3a), 58.3 (C-5'), 60.6 (C-2',4'), 71.2 (C-3'), 75.4 (C-1'), 88.7 (C-7a), 135.0 (C-5), 140.3 (C-6), 156.4 (C-3); m/z (EI) Found: M^++H 267.11047 $C_{13}H_{17}NO_5$ requires M^++H 267.11067.

3.8 ROMP of glycosyl isoxazolino norbornenes

3.8.1 Homopolymerisation

GENERAL PROCEDURE: Same procedure as that for the polymerisation of isoxazolino- / isoxazolidino- norbornenes (3.5.1) except that reaction media was dichloromethane (DCM) due to the insolubility of sugar isoxazolino norbornenes **168** and **169** in cyclohexane.

3.8.1.1 ROMP of xylose NBE 168



178

Sample code: **JM086***

Sample code: **JM103****

*Initiation using **1**; ** initiation using **2**

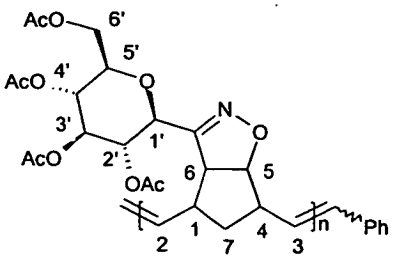
Xylose NBE **168**, (0.1 g, 0.25 mmol, 30 equivs.) was dissolved in dichloromethane and to this was added a solution of the ruthenium complex **1** or **2** (0.007 g, 0.008 mmol, 1 equiv.) in dichloromethane. The product **178** was afforded as a grey polymeric solid; δ_H (250 MHz, $CDCl_3$) 1.18, 1.36, 1.67, 1.84 (protons of five-membered ring), 1.92-1.97 (9H, m, 3x$COCH_3$), 2.51, 2.82 (protons of five-membered ring), 3.29 (1H, m, H-5'), 3.56 (1H, m, H-6), 4.11 (1H, m, H-5'), 4.28 (1H, m, H-1'), 4.72 (1H, m, H-5), 5.02, 4.85 (2H, m, H-2',4'), 5.18 (1H, m, H-3'), 5.32-5.60 (2H, m, H-2,3), 6.38, 6.55 (2H, m, CH=CH_2), 6.91, 6.78 (1H, m, PhHC=C), 7.27-7.29 (5H, m, PhH), 7.31 (1H, s, CH=CH_2); δ_C (90 MHz, $CDCl_3$) 20.9, 21.1, 21.6 (3x$COCH_3$), 39.0 (C-7), 47.0, 51.3 (C-1,4), 59.0 (C-6), 67.3 (C-5'), 69.4, 69.6 (C-2',4'), 73.6 (C-3'), 75.2 (C-1'), 92.0 (C-5), 131.5-133.8 (olefinics), 156.6 (C-3a), 169.9, 170.2, 170.6 (3x$COCH_3$).

I	[M]:[I]	yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI[a]	Propagating species ppm
1	30:1	87	1.57	2.39	40	1.52	19.5
2	30:1	75	47.05	28.67	729	1.64	[b]

[a]Determined by GPC in THF against polystyrene standards (860 – 2.43 million); [b]not observable by ^1H NMR

Table 3.12 – ROMP of **168** with **1** and **2**

3.81.2 ROMP of glucose NBE 169



179

Sample code: **JM167** (Initiation using **2**)

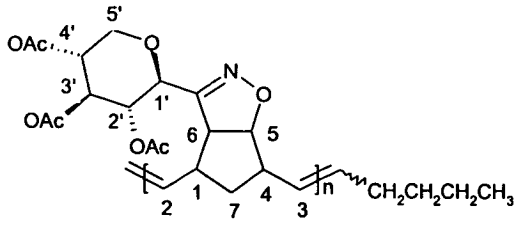
Glucose NBE **169**, (0.1 g, 0.21 mmol, 30 equivs.) was dissolved in dichloromethane and to this was added a solution of initiator **2** (0.006 g, 0.007 mmol, 1 equiv.) in dichloromethane. Precipitation in methanol afforded the product **179** as a grey polymeric solid; δ_H (250MHz, $CDCl_3$) 1.72, 1.63, 1.23 (protons from five-membered ring), 1.95 (4x$COCH_3$), 2.83, 2.60 (protons from five-membered ring), 3.52 (H-5'), 3.73 (H-6), 4.03 (H-1'), 4.23 (H-5), 4.65 (H-6'), 5.24, 5.05 (H-2',4'), 5.32 (H-3'), 5.57-5.66 (olefinics), δ_C (90 MHz, $CDCl_3$), 20.5, 20.6, 20.7 (4x$COCH_3$), 39.0, 42.4 (C-7), 46.6, 51.8 (C-1,4), 59.5 (C-6), 62.6 (C-6'), 65.6, 67.7 (C-2',4'), 71.8 (C-1',3'), 76.5 (C-5'), 91.2 (C-5), 129.0-134.2 (olefinics), 155.3 (C=N), 169.5 170.0, 170.5 (4x$COCH_3$).

I	[M]:[I]	Yield / %	$10^{-4}M_w$	$10^{-4}M_n$	av DP	PDI[a]	Propagating species ppm
2	30:1	71	15.44	8.37	212	1.84	[b]

[a]Determined by GPC in THFagainst polystyrene standards (860 – 2.43 million); [b]not observable by ^1H NMR

Table 3.13 – ROMP of **169** with **2**

3.8.1.3 ROMP of xylose NBE 168 in presence of hex-1-ene



184

Sample code: **JM219**

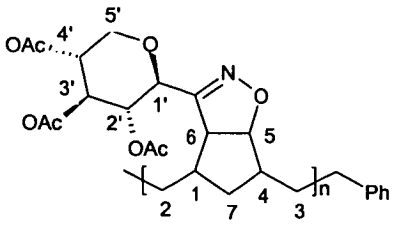
Xylose NBE **168** (0.05 g, 0.131 mmol, 100 equivs.) and hex-1-ene (0.0016 g, 0.02 mmol, 15 equivs.) was dissolved in dichloromethane and to this was added a solution of **1** (0.002 g, 0.002

mmol, 1.5 equivs.) in dichloromethane. The reaction was stirred at room temperature for 24 h before usual workup. The product **184** was afforded as a brown solid (62%); σ_C = 0.62; δ_H (360MHz, $CDCl_3$) 0.85 (3H, m, CH_3); 1.18, 1.36, 1.67, 1.84 (protons of five-membered ring), 1.92-1.97 (9H, m, 3x$COCH_3$), 2.51, 2.82 (protons of five-membered ring), 3.29 (1H, m, H-5'), 3.56 (1H, m, H-6), 4.11 (1H, m, H-5'), 4.28 (1H, m, H-1'), 4.72 (1H, m, H-5), 4.85, 5.02 (2H, m, H-2',4'), 5.18 (1H, m, H-3'), 5.31-5.60 (2H, m, H-2,3); δ_C (63MHz, $CDCl_3$) 20.5 (3x$COCH_3$, CH_3), 29.6 (3xCH_2), 39.0 (C-7), 46.1, 50.7 (C-1,4), 57.0 (C-6), 66.6 (C-5'), 68.8, 69.1 (C-2',4'), 72.9 (C-3'), 74.6 (C-1'), 91.2 (C-5), 130.1-134.2 (C=C), 156.0 (C=N), 169.2, 170.0 (3x$COCH_3$).

Sample code	[hex-1-ene] / [1]	yield / %	$10^{-4}M_n$	av DP[a]
JM219	0.10	62	0.60	15

[a]Determined by NMR analysis

3.8.2 Reduction of glyco isoxazolino polymers 178



185

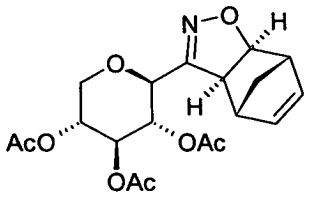
Sample code: **JM215**

A sample of the glycopolymer **178** was dissolved in chlorobenzene (10 ml), *p*-toluenesulfonylhydrazide (500 mgs) was then added and the mixture heated at reflux (130 °C) with stirring for 2.5h. The reaction mixture was observed to effervesce as the reaction proceeded. The mixture was the added to methanol (250 ml), and the resulting beige precipitate was filtered, washed twice with methanol and dried *in vacuo* to afford the product **185** as a grey powder (69%); δ_H (250MHz, $CDCl_3$) 0.88 (2H, m, H-2,3), 1.26-1.70 (4H, m, H-1,4,7), 2.10 (9H, bs, 3x$COCH_3$), 3.20-3.35 (2H, m, H-5',6), 4.01-4.31 (2H, m, H-5,1'), 4.60, 4.97-5.33 (3H, m, H-3',2',4'); δ_C (90 MHz, $CDCl_3$, 45 °C) 20.7 (3x$COCH_3$), 20.8, (CH_3), 29.6 (CH_2PH), 31.9, 34.1 (C-2,3), 38.2 (C-7), 44.1, 47.7 (C-1,4), 58.8 (C-6), 66.8 (C-5'), 69.3, 70.9 (C-2',4'), 73.4 (C-3'), 74.8 (C-1'), 92.6 (C-5), 159.6 (C=N), 169.5, 169.9 (3x$COCH_3$).

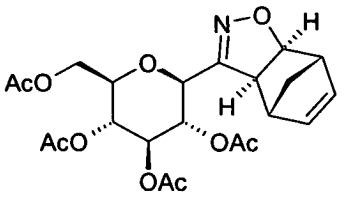
3.9 Random copolymerisation

Random copolymers (C/Ps) were synthesised using the same procedure as that described in 3.6.1.

CPE



168



169

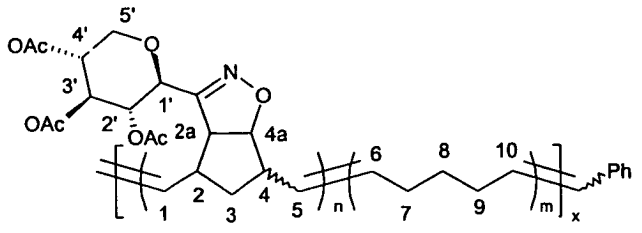
NBE

monomer[a]	[M1]:[M2]:[I][a]	C/P	I	Yield / %	$10^{-4}M_n$[b]	$10^{-4}M_n$[c]	av DP[d]	PDI
CPE/**168**	[40]:[10]:[1]	**186**	**2**	78	0.66	[e]	[e]	[e]
CPE/**169**	[40]:[10]:[1]	**187**	**2**	82	0.74	[e]	[e]	[e]
168/NBE	[10]:[40]:[1]	**188**	**1**	64	0.77	2.12	24/120	3.12
168/NBE	[10]:[40]:[1]	**189**	**2**	64	0.77	3.62	47/188	1.86
169/NBE	[10]:[40]:[1]	**190**	**2**	82	0.84	2.74	36/142	2.07
168/169	[67]:[67]:[1]	**191**	**1**	59	5.75	5.43	69/69	1.57

[a]The composition of comonomers and the equivalents of each. [b]Calculated from monomer to catalyst ratio. [c]Measured using GPC in THF against polystyrene standards (860 – 2.43 million). [d][M1]:[M2] in copolymer calculated from ^{1}H NMR. [e]GPC trace showed a bimodal molecular weight distribution.

Table 3.14 – Random copolymerisations of isoxazolino norbornenes.

3.9.1 Random copolymer 186 of CPE / xylose NBE 168



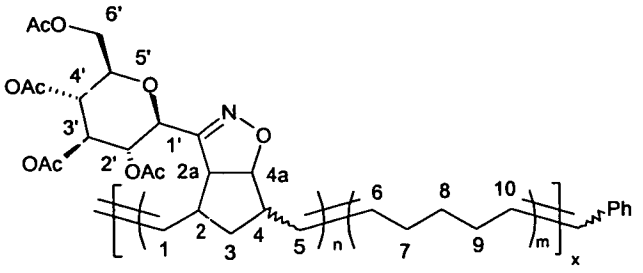
186

Sample code: **JM156**

Cyclopentene (27.8 mg, 0.41 mmol, 10 equivs.) and xylose NBE **168** (40 mg, 0.10 mmol, 40 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **2** (2 mg, 0.04 mmol, 1 equiv.) and the reaction stirred at rt for 24h. Upon work-up the product **186** was afforded as a brown tar (78%); δ_H (250MHz, $CDCl_3$) 0.81-1.75 (H-7,8,9), 1.97 (3x$COCH_3$), 2.47,

2.69, 2.80, (H-2,3,4), 3.24 (H-5'), 3.40 (H-2a), 4.06 (H-1'), 4.21 (H-4a), 4.64, 4.85 (H-2',4'), 5.21 (H-3'), 5.56-5.31 (H-1,5,6,10), 6.48 (C=CH_2), 6.90 (PhHC=C), 7.33 (PhCH); δ_C (90 MHz, $CDCl_3$) 19.7 (3xCOCH_3), 31.8, 28.7, 26.1 (C-7,8,9), 39.0 (C-3), 47.0, 51.3 (C-2,4), 59.0 (C-2a), 65.7 67.9, 68.2, 72.2, 73.7 (C-1', 2', 3', 4', 5'), 92.0 (C-4a), 131.2-129.3 (C-1,5,6,10), 156.6 (C=N), 169.6, 169.2, 168.8 (3xCOCH$_3$).

3.9.2 Random copolymer 187 of CPE / glucose NBE 169

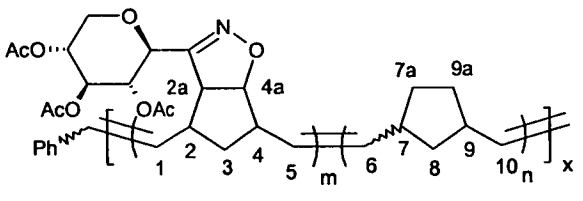


187

Sample code: **JM171**

Cyclopentene (29.2 mg, 0.038 mmol, 10 equivs.) and glucose NBE **169** (50 mg, 0.107 mmol, 40 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **2** (2.3 mg, 0.0027 mmol, 1 equiv.) and the reaction stirred at room temperature for 24h. Upon work-up the product **187** was afforded as a brown tar (82%); δ_H (250MHz, $CDCl_3$) 1.18-1.48 (2H, m, H-3,8), 1.76 (1H, m, H-3), 2.09-1.99 (16H, m, H-7,9, 4xCOCH_3), 2.81, 2.94 (2H, m, H-2,4), 3.49 (1H, m, H-2a), 3.73 (1H, m, H-5'), 4.12, 4.20 (2H, m, H-6'), 4.36 (2H, m, H-1',3'), 4.73 (1H, m, H-4a), 5.08 (2H, m, H-2',4'), 5.23 (2H, m, H-1',3'), 5.33-5.51 (4H, m, H-1,5,6,10), 5.67 (2H, m, HC=CH_2), 7.33 (1H, m, PhCH); δ_C (90 MHz, $CDCl_3$) 20.5 (4xCOCH_3), 31.9, 29.4, 26.6 (C-7,8,9), 40.1 (C-3), 50.6, 46.0 (C-1,4), 58.2 (C-2a), 62.2 (C-6'), 68.0, 69.4 (C-2',4'), 73.6 (C-3'), 73.8 (C-1'), 75.8 (C-5'), 91.9 (C-4a), 128.1-133.0 (HC=CH), 156.0 (C=N), 169.2, 169.6, 170.0, 170.4 (4xCOCH$_3$).

3.9.3 Random copolymers 188 and 189 of NBE / xylose NBE 168



188*/189**

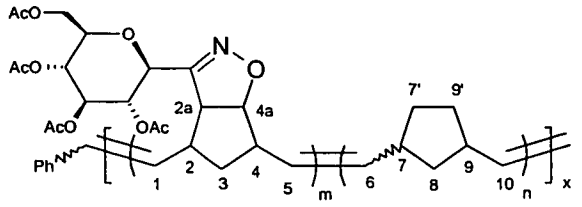
Sample code: **JM243***

Sample code: **JM237****

*Initiated with **1**, **initiated with **2**

Xylose NBE **168** (46.2 mg, 0.117 mmol, 10 equivs.) and norbornene (44.2 mg, 0.47 mmol, 40 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **1** or **2** (10.19 mg, 0.012 mmol, 1 equiv.) and the reaction stirred at rt for 24h. Upon work-up, the product was afforded as a grey polymeric solid (71%); δ_H (250MHz, $CDCl_3$) δ_H (250MHz, $CDCl_3$) 0.98-1.07 (4H, m, H-3,8), 1.35, 1.80 (4H, m, H-7a, 9a), 1.86 (2H, m, H-8), 2.03 (9H, bs, 3x$COCH_3$), 2.43, 2.80 (2H, m, H-7,9), 2.96 (2H, m, H-2,4) 3.31 (2H, m, 2xH-5'), 3.47 (H, m, H-2a), 4.15 (2H, m, 2xH-5'), 4.24 (2H, m, H-3'), 4.69 (1H, m, H-4a), 4.94 (1H, m, H-1'), 5.21 (6H, m, H-2',4', H-1,5,6,10), 5.34 (4H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 20.6 (3x$COCH_3$), 32.0, 32.2, 32.7, 32.9 (C-7a, 9a), 38.2, 38.5 (C-7,9), 41.2, 41.9, 42.6 (C-8), 43.0, 43.3 (C-7,9), 45.9, 46.5 (C-3) 50.3, 51.0 (C-2,4), 57.3-59.7 (C-2a), 66.5 (C-5'), 68.6, 69.0, 69.8 (C-2', 4'), 73.0, 73.2 (C-3'), 74.2, 74.4 (C-1'), 91.8, 93.0 (C-4a), 125.7-137.1 (C-1,5,6,10 + end groups), 156.2 (C=N), 169.6, 169.9 (3x$COCH_3$).

3.9.4 Random copolymer 190 of NBE / glucose NBE 169

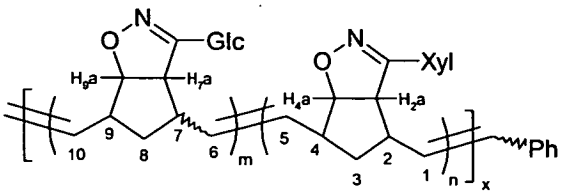


190

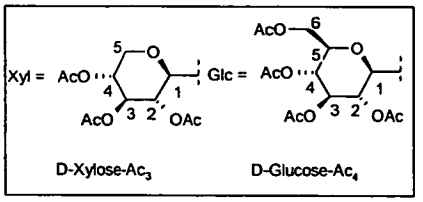
Sample code: **JM238**

Glucose NBE **169** (46.7 mg, 0.092 mmol, 10 equivs.) and norbornene (34.53 mg, 0.38 mmol, 40 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator **2** (7.64 mg, 0.009 mmol, 1 equiv.) and the reaction stirred at rt for 24h. Upon work-up the product **190** was afforded as a grey polymeric solid (83%); δ_H (250MHz, $CDCl_3$) 1.00-1.05 (4H, m, H-8,3), 1.35, 1.43 (2H, m, H-7a,9a), 1.81, 1.86 (2H, m, H-7a,9a), 2.01 (12H, bs, 4x$COCH_3$), 2.44, 2.79 (2H, m, H-7,9), 3.01, 3.03 (2H, m, H-2,4), 3.48 (2H, m, H-2a), 3.73 (1H, m, H-5') 4.13 (1H, m, H-6'), 4.35, 4.43 (2H, m, H-1',3'), 4.71 (1H, m, H-4a), 5.02, 5.06 (2H, m, H-2',4'), 5.21 (6H, m, H-1',3', H-1,5,6,10), 5.43 (4H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 20.4, 20.5, 20.6 (4x$COCH_3$), 32.0, 32.2, 32.7, 32.9 (C-7', 9'), 38.2, 38.4 (C-7,9), 41.2, 41.9, 42.6 (C-8), 42.0, 43.3 (C-7,9), 45.8, 46.5 (C-3), 50.7, 51.1 (C-2,4), 57.1, 59.5 (C-2a), 62.0 (C-6'), 67.9, 68.9, 69.4 (C-2',4'), 73.5, 73.8 (C-1,3), 75.6 (C-5'), 92.9 (C-4a), 125.4-137.1 (C-1,5,6,10 + end groups), 155.8, 156.4 (C=N), 169.2, 169.3, 170.0, 170.4 (4x$COCH_3$).

3.9.5 Random copolymer 191 of Xylose NBE 168 / glucose NBE 169



191

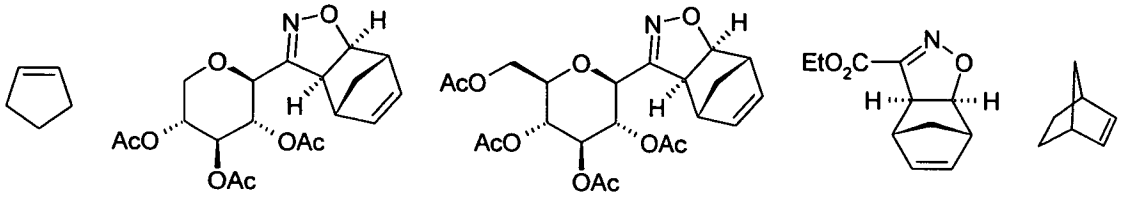


Sample code: **JM236**

Xylose NBE **168** (30 mg, 0.076 mmol, 67 equivs.) and glucose NBE **169** (35.3 mg, 0.076 mmol, 67 equivs.) were dissolved in dichloromethane (1.0 cm^3) and to this was added Grubbs initiator 1 (0.94 mg, 0.0011 mmol, 1 equiv.) and the reaction stirred at rt for 24h. Upon work-up the product was afforded as a grey polymeric solid (59%); δ_H (250MHz, $CDCl_3$) 1.99 (21H, bs, 7x$COCH_3$), 1.43, 2.27, 2.59 (8H, m, H-2,3,4,7,8,9), 3.35 (4H, m, 2xH-5'), 3.54-3.60 (2H, m, H-2a,7a), 4.19 (2H, m, 2xH-1'), 4.34 (2H, m, H-4a,9a), 4.79-4.91 (1H, m, H-6'), 5.10, 5.24 (4H, m, 2xH-2',4'), 5.46 (2H, m, 2xH-3'), 5.55-5.82 (4H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 20.5, 20.6 (7x$COCH_3$), 38.4, 39.6, 40.0 (C-3,8), 46.0, 50.6 (C-2,4,7,9), 61.9 (C-2a, 7a), 66.6, 68.8, 69.1, 72.8, 73.7, 74.6 (C1'-6'), 91.5 (C-4a, 9a), 130.6-135.1 (C=C), 156.0 (C=N), 169.0, 169.6, 170.0, 170.4 (7x$COCH_3$).

3.10 Block copolymerisation

Block copolymerisation of glyco homopolymers and CPE was carried out using the procedure described by Grubbs *et al.*[137] Monomer one (M1) was dissolved in dichloromethane and to this was added the ruthenium initiator **1** or **2**. The reaction was stirred at room temperature for 24h after which time a solution of monomer two (M2) in dichloromethane was added to the polymerisation and stirred for a further 24 hours at room temperature. The reaction was then heated at 50 °C for six hours after which time ethyl vinyl ether was added to terminate the polymerisation. The mixture was then added to methanol containing 2,6-di-tert-butyl-4-methylphenol affording a precipitate which was filtered, washed twice with methanol and then dried *in vacuo* to afford the block copolymer. The table below outlines the molecular weight data recorded for the block copolymers using GPC.



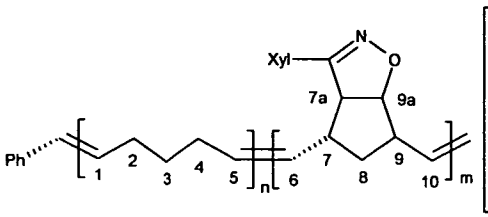
CPE **168** **169** **82** **NBE**

Monomer[a]	[M1]:[M2]:[I][a]	C/P	I	Yield / %	$10^{-4}M_n$[b]	$10^{-4}M_n$[c]	av DP[d]	PDI[a]
CPE/**168**	[67]:[67]:[1]	**192**	**1**	81	3.09	[e]	[e]	[e]
CPE/**169**	[67]:[67]:[1]	**193**	**2**	72	3.09	2.84	21/86	2.18
NBE/**169**	[40]:[40]:[1]	**194**	**2**	83	2.40	8.58	211/107	2.13
82/168	[67]:[67]:[1]	**195**	**1**	79	5.75	4.01	51/51	1.17
168/169	[67]:[67]:[1]	**196**	**1**	76	3.74	19.61	892/223	2.07

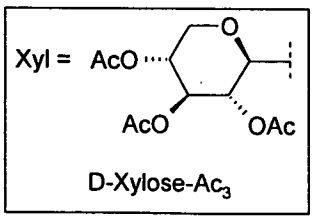
[a]The composition of comonomers and the equivalents of each. [b]Calculated from monomer to catalyst ratio. [c]Measured using GPC in THF against polystyrene standards (860 – 2.43 million). [d][M1]:[M2] in copolymer calculated from ^{1}H NMR. [e]Not determined

Table 3.15 – Block copolymerisations of isoxazolino norbornenes.

3.10.1 Block copolymer 192 of CPE / xylose NBE 168



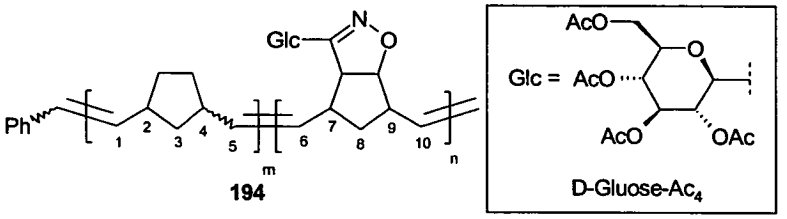
192



Sample code: **JM204**

Cyclopentene (8.7 mg, 0.13 mmol, 67equivs.) was dissolved in dichloromethane and to this was added a solution of ruthenium complex **1** or **2** (1.6 mg, 0.002 mmol, 1equiv.) in DCM. After 24h stirring, xylose NBE **168** (50 mg, 0.13 mmol, 67 equivs.) in DCM was added and the reaction stirred for a further 24h, before heating at 50 °C for 6h. Work-up was as outlined above to afford a brown tar (78%); δ_H (300MHz, $CDCl_3$) 0.78 (4H, m, H-8,3), 1.01-1.75 (4H, m, H-2,4), 1.92 (9H, m, 3x$COCH_3$) 2.46, 2.68, 2.86 (4H, m, H-7,8,9), 3.24 (1H, m, H-5'), 3.42 (1H, m, H-7a), 4.08 (1H, m, H-1'), 4.26 (1H, m, H-9a), 4.64, 4.64 (2H, m, H-2',4'), 5.21 (1H, m, H-3'), 5.31-5.55 (4H, m, H-1,5,6,10), 6.48 ($C=CH_2$), 6.88 (C=CHPh), 7.36 (PhCH); δ_C (300MHz, $CDCl_3$) 19.7 (3x$COCH_3$), 26.1, 28.7, 31.8 (C-2,3,4), 36.1 (C-8), 42.5, 47.1, 49.9 (C-7,9), 57.0 (C-7a), 65.7 (C-5'), 67.9, 68.2 (C-2',4'), 72.2 (C-3'), 73.7 (C-1'), 91.5 (C-9a), 124.0 ($C=CH_2$), 129.3-131.2 (C-1,5,6,10), 134.2 (C=CHPh), 155.0 (C=N), 168.7 (3x$COCH_3$).

3.10.2 Block copolymer 194 of NBE and glucose NBE 169

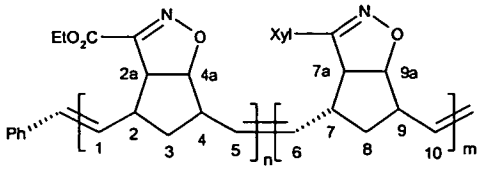


194

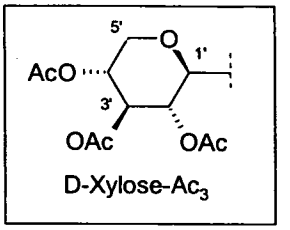
Sample code: **JM241**

Norbornene (6.9 mg, 0.073 mmol, 67 equivs.) was dissolved in dichloromethane (1.5 ml) and to this was added the Grubbs initiator **1** (0.89 mg, 0.0011 mmol, 1 equiv.) in dichloromethane (1.0 ml) and the reaction stirred for 24h. A second aliquot of glucose NBE **169** (33.9 mg, 0.073 mmol, 67 equivs.) dissolved in dichloromethane (1.0 cm^3) was then added and the reaction and stirred for a further 24h. The reaction mixture was then heated at 60 °C for 6h before termination with ethyl vinyl ether. Upon work-up, the product **194** was afforded as a light grey polymeric solid (76%); δ_H (250MHz, $CDCl_3$) 0.98-1.02 (4H, m, H-8,3), 1.36, 1.43 (2H, m, H-7a,9a), 1.80, 1.85 (2H, m, H-7a,9a), 2.02 (12H, bs, 4x$COCH_3$), 2.38, 2.77 (2H, m, H-7,9), 3.00, 3.04 (2H, m, H-2,4), 3.48 (2H, m, H-2a), 3.73 (1H, m, H-5') 4.13 (1H, m, H-6'), 4.35, 4.43 (2H, m, H-1',3'), 4.71 (1H, m, H-4a), 5.02, 5.06 (2H, m, H-2',4'), 5.21 (6H, m, H-1',3', H-1,5,6,10), 5.18-5.35 (4H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 20.6 (4x$COCH_3$), 32.0, 32.2, 32.7, 32.9 (C-7', 9'), 38.3, 38.5 (C-7,9), 41.2, 41.9, 42.6 (C-8), 42.9, 43.3 (C-7,9), 45.9, 46.5 (C-3), 50.7, 51.1 (C-2,4), 58.5, 59.6 (C-2a), 62.7 (C-6'), 66.5, 68.6, 69.0 (C-2',4'), 73.1, 74.3 (C-1',3'), 76.5 (C-5'), 91.9, 93.1 (C-4a), 125.7-137.1 (C-1,5,6,10 + end groups), 156.2 (C=N), 169.5, 169.6, 169.9, 170.0 (4x$COCH_3$).

3.10.3 Block copolymer 195 of ethoxycarbonyl NBE 82 and glucose NBE 169



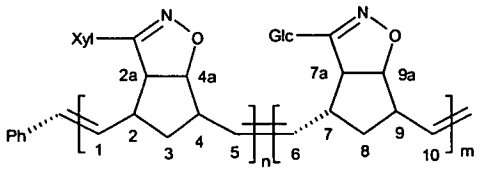
195



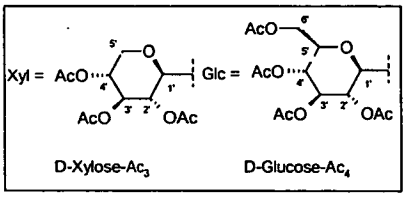
Sample code: **JM161**

Ethoxycarbonyl NBE **82** (21.5 mg, 0.104 mmol, 67equivs.) was dissolved in dichloromethane and to this was added a solution of the ruthenium complex **2** (0.09 mg, 0.0015 mmol, 1equiv.) in DCM. After 24h stirring, xylose NBE **168** (41 mg, 0.104 mmol, 67equivs.) in DCM was added and the reaction stirred for a further 24h, before heating at 50 °C for 6h. Work-up was as outlined above to afford the product **195** as a cream coloured powder (83%); δ_H (500MHz, $CDCl_3$) 1.22-1.34 (3H, m, $COCH_2CH_3$), 1.90-1.94 (bs, 9H, $3xCOCH_3$), 2.63 (m, 8H, protons from five-membered ring), 3.33-3.41 (bs, 2H, $CO_2CH_2CH_3$), 5.16, 4.92, 4.88, 4.26, 4.23 (6H, m, H-1' – H-5'), 5.71-5.35 (2H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 13.8 ($CO_2CH_2CH_3$), 20.4 ($3xCOCH_3$), 39.4 (C-3,8), 42.4, 46.2 (C-2,4,7,9), 57.3 (C-2a,7a), 61.8 ($CO_2CH_2CH_3$), 66.3 (C-5'), 68.6, 69.0 (C-2',4'), 72.8 (C-3'), 74.3 (C-1'), 91.4-95.2 (C-4a,9a), 128.9-134.3 (olefinics), 153.6, 156.6 (2xC=N), 160.5 ($CO_2CH_2CH_3$), 168.9 ($3xCOCH_3$).

3.10.4 Block copolymer 196 of xylose NBE 168 / glucose NBE 169



196



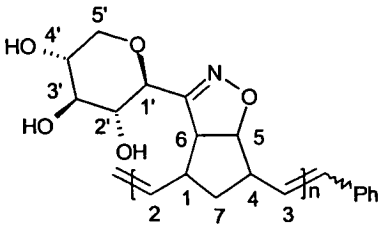
Sample code: **JM232**

Xylose NBE **168** (37.6 mg, 0.096 mmol, 70 equivs.) was dissolved in dichloromethane (1.5 ml) and to this was added the ruthenium initiator **1** (1.16 mg, 0.0014 mmol, 1 equiv.) in dichloromethane (1.0 ml) and the reaction stirred for 24h. A second aliquot of glucose NBE **169** (44.5 mg, 0.096 mmol, 70 equivs.) dissolved in dichloromethane (1.0 cm^3) was then added and the reaction stirred for a further 24h. The reaction mixture was then heated at 60 °C for 6h before termination with

ethyl vinyl ether. Upon work-up the product **196** was afforded as a grey polymeric solid (79%); δ_H (250MHz, $CDCl_3$) 1.98 (21H, bs, 7x$COCH_3$), 1.43, 2.57, 1.43 (8H, m, H-2,3,4,7,8,9), 3.34 (4H, m, 2xH-5'), 3.45-3.64 (2H, m, H-4a, 9a), 4.14 (2H, m, 2xH-1'), 4.35 (2H, m, H-2a,7a), 4.79-4.91 (1H, m, H-6'), 5.09, 5.26 (4H, m, H-2',4'), 5.44 (2H, m, 2xH-3'), 5.51-5.75 (4H, m, H-1,5,6,10); δ_C (90 MHz, $CDCl_3$) 20.5, 20.6 (7x$COCH_3$), 38.5 (C-7), 42.6, 46.0, 50.7 (C-1,4), 57.1 (C-2a,4a), 61.9, 66.6, 68.8, 69.1, 72.8, 74.5 (C-1'-6'), 91.8 (C-4a,7a), 127.9, 130.9, 132.3 (C=C), 156.0 (2xC=N), 169.6, 170.1, 170.4 (7x$COCH_3$).

3.11 Deacetylated carbohydrate functionalised polymers

3.11.1 ROMP of deacetylated xylose NBE 176 under aqueous conditions



Sample code	catalyst system	conditions
JM221	$RuCl_3.xH_2O$	H_2O, 60 °C, 18h
JM223	**1**	H_2O/MeOH
JM234	**2**	Emulsion conditions

3.11.1.1 Ruthenium trichloride hydrate

Adopting the procedure of Grubbs *et al.*[186] a flask containing *exo*-3-(2',3',4'-tri-*O*-hydroxy-β-D-xylopyranosyl)-3a,4,7,7a-tetrahydro-4,7-methano-benzo[d]isoxazole **176** (0.023 g, 0.085 mmol, 33 equivs.) and $RuCl_3.xH_2O$ (0.0006 g, 0.0028 mmol, 1.0 equiv.) was added degassed H_2O (1.5 ml). The resulting black solution was heated at 55-60 °C. After 18h, the solution was washed with acetone (2 ml) and methanol (2 ml) to afford a discoloured solid. The solid was dissolved in water (10 ml), concentrated to 2 ml, and precipitated by the addition of methanol (10 ml). The supernatant liquid was decanted and the white precipitate was washed with methanol (2 x 1 ml). Excess solvent was evaporated under reduced pressure to afford a grey solid (92 %). The product was identified as being unreacted monomer **176**.

3.11.1.2 Emulsion conditions using 2

Polymerisation under emulsion conditions using **2** adopted from the procedure of Grubbs *et al.*[187] To the solution of deacetylated xylose NBE **176** (0.05 g, 0.176 mmol, 1.0 equiv) and DTAB (0.09 g, 0.3 mmol, 1.6 equivs.) in H_2O (310μl), was added the initiator **2** (0.003 g, 0.0035 mmol, 0.02 equivs.) in $(CH_2Cl)_2$ (150μl) and the whole was stirred vigorously for 20 hr at room temperature.

Ethyl vinyl ether (0.1 ml) was added and the mixture was warmed up to 60 °C for 3.5 hr and then concentrated. The residue was dissolved in H_2O (5 ml) and washed with $CHCl_3$ (3 x 3ml). Concentration of the water layer gave the crude mixture. The crude brown film was washed with MeOH (3 x 5 ml) to give a pale brown film (71%); δ_H (250MHz, D_2O); 0.81, 1.22, 1.71-1.93, 3.06, 3.26, 4.68-4.76; δ_C (90 MHz, D_2O) 14.7, 23.4, 27.1, 30.26, 32.6, 35.9, 53.9, 67.6, 78.8, 101.5.

3.11.1.3 Methanol / water using 1

The polymerisation was carried out using the Grubbs ruthenium alkylidene 1 in a H_2O/MeOH solvent mixture according to the method described by Kiessling *et al.*[188] Thus deacetylated xylose NBE **176** (0.02g, 0.06 mmol, 33 equivs.) was dissolved in methanol (42 µl) and H_2O (11 µl) and the resulting solution degassed with nitrogen. The initiator 1 (0.002 g, 0.002 mmol, 1 equiv.) was dissolved in dichloromethane (280 µl) and added to the monomer. The reaction went from purple to green with vigorous stirring. Additional degassed methanol (210 µl) and degassed H_2O (75 µl) were added to keep the monomer in solution. After 2h, the reaction was quenched with ethyl vinyl ether (50 mg), heated to 45 °C and stirred for 3h. The solvent was removed *in vacuo* and the resulting syrup was taken up in MeOH and the polymer was filtered off and washed with MeOH (3 x 5 ml) to remove unreacted monomer and ruthenium initiator 1 affording a dark brown solid (87%); δ_H (250MHz, DMSO) 1.14-1.23, 1.66-1.75. 2.50, 3.15-3.56, 3.76-3.79, 4.42, 5.02-5.16, 6.72, 7.12-7.42, 7.68.

3.11.2 Deacetylation of xylose isoxazoline functionalised polymer (n = 3) 178

The deacetylation reaction was carried out using the method of Schrock *et al.*[133] with the exception that the methoxide source was generated from MeOH/TEA as reported by Bazin *et al.*[184] Glycopolymer **178** (50 mgs, 0.04 mmol, 1.6 equivs.) was dissolved in THF (5 ml) containing a triethylamine (2.5 mgs, 0.025 mmol, 1 equiv.) methanol (0.5 ml) mixture. This was stirred at 45 °C for 12h. The solvent was removed *in vacuo* to yield the deprotected polymer as a tan tar (91%); δ_H (250MHz, D_2O) 1.12-1.27, 1.40-1.49, 1.89-1.96, 2.73-2.78, 3.47-3.58, 4.00, 5.10-5.35, 6.39; δ_C (69MHz, D_2O) 23.4, 23.6, 26.8, 29.8, 30.1, 30.3, 30.4, 32.7, 47.7, 53.9, 67.1, 67.1, 69.9, 70.2.

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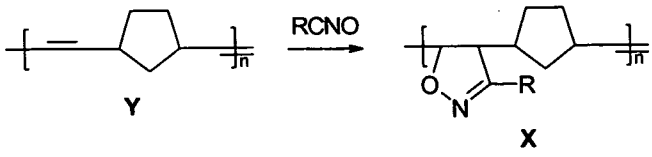
Appendix 1 – N-elemental analysis of modified polymers

Modification to polyNBE



R	M_w X
Ph	226
EtO_2C	222
MeO_2C	208

Case 1. Modification of polyNBE with ethoxycarbonylformonitrile oxide

Molecular weight of modified polymer is 222X + 107Y

$$\%N = \frac{14 \times 100X}{222X + 107Y}$$

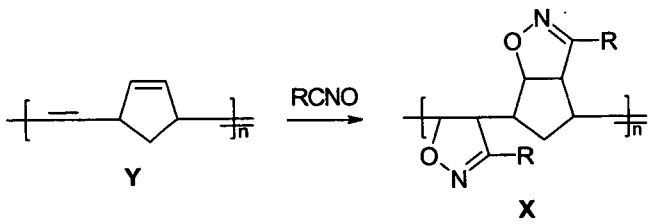
By elemental analysis, %N in polymer = 2.37%

Therefore, the ratio of unreacted alkene groups to modified groups = 78:22.

(*i.e.* for every 10 units approximately 8 are unsaturated and 2 are modified)

The structure of the modified polymer by elemental analysis requires C 64.85, H 7.26, N 6.30%, found C 59.20, H 6.71, N 2.37%.

Modification to polyNBD



R	M_w X
Ph	343
EtO_2C	335
MeO_2C	307

Case 2. Modification of polyNBD with ethoxycarbonylformonitrile oxide

Molecular weight of polymer is 335X + 105Y

$$\%N = \frac{2 \times 14 \times 100X}{335X + 105Y}$$

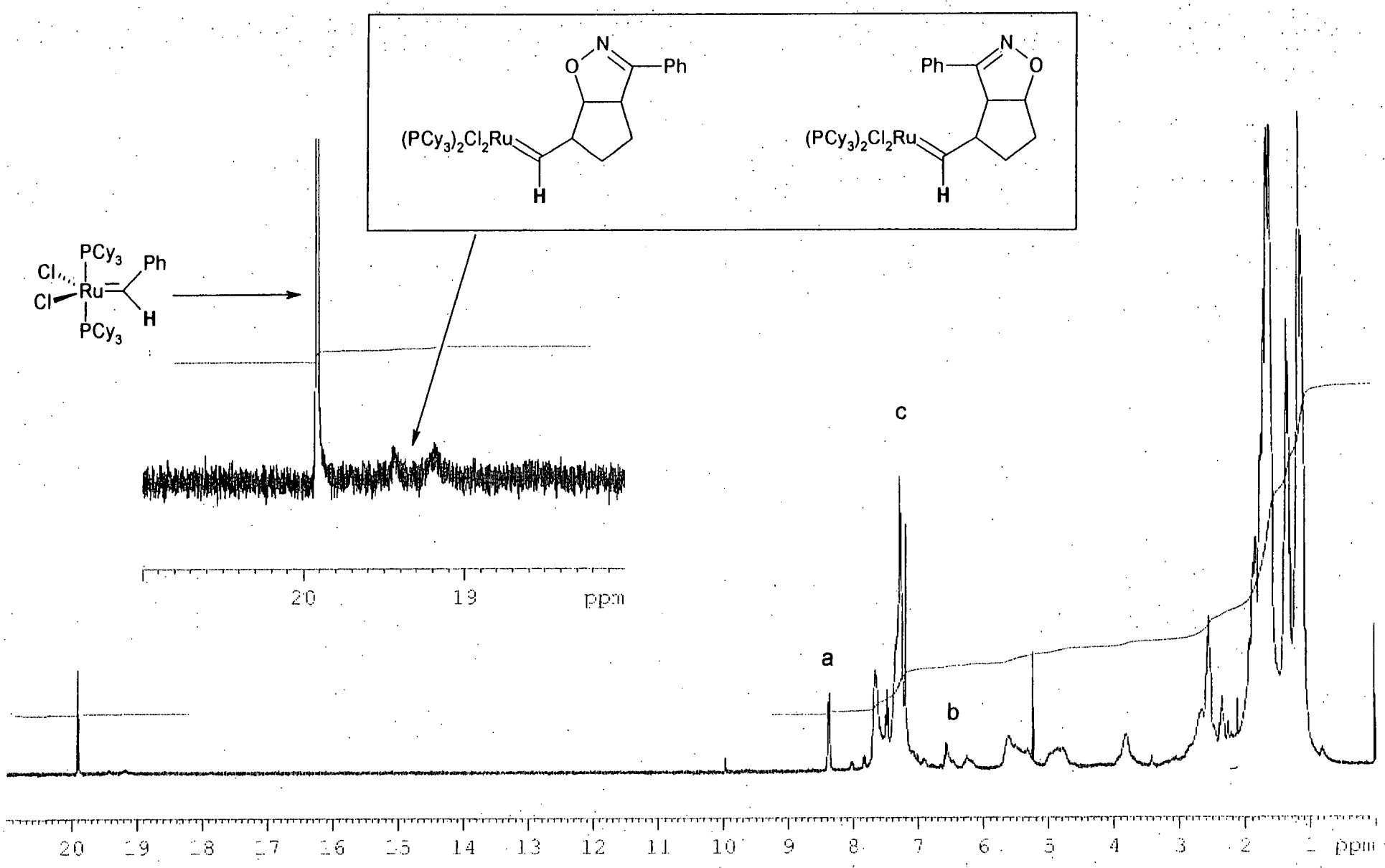
By elemental analysis, %N in polymer = 4.31%

Therefore, the ratio of unreacted alkene groups to modified groups = 3:1.

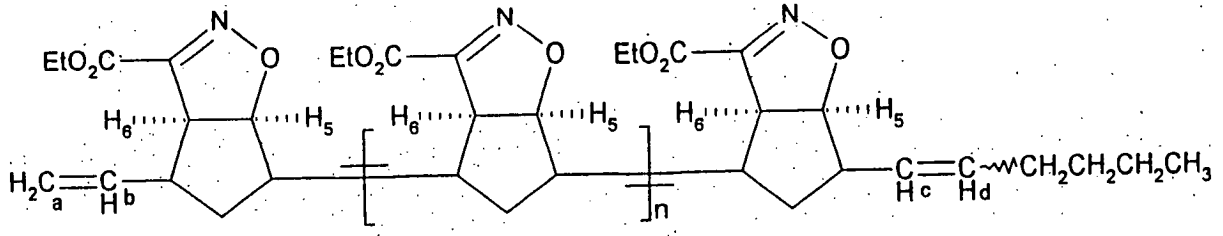
(*i.e.* for every 10 units approximately 7 are unsaturated and 3 are modified)

The structure of the modified polymer by elemental analysis requires C 57.48, H 5.12, N 8.38%, found C 60.18, H 5.58, N 4.31%.

Appendix 2: Monitoring the propagating species in ROMP of *exo*-3-phenyl -3a,4,5,6-tetrahydro-4,7-methano-benzo[d]isoxazole 81 using ^{1}H NMR spectroscopy



Appendix 3: Identification of end groups ethoxy isoxazolino functionalised oligomer (n = 4) in ^{13}C NMR spectrum



$\underline{C}H_3CH_2CO_2$
+ CH_3