Oxy-Cope and Claisen Rearrangements on Carbohydrate Templates: Expedient Syntheses of 9-Membered Ring Ethers and Pseudo-Sugars

A Thesis
Submitted for the degree of
Doctor of Philosophy

By

A.V.R.L. SUDHA

School of Chemistry
University of Hyderabad
Hyderabad 500 046
INDIA

March 1998

TO MY

FIRST FRIEND AND TEACHER

AMMA

CONTENTS

DECLARATION

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad under the supervision of Professor M. Nagarajan.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

A.V.R.L. SUDHA

CERTIFICATE

This is to certify that the work described in this thesis entitled *Oxy-Cope and Claisen Rearrangements on Carbohydrate Templates: Expedient Syntheses of 9-Membered Ring Ethers and Pseudo-Sugars* has been carried out by Ms **A.V.R.L. Sudha** under my supervision and the same has not been submitted elsewhere for any degree.

M. NAGARAJAN
(THESIS SUPERVISOR)

DEAN
School of Chemistry,
University of Hyderabad,
Hyderabad - 500 046
INDIA

ACKNOWLEDGEMENTS

I wish to express my respect and deep sense of gratitude to Professor M. Nagarajan, my research supervisor, for his excellent guidance and inspiring discussions about the subject I am indebted to him for teaching me not only chemistry but many other things I can never forget his fatherly affection and friendly behaviour towards us

I thank Professor P. S. Zacharias, Dean, School of Chemistry for his support. My due respects to all other faculty members for their stimulating lectures during my post-graduation days and their help throughout my Ph. D tenure My sincere thanks to Prof. D Basavaiah and Dr. M. J. Swamy for extending instrumental facilities. I thank Professor S. Chandrasekharan, I, I. Sc, Bangalore for providing microanalysis for some of my samples.

It gives me great pleasure to thank all my labmates, Murali, Narkunan, Vasudeva, Prabhavathi, Manjula, Ramana and Lakshmikanthan, for creating lively, friendly, co-operative and pleasant atmosphere in the lab.

My association with Manjula and Ramana is a memorable experience in my life. 1 enjoyed all my moments with them including our petty quarrels over silly things. Manjula (honorary editor of the lab) and Ramana are acknowledged for their invaluable help in the preparation of this thesis

I am also thankful to my friends Bhanu, Ranganayaki, Sumithra, Murali, Shiva, Malli and Markandeyulu for adding cheerful moments to my memory bank.

I would like to thank Mr. Y. Hanumantha Rao who has not only been a teacher to me, but also a friend, guide and source of inspiration.

I acknowledge Prasanna, Prasad, Chandrakala, Anitha, Vijju, Madhavi, Ramalakshmi, Mangai, Sailaja, Venkat, Anthony, Giribabu and Arounaguiri for making my stay in school an enjoyable one. Special thanks to Ramakrishnan for his timely help.

I feel fortunate to have wingmates like Rama, Rukmini and Parvathi who always made me feel at home.

I am grateful to my parents for their support and encouragement all these years. I am very lucky to have brothers like Prasad and Vinu with whom I shared my wonderful childhood.

Words fail to express my feelings towards Swamy. He has been my best friend all these years and has been very understanding, caring and co-operative. My weekends with him always filled me with new enthusiasm and energy to see me through rest of the week.

I would like to express my respect to my parents-in-law who are pleasant people and are proud of my career.

Thanks are also due to the supporting staff of the school for their assistance. Especially, Mr. Shetty, Mr. Venkata Rao, Mr. Ramakrishna, Mr. Vijaya Bhaskar, Mr. Anand, Mr. Dilip, Ms. Ayesha, Mr. Raghava, Ms. Vijayalakshmi, Mr. Ramana and Mr Santosh. A special word of appreciation to Mr. Satyanarayana and Mr. Bhaskar Rao for recording beautiful spectra during my research period.

Dr. K. V. Reddy and his staff at C.I.L have been very helpful and I wish to thank them. I thank the university authorities for providing necessary facilities to carry out my research. Finally, I thank CSIR for the financial assistance.

ABBREVIATIONS

Ac	acetyl
A	Angstrom
aq	aqueous
AT	aryl
AIBN	2,2'-azobisisobutyronitrile
Bz	benzoyl
Bn	benzyl
9-BBN	9-borabicyclo[3.3.1]nonane
Bu	butyl
Cat	catalytic
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	1,3-dicyclohexylcarbodiimide
DIBAL-H	diisobutylaluminum hydride
DME	1,2-dimethoxyethane
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
Et	ethyl
FVP	flash vaccum pyrolysis
HMPA	hexamethylphosphoric triamide
h	hour(s)
LDA	lithium diisopropylamidc
m-CPBA	*m*-chloroperbenzoic acid
Ms	methanesulfonyl (mesyl)
Me	methyl
ml	millilitre(s)
mmol	millimole(s)
min	minute(s)

NuH	nucleophile
Ph	phenyl
Pr	propyl
Py	pyridine
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
rt	room temperature
TBAF	tetra-n-butylammonium fluoride
TBDMS	t-butyldimethylsilyl
TBDPS	t-butyldiphenylsilyl
THF	tetrahydrofuran
Ts	p-toluenesulfonyl (tosyl)
TFA	trifluoroacetic acid
TMS	trimethylsilyl
Tr	triphenylmethyl (trityl)

ABSTRACT

This thesis deals with the synthesis of medium ring ethers and pseudo-sugars from sugars using oxy-Cope and Claisen rearrangements, respectively. The thesis consists of three sections, namely, introduction, results and discussion and experimental section followed by relevant references. The results and discussion is divided into two parts. Part I deals with the preparation of chiral hexahydrooxoninones and attempts towards synthesis of oxecanones from carbohydrates. Part II deals with the synthesis of pseudo-sugars from sugars *via* chiral carbocycles.

The introduction briefly presents various available methods for the synthesis of medium ring ethers and lactones, conversion of carbohydrates to carbocycles and syntheses of pseudo-sugars.

RESULTS AND DISCUSSION: PART I: SYNTHESIS OF MEDIUM RING ETHERS.

The oxy-Cope rearrangement is one of the most widely used sigmatropic reactions for ring expansion purposes. We chose to make chiral 9- and 10-membered ring ethers from carbohydrates utilizing oxy-Cope rearrangement as a key step For construction of the requisite precursor in furanoses, 1,2:5,6-di-*O*-cyclohexylidene-3-*C*-vinyl-α-D-allofuranose (212) was chosen as a suitable substrate. The allofuranose 212 on selective removal of the 5,6-*O*-cyclohexylidene group and penodate oxidation gave the aldehyde 214 Wittig methylenation of the aldehyde 214 with formylmethylenetriphenylphosphorane and subsequent decarbonylation with Wilkinson's catalyst yielded the diene 217. The diene 217 was ring expanded to the chiral hexahydrooxoninone 219 under thermal oxy-Cope rearrangement conditions.

Encouraged by this, substituted analogues of the diene 217, 220a-223b were prepared by condensing the aldehyde 214 with different stable ylides. Most of these dienes underwent ring enlargement to yield functionalized 9-membered ethers, 227, 228 and 229.

Similarly, to prepare chiral 10-membered ethers from pyranoses, methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexo-pyranosid-4-ulose (239) was identified as suitable starting material. The ulose 239 on Gngnard reaction with ethynylmagnesium bromide, followed by semi-hydrogenation afforded a mixture of epimeric C-4 vinyl derivatives 241. Further reactions were conducted on the mixture Detritylation of 241 and subsequent oxidation of the resulting diol 243 furnished the aldehyde 244. Methylenation of the aldehyde 244 with methylenetriphenylphosphorane gave the required diene 245. Subsequently, the dienes 246a, 246b and 247 were synthesized from the aldehyde 244. Attempted anionic and thermal oxy-Cope rearrangements of these dienes 245-247 under various conditions resulted in either recovery of starting material or decomposition

PART II: SYNTHESIS OF PSEUDO-SUGARS *VIA* CHIRAL CARBOCYCLES:

Conversion of carbohydrates to carbocycles is an area which has attracted considerable attention in recent times, due to the omnipresence of 5- and 6-membered carbocycles in several natural products. Pseudo-sugars are carbocyclic analogues of carbohydrates and are found as components of important antibiotics.

We realized that the Claisen rearrangement could serve as a key step to convert carbohydrates to carbocycles which could be further functionalized to pseudo-sugars.

To this end, the known alcohol, 1,5-anhydro-3,4-di-*O*-benzyl-D-*arabino*-hex-1-enitol (250) was arrived at as a convenient starting material. The alcohol 250

on oxidation yielded the aldehyde **251,** which on Wittig reaction with methylenetriphenylphosphorane furnished the diene **253** The thus formed allyl vinyl ether 253 underwent Claisen rearrangement at 240", to yield the chiral carbocycle **254**

In order to generalize the above strategy, carbethoxy and acetyl substituted dienes. 256 and 257 were prepared. Claisen rearrangement of 256 and 257 under similar conditions as those for 253 furnished chiral carbocycles 258 and **259,** respectively.

As the aldehyde 254 was observed to epimerize on standing at room temperature, the crude aldehyde 254 was reduced with sodium borohydride to provide the alcohol 255. Catalytic osmium tetroxide hydroxylation of the double bond in 255 from the less hindered α-face gave the triol 262. which on debenzylation yielded pseudo-α-D-glucopyranose **(263)**

The primary hydroxyl group in 255 was protected as its benzyl ether to yield the tribenzyl ether **264.** A mixture of partially benzylated pseudo-a-D-mannopyranose 265 and pseudo-β-D-glucopyranose 266 was obtained in one step from 264 involving a sequence of epoxidation and ring opening using *m*-CPBA, water and 10% H_2SO_4. 265 and 266 were separated and subjected to hydrogenolysis to yield pseudo-α-D-mannopyranose (267) and pseudo-β-D-glucopyranose **(268),** respectively.

cis-Hydroxylation of the alkene 264 under Woodward's conditions and subsequent debenzylation afforded pseudo-α-D-glucopyranose **(263)** instead of the anticipated pseudo-β-D-mannopyranose

The aldehyde **270** which was obtained from epimerization of **254,** on sodium borohydride reduction, osmium tetroxide hydroxylation and debenzylation gave pseudo-p-L-idopyranose **(273).**

Utility of the oxy-Cope rearrangement in the ring expansion of furanosides to functionalized 9-membered ring ethers has been demonstrated for the first time. These chiral 9-membered nng ethers can serve as precursors for 9-membered lactones and other systems. A simple and convenient methodology has been developed for the preparation of pseudo-sugars as well as for the conversion of sugars to carbocycles.

All the relevant experimental details were given ın the experimental section. All the new compounds prepared in the course of this thesis were characterized by spectral and analytical data as appropriate.

INTRODUCTION

INTRODUCTION

Carbohydrates are widespread amongst natural products and are endowed with rich stereochemistry. They are abundant in Nature as for example, in sugarcane, sugar beet, trees and chitin. The more common ones are often cheaper than other enantiopure compounds of natural origin or even basic organic chemicals from petrochemical sources.[1] Availability of carbohydrates in cyclic and acyclic forms and with different chain lengths make them an attractive source of chiral molecules. Till recently, carbohydrates were not preferred for synthetic manipulations, as they were believed to be complex, polyoxy, polyfunctional molecules with a less selective role in biological processes when compared to proteins and nucleic acids

Interesting findings in cell biology, immunology and biochemistry during the last two decades, has unveiled the hitherto unknown role of carbohydrates in biological processes.[2] The carbohydrate portion of glycoconjugates plays a decisive role in biological recognition of membranes. Selective interactions of carbohydrates with receptors regulate intercellular transport of enzymes. They are of importance in the regulation of cell growth and various immunological processes. Biocompatibility and biodegradability of carbohydrates have made them indispensable for industrial applications. D-glucose. for example, is used as a nutrient, feed stock for sorbitol and high fructose corn syrup and as a carbon source for industrial fermentations. Many polymers, detergents and food additives have also been derived from carbohydrates.[3]

During the last three decades, many monosaccharides have been recognized as essential constituents of drugs. Aminohexoses such as daunosamine and related compounds are the glycosidic components of the anthracycline antibiotics

daunomycin and adriamycin which exhibit strong activity against solid tumors and soft tissue sarcomas. The aminooctose lincosamine is an essential component of the antitumor antibiotic lincomycin. Macrolide antibiotics and antitumeral agents such as calicheamycin and analogues contain amino and deoxy-sugars

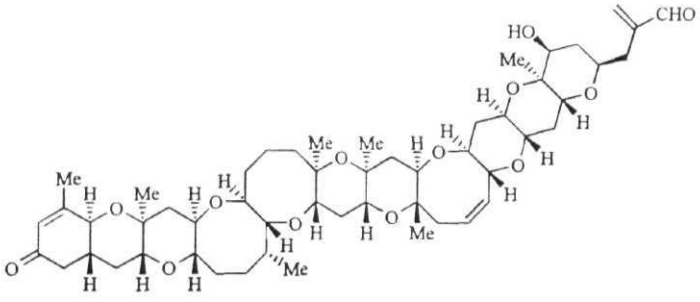
These important observations have infused new enthusiasm amongst synthetic chemists to explore various facets of carbohydrate chemistry. As a result, carbohydrates are being looked at from a different view point and are considered as Nature's supply of "*chiralpool*" molecules to construct enantiomerically pure synthetic targets.[4] Thus, the stereocherrucal and operational advantages of carbohydrates has led to the synthesis of modified sugars, non-natural sugars, molecules containing butyrolactone and valerolactone type rings, cyclic molecules, heterocyclic compounds, carbocyclic compounds and macrolides. The inherent steric, stereoelectronic and coordinating properties of carbohydrate templates have been utilized to induce high asymmetric induction in Diels-Alder reactions, hetero Diels-Alder reactions, (2+2) cycloadditions, cyclopropanations and Michael additions.[5]

This thesis deals with the syntheses of medium ring compounds, pseudo-sugars and conversion of carbohydrates to carbocycles. A brief summary of the existing literature in connection with above mentioned compounds is given in the following pages.

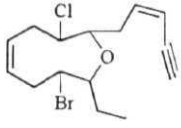
SYNTHESIS OF MEDIUM RING ETHERS AND LACTONES:

Recent interest in the synthesis of medium ring compounds stems from the fact that they occur widely in Nature, particularly in marine natural products such as brevetoxin A and B[6] (1) and in many laurencia non-terpenoid metabolites.[7] Metabolites of the red alga laurencia such as isolaurepinnacin, laurencin and

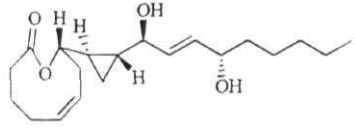
laurenyne and obtusenyne[8] (2) possess 7-, 8- and 9-membered ethers in their structures, respectively. Bioactive marine metabolites such as halicholactone (3) and neohalicholactone contain unsaturated 9- membered lactones as an integral part of their structures.[9] Of the functionalized 10-membered lactones, diplodialides A. B, C and D. phoracantholides I and J. diplodialide A exhibits significant inhibitory activity against progesterone 1 1α-hydroxylase.[10]



BREVETOXIN B (1)



OBTUSENYNE (2)



HALICHOLACTONE (3)

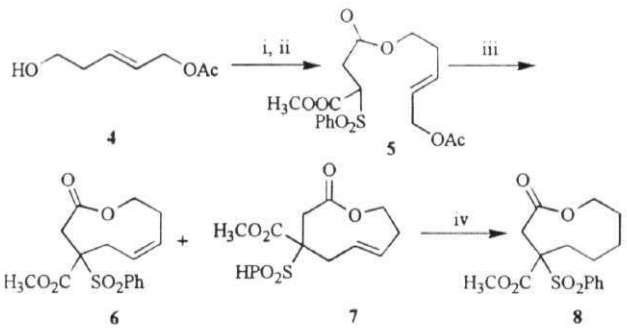
Figure 1

Unfavorable entropy factors in effecting ring closure and non-bonding interactions inherent in medium ring structures make their synthesis a difficult task. The methods available for the synthesis of medium ring compounds can be broadly

classified into three types, based on the type of reaction involved, as 1) cyclization of acyclic precursors, 2) modification of existing medium ring compounds and 3) ring expansion reactions. Syntheses of medium ring compounds have been achieved using each of these methods and some typical examples are detailed below.

1. CYCLIZATION OF ACYCLIC PRECURSORS:

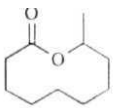
Trost has developed a general method for the construction of medium and large nng compounds through **C-C** bond formation It is based on the application of palladium catalyzed allylic alkylation in an intramolecular process The yields



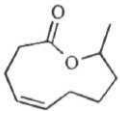
Scheme 1. *Reagents and conditions:* i) $BrCH_2COBr$, Py, CH_2Cl_2, 0°; ii) NaH, $PhSO_2CH_2CO_2CH_3$, DMF, 0°; iii) NaH, $Pd(Ph_3P)_4$, THF, reflux; iv) H_2, 5% $Pd\text{-}BaCO_3$, absolute ethanol, 2 atm.

of cyclization obtained by this method are independent of ring size and no dimeric products are formed. Thus, the allylic acetate 4 was converted to 5, which on cyclization gave two 9-membered lactones 6 and 7, These on hydrogenation gave the

saturated lactone 8 (Scheme 1) The 10-membered lactones phoracantholide I (9) and J (10) were synthesized using this protocol.[11]



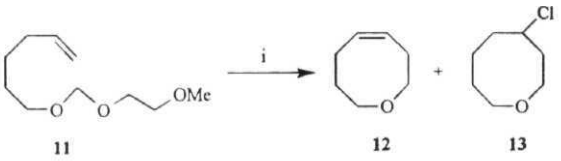
rac-PHORACANTHOLIDE I (9)



rac-PHORACANTHOLIDE J (10)

Figure 2

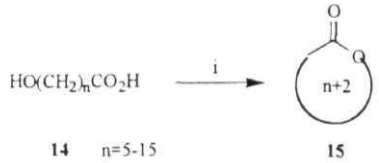
Lewis acid catalyzed cyclization of simple unsaturated acetals to A-unsaturated 8- and 9-membered ring etliers has been demonstrated by Overman. This method is illustrated by treating the acetal **11** with 2 equivalents of $SnCl_4$ to provide the oxocene 12 (Scheme 2). Mono- and disubstituted alkenes on cyclization afforded only 8-membered ring products, whereas 7-membered rings were observed in the case of trisubstituted alkenes.[12]



Scheme 2. *Reagents and conditions:* i) SnCU, -20°, 13h.

Lewis acid catalyzed macrolactonization of ω-hydroxycarboxylic acids 14 to lactones 15 has been examined by Yamamoto.[13] *p*-Nitrobenzoic anhydride and a catalytic amount of scandium triflate were found to be a perfect combination for internal esterification of ω-hydroxycarboxylic acids to medium and large ring

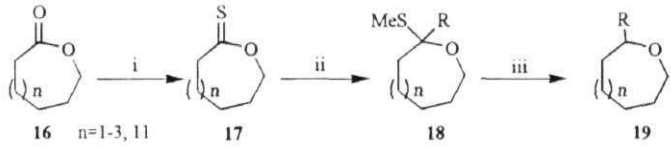
lactones as shown in the scheme below (Scheme 3). This method permits selective monomeric lactonization to produce medium ring lactones, without forming large quantities of diolides



Scheme 3. *Reagents and conditions:* i) $Sc(OTf)_3$ (10-20 mol%), $(p\text{-}NO_2C_6H_4CO)_2O$ (2 eq.), CH_3CN, THF, reflux.

2. MODIFICATION OF EXISTING RING SYSTEMS:

Stereoselective syntheses of various medium ring ethers from the corresponding lactones have been developed by Nicolaou. Medium ring thionolactones 17 were obtained from the corresponding lactones 16 by treatment with Lawesson's reagent Condensation of the resultant thionolactones with nucleophiles, followed by quenching with methyl iodide afforded the



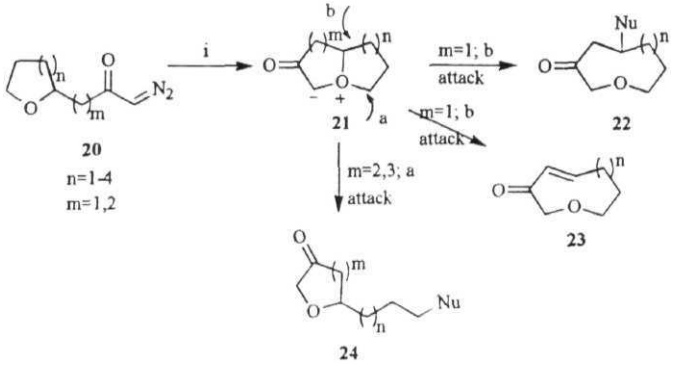
Scheme 4. *Reagents and conditions:* i) Lawesson's reagent; ii) RM, MeI; iii) Ph_3SnH, AIBN, toluene, reflux.

corresponding alkylated thioacetals **18** These thioacetals on reductive desulfurisation with triphenyltin hydride under radical conditions gave the corresponding cyclic ethers **19** (Scheme 4). This strategy provides an easy access to model systems of rings B and D of brevetoxin A and rac-lauthisan [14]

3. RING EXPANSION METHODS[15]:

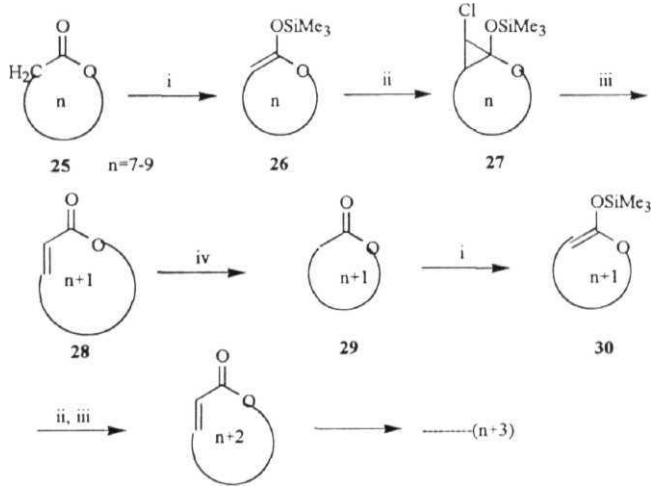
Ring expansion reactions can be achieved in three ways, by a) cleaving the shortest bridge in a bicycle, b) incorporating a side chain placed at a suitably functionalized atom of the ring into the ring and c) forming a new bond and breaking an old bond between two side chains situated appropriately on the same ring

a) CLEAVING THE SHORTEST BRIDGE IN A BICYCLE:



Scheme 5. *Reagents and conditions:* i) $Rh_2(OAc)_4$, NuH

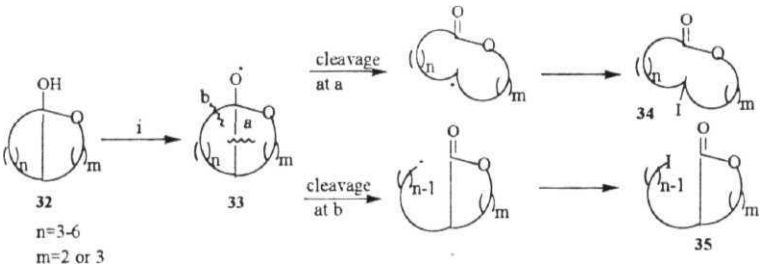
Recently, Oku has described the construction of 8- to 10- membered cyclic ketoethers by rhodium(II) catalyzed three carbon ring enlargement of diazoacetonyl substituted cyclic ethers *via* bicyclic ethereal oxonium ylide intermediates (Scheme 5). The intermediate bicyclic oxonium ion 21 can be attacked by the nucleophile in two modes leading to either ring switched or ring enlarged products. In the presence of nucleophiles more acidic than methanol and moderately acidic nucleophiles. the nucleophilic attack by the conjugate base Nu on the bridgehead position gave rise to ring enlarged products 22 and 23 when m=l ('b' attack). In the case of m=2 and 3, attack of nucleophile at less hindered positions ('a' attack) facilitated release of strain energy to afford ring switched products exemplified by **24**.[16]



Scheme 6. *Reagents and conditions:* i) LDA. TMSCl, THF; ii) $NaN(SiMe_3)_2$, CH_2Cl_2, pentane, -15°, in) toluene, reflux; iv) H_2, Pd/C.

An elegant method developed by Rousseau for the construction of medium nng lactones consists of thermal rearrangement of cyclopropanes formed by carbene addition to trimethylsilyl enol ethers, affording one carbon ring expanded products Thus. for example. the saturated lactone 25 on enolization followed by cyclopropanation gave the cyclopropyl compound 27. which on refluxing in toluene and h> drogenation gave the one carbon ring expanded product 29 (Scheme 6) This method could be iterative. as the product of thc initial rearrangement can be suitably modified to form the substrate for a second rearrangement [17]

An interesting approach to medium ring lactones has been reported by Suginome Several catacondensed lactols were converted to ring-enlarged products through light induced regioselective β-scission of alkoxy radicals generated from

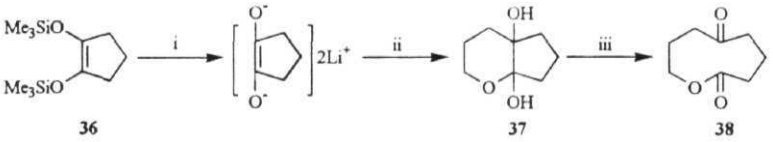


Scheme 7. *Reagents and conditions* i) HgO. I₂. 100W high pressure Hg arc.

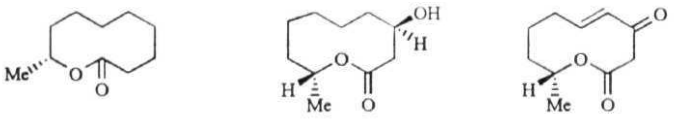
their hypoiodites Out of the two possible modes of cleavage for the catacondensed lactol 32. cleavage at 'a' would lead to a nng expanded product 34. whereas cleavage at 'b' would result in generation of a side chain to give 35 (Scheme 7) In all cases. preponderant cleavage at 'a" to form secondary carbon radicals resulted in high yields of ring expanded products. 6/5 Fused lactols on ring enlargement gave 9-

membered lactones whereas 10-membered lactones were obtained either from 6/6 or 7/5 fused lactols. This method has been exploited in the synthesis of R-(-)-phoracantholide I, a 10-membered lactone.[18]

Ketolactones of medium ring size were prepared by alkylation of 1,2-enediolates, followed by oxidation of the resultant bicyclic glycol (Scheme 8). Thus, 1,2-bis(trimethylsilyloxy)cyclopentene 36 on treatment with methyllithium and 3-bromopropanol afforded the glycol 37, which was oxidatively cleaved with lead tetraacetate to the desired lactone 38. Following this protocol, 7-ketoundecanolide was obtained, but in low yields Suitable manipulation of 6-ketononalide led to the synthesis of racemic decan-9-olide (39), diplodialide C (40) and diplodialide A (41) (Figure 3)."



Scheme 8. *Reagents and conditions:* **i)** CH_3Li, DME; **ii)** $Br(CH_2)_3OH$, THF, **HMPA; iii)** $Pb(OAc)_4$.

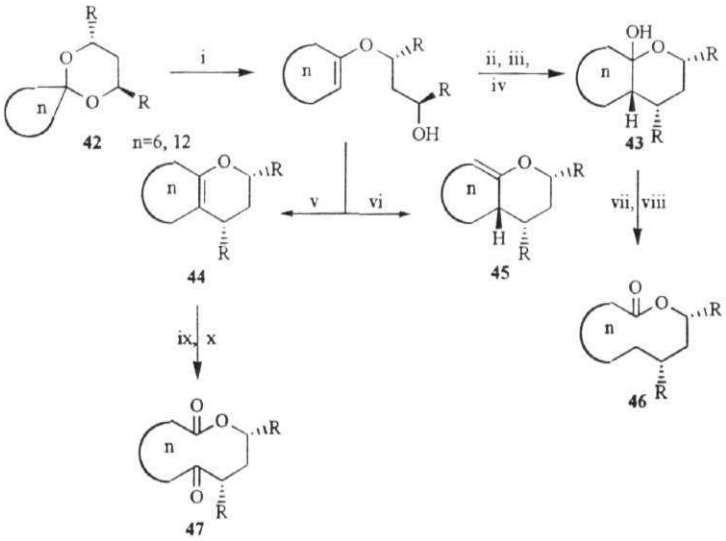


DECAN-9-OLIDE (39) **DIPLODIALIDE C (40)** **DIPLODIALIDE A (41)**

Figure 3

Synthesis of medium and large ring compounds from stereospecifically annulated hydroxy vinyl ethers has been described by Yamamoto. Treatment of

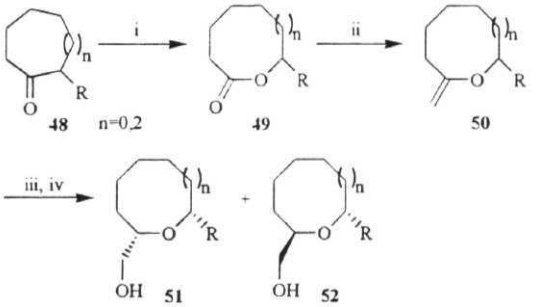
spiroacctals 42 with tri-isobutylaluminum gave the corresponding hydroxy vinyl ethers These **hydroxy** vinyl ethers formed hemiacetals 43 and isomeric bicyclic vinyl ethers 44 and 45 under different reaction conditions. These compounds were easily transformed into cyclic lactones 46 and ketolactones 47, respectively, by routine methods (Scheme 9).[21]



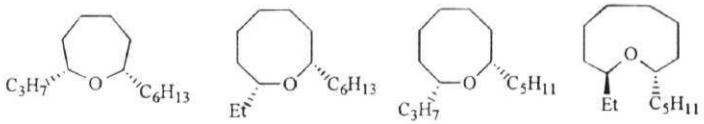
Scheme 9. *Reagents and conditions:* i) i-Bu,Al; ii) Tf_2O (1.2 eq.), i-Pr_2EtN, CH_2Cl_2, -78°; iii) aq. $NaHCO_3$; iv) -78° to rt; v) Tf_2O (1.2 eq.), i-Pr_2EtN, toluene, -78 to 25°; \i) Tf_2O (1.2 eq), i-Pr_2EtN, CH_2Cl_2, -78 to 25"; vii) $PhI(OAc)_2$, I_2, hv, cyclohexane; viii) Bu_3SnH, AIBN, THF; ix) O_3, MeOH, -78°; x) Me_2S.

b) INCORPORATING A SIDE CHAIN INTO THE RING:

The Baeyer-Villiger oxidation has been exploited by Holmes in his syntheses of 2,n disubstituted oxacycles (n=ring size). 2-Substituted cycloalkanones 48 on Baeyer-Villiger oxidation gave ring expanded lactones 49, which were methylenated by Tebbe's reagent. The resultant enolethers 50 on hydroboration followed by oxidation afforded the required medium ring ethers 51 and 52 (Scheme 10).[21]



Scheme 10. *Reagents and conditions:* i) CF_3CO_3H, Na_2HPO_4, CH_2Cl_2, 0° to rt; ii) $Cp_2Ti[\mu\text{-}(CH)_2\text{-}\mu\text{-}Cl]AlMe_2$, THF, toluene. Py (cat), -40° to rt; iii) a) borane-THF, rt or b) diisoamylborane, THF, 0°; iv) H_2O_2, NaOH, 0°.

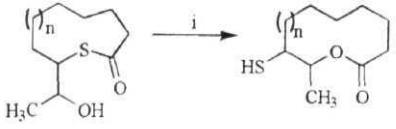


ISOLAUREPAN (53) **LAUTHISAN (54)** **LAURENAN (55)** **OBTUSAN (56)**

Figure 4

Synthesis of fully saturated carbon skeletons corresponding to isolaurepan. lauthisan, laurenan and obtusan **have** been achieved by this method (Figure **4**)

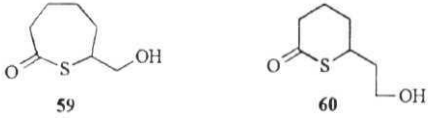
Vedejs has reported a new method for the synthesis of medium ring lactones involving acid catalyzed sulphur to oxygen acyl transfer as a key step for the conversion of hydroxyalkyl thiol lactones to mercaptolactones. In this context, the thiol lactone 57 was rearranged to mercaptolactone 58 in the presence of camphorsulfonic acid by an S to **0 acyl** transfer process (Scheme 11).[22]



57 n=0,1 58

Scheme **11.** *Reagents and conditions* i) *rac*-Camphor-10-sulphonic acid, CH_2Cl_2.

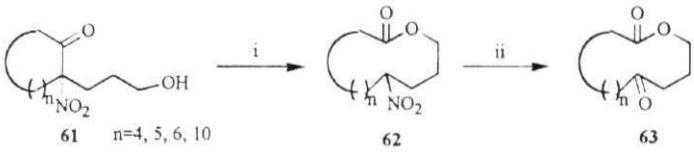
However, in the case of 6- and 7-membered thiol lactones **59** and 60, S to 0 acyl transfer was incomplete.



59 60

Figure 5

2-(ω-Hydroxybutyl)-2-nitrocycloalkanones 61, obtained from nitrocyclo-alkanones, on base catalyzed isomerization gave the nitrolactones 62 which on suitable functional group adjustments yielded ketolactones 63 as outlined in Scheme 12.[23]

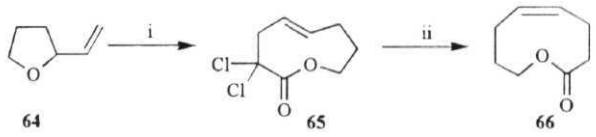


Scheme 12. *Reagents and conditions:* i) NaH (cat. amount), DME, reflux; ii) Et_3N, aq. $(NH_4)_2[Ce(NO_3)_6]$, CH_3CN, reflux.

c) **FORMING A NEW BOND AND BREAKING AN OLD BOND BETWEEN TWO SIDE CHAINS PLACED APPROPRIATELY ON THE RING:**

Sigmatropic reactions such as the Claisen and Cope rearrangements come under this type of ring expansion reactions.

An efficient stereoselective synthesis of unsaturated 9-membered lactones by Taylor comprises application of Malherbe-Bellus variant of the Claisen rearrangement Reaction of 2-vinyltetrahydrofuran 64 and dichloroketene resulted in



Scheme 13. *Reagents and conditions:* **i)** Cl_3CCOCl, **Zn; ii)** Bu_3SnH, AIBN, **benzene, reflux.**

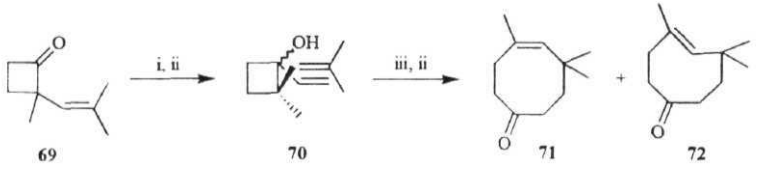
the unsaturated dichlorolactone 65, which on dechlorination and concomitant isomerization gave the *cis*-unsaturated lactone 66 (Scheme 13)[24].

Various substituted unsaturated 9-membered lactones were prepared by this method

Scheme 14. *Reagents and conditions:* **i) 120".**

The Cope rearrangement of divinylcyclobutane to 1,5-cyclooctadiene was demonstrated by Vogel. *cis*-Divinylcyclobutane 67, on Cope rearrangement at 120°, gave the cyclooctadiene 68 (Scheme 14).[25]

As the Cope rearrangement is very often reversible, the oxy-Cope rearrangement which renders the rearrangement irreversible, has become very popular. Gadwood has reported the synthesis of 1,2-dialkenylcyclobutanols and their rearrangement to substituted cyclooctenones *via* the oxy-Cope rearrangement.



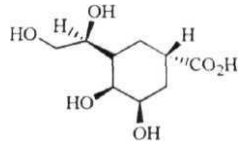
Scheme 15. *Reagents and conditions:* **i)** vinyllithium, Et_2O, -78°; **ii) AcOH, iii)** KH, **THF. 25°.**

In a typical example. 2-methyl-2-(2-methylpropen-l-yl)cyclobutanone 69 on reaction with vinyllithium gave cyclobutanol 70. which on treatment with KH underwent anionic oxy-Cope rearrangement to afford Z- and E-cyclooctenones 71 and 72 (Scheme 15).[26]

As this brief survey indicates, while several methods are available for the construction of medium ring ethers, the Cope rearrangement and its variants have not been used for this purpose

CONVERSION OF SUGARS TO CARBOCYCLES:

The ubiquity of cyclopentane and cyclohexane rings among natural products has elicited intense interest in the synthesis of functionalized, enantiomerically pure carbocycles.[28] Myo-inositol, a cyclohexanehexol, with its several important biological functions, has attracted the attention of many synthetic chemists since the time of Fischer. The carbocyclic analogue of β-2-deoxy-KDO (73), a complex cyclohexane, is expected to be more lipophilic than its sugar counterpart and hence more potent towards inhibition of CMP-KDO synthetase.[28] Fused ring carbocycles, such as chiral hexahydrobenzofurans were recognized as potential precursors for the broad spectrum antibiotics, milbemycins and avermectins.[29] Several syntheses of phyllanthocin, an anti-P388 leukemia plant product, share the common feature of using a preformed cyclohexane ring as a template for constructing the requisite furanoid moiety.[30] The glycoprotein processing inhibitor, mannostatin A, is formed *via* the key intermediacy of a chiral cyclopentanone.[31] Functionalized, chiral cyclopentanes have been widely utilized in the synthesis of a variety of isomeric cyclopentanepentols, aminocyclopentanetetrols and diaminocyclopentanetriols.[32]

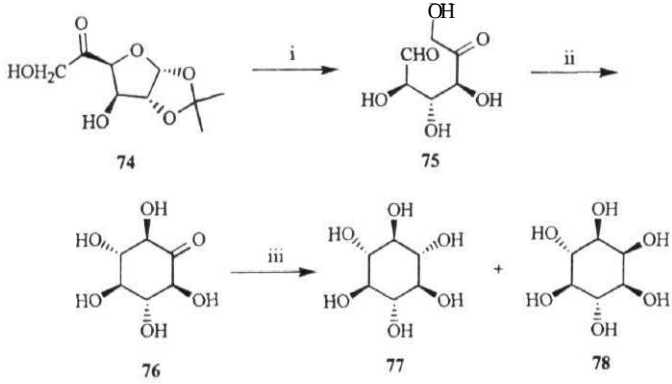


CARBOCYCLIC ANALOGUE OF β 2-DEOXY KDO (73)

Figure 6

Carbohydrates have long been recognized as synthetic precursors for many complex molecules in Nature, but exploration of the synthetic versatility of carbohydrates by chemists is of recent origin. Fischer's synthesis of nitroinositols from 6-deoxy-6-nitrohexose[27] can be termed as a stepping stone for carbohydrates to carbocycles conversion Since then, synthesis of many carbocycles have been accomplished, taking advantage of the ability of carbohydrates to transfer chirality. In the following pages, a brief account of the available methods for conversion of carbohydrates to carbocycles is given. Depending upon the key step involved in the conversion, they can be classified under the following headings

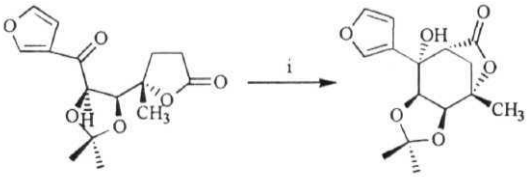
ALDOL REACTIONS:



Scheme 16. *Reagents and conditions:* i) Dowex 50W X-8 (H^+), 38-40°, 48h; ii) NaOH; iii) $NaBH_4$.

Aldol cyclization of 1,5-dicarbonyl sugar derivatives to cyclohexane derivatives has been reported by Kiely and Fletcher. Thus, for example, the 1,5-dicarbonyl compound, D-*xylo*-hexos-5-ulose 75 obtained from ketoalcohol 74, on treatment with alkali gave inosose 76. Subsequent reduction of the ketone functionality with $NaBH_4$ gave myo-and scyllo-inositols 77 and 78, respectively (Scheme 16).[33]

CLAISEN CONDENSATION:



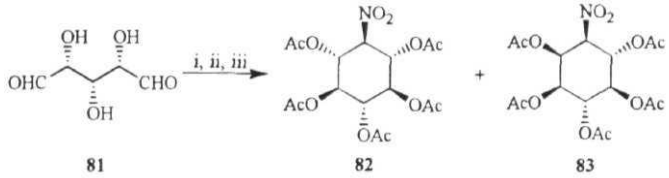
Scheme 17. *Reagents and conditions:* i) LDA, THF, -78° .

Williams has investigated the utility of intramolecular Claisen condensation for the stereoselective preparation of β-hydroxylactones as exemplified by 80 from 1,7-dicarbonyl compounds e.g., 79 (Scheme 17). This strategy has been used to produce a synthon for a component of the milbemycin and avermectin family of macrocvclic metabolites.[29]

DIALDEHYDE-NITROMETHANE CYCLIZATION:

An elegant approach for the synthesis of nitroinositols was developed by Lichtenthaler through the intermediacy of nitro-stabilized species. Cyclization of the *xylo*-trihydroxyglutardialdehyde 81, obtained from 1,2-*O*-isopropylidene-α-D-

glucofuranose, in the presence of a base and nitromethane afforded a mixture of

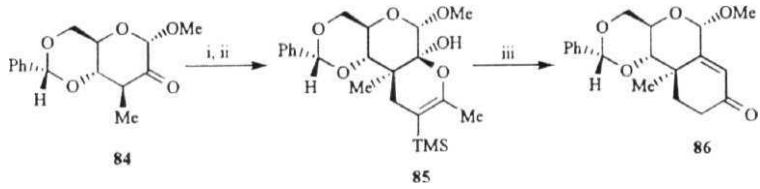


Scheme 18. *Reagents and conditions:* i) CH_3NO_2, NaOH; ii) H$^+$; iii) Ac_2O, H$^+$

scyllo- and *myo*-1-deoxynitroinositols 82 and 83, respectively (Scheme 18).[34] Replacement of nitromethane with ^{14}C-nitromethane in the above cyclization led to 2-^{14}C-myoinositol, which is important for biochemical studies.

ROBINSON ANNULATION:

Recently, Jenkins reported the first Robinson annulation on a carbohydrate derivative. The alcohol 85, derived from the enolate of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-*arabino*-hexopyranosid-2-ulose (84), on treatment with

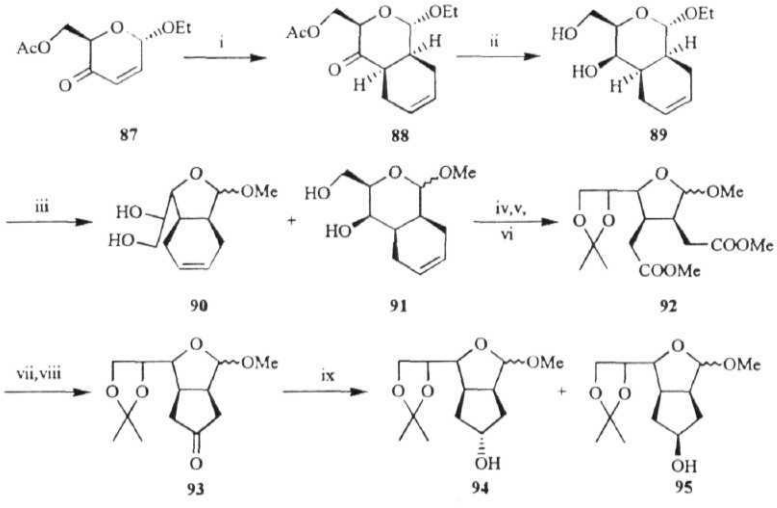


Scheme 19. *Reagents and conditions:* i) lithium teramethylpiperidide, Et_2O, 0°, 1h; ii) 3-(trimethylsilyl)but-3-en-2-one, -78° to rt, 1h; iii) KOH, MeOH. 80°, 6h.

KOH in methanol underwent reverse type of Michael addition to yield the Robinson annulation product 86 (Scheme 19).

DIELS-ALDER REACTION:

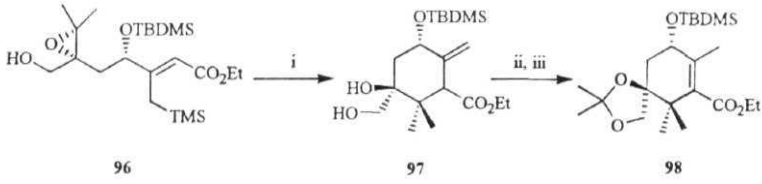
Fraser-Reid has done pioneering work on annulated sugars, utilizing the dienophilic nature of the sugar enone 87, in its Diels-Alder reaction with 1,3-butadiene. The resultant cyclohexenopyranoside 88 was modified suitably to form the fused cyclopentane furanosides 94 and 95 (Scheme 20).[36]



Scheme 20. *Reagents and conditions:* i) 1,3-butadiene, $AlCl_3$, CH_2Cl_2, -78 to 40°; ii) $LiAlH_4$, THF. rt; iii) MeOH, 6% methanolic HC1; iv) 2,2-dimethoxypropane, p-TsOH.H_2O, CH_2Cl_2; v) acetone and phosphate buffer, $NaIO_4$, $KMnO_4$; vi) diazomethane, ether; vii) t-BuOK, benzene; viii) NaCl, DMSO, H_2O, 120-125°; ix) Li AlH_4, dimethoxyethane, -40°.

EPOXY-ALLYLSILANE BASED CYCLIZATIONS:

Lewis acid mediated ring closure of epoxy-allylsilanes was used by Frejd in his enantiospecific synthesis of Taxol A-ring building unit The epoxy-alhlsilane 96. obtained from L-arabinose through a multistep sequence, was subjected to ring closure in the presence of $BF_3{:}Et_2O$ to afford the functionalized cyclohexane 97 which served as a precursor to the Taxol A-nng system 98 (Scheme 21).[37]

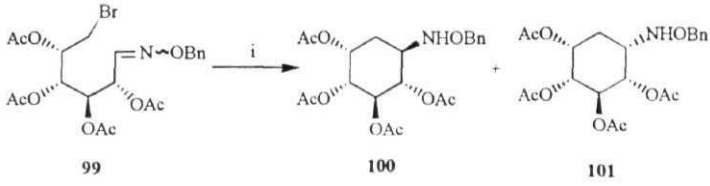


96 97 98

Scheme 21. *Reagents and conditions:* i) $BF_3{:}OEt_2$, CH_2Cl_2, 0°; ii) $BF_3{:}OEt_2$, CH_2Cl_2, acetone; iii) DBU, 185°, 1h.

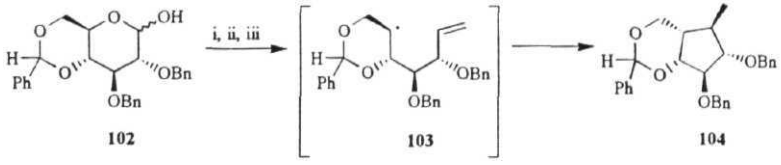
FREE-RADICAL CYCLIZATIONS:

Synthesis of enantiomerically pure polyhydroxylated cyclohexane derivatives based on 6-exo free radical cyclization was developed by Contelles. In this context, a variety of 6-bromo-6-deoxy-hexose derivatives were prepared ha\ing different unsaturated radical trapping groups at C-1. The yields and stereoselectivities of cyclization were found to be dependent upon structural factors and nature of the trapping groups. Thus, for example, the tri-n-butyltin hydride mediated cyclization of the oxime ether 99 afforded a mixture of the aminocyclitols 100 and 101 (Scheme 22).[38]



Scheme 22. *Reagents and conditions:* i) n-Bu_3SnH, AIBN, toluene, reflux.

Hex-5-enyl radical cyclization has been exploited by RajanBabu in his preparation of optically active carbocycles from carbohydrates The radical 103. obtained from the aldopyranose 102 underwent cyclization to give exclusively the chiral cyclopentane 104 (Scheme 23).[39]

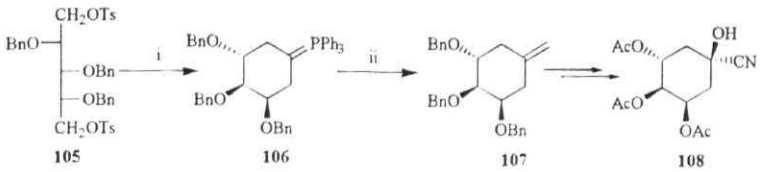


Scheme 23. *Reagents and conditions:* i) $Ph_3P{=}CH_2$; ii) $(imidazolyl)_2C(S)$, $ClCH_2CH_2Cl$, reflux; in) Bu_3SnH, AIBN, toluene, reflux.

REACTIONS OF PHOSPHORUS-STABILIZED SPECIES:

Bestmann, in his total synthesis of quinic acid and shikimic acid from D-arabinose has utilized the fact that short alkanes having halogen or **sulfonyloxy** substituents at the a- and co-positions react with methylenetriphenylphosphorane to give carbocyclic products that incorporate a carbon atom derived from the reagent. The D-arabinose derivative **105** was converted to the cyclohexylidene ylide 106 which on reaction with formaldehyde gave **107**. A sequence of reactions on **107** led

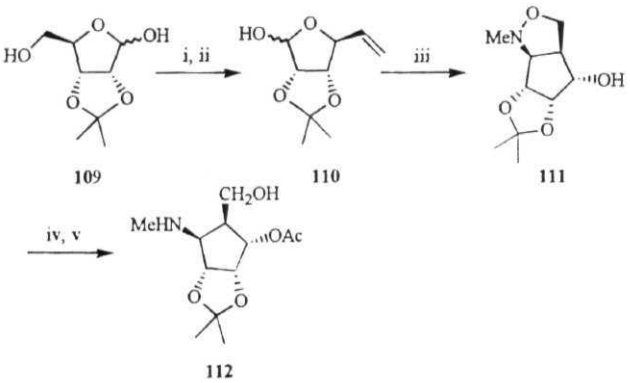
to a common intermediate **108** from which both quinic and shikimic acids were synthesized (Scheme 24).[40]



Scheme 24. *Reagents and conditions:* i) $Ph_3P{=}CH_2$; ii) CH_2O.

INTRAMOLECULAR NITRONE CYCLOADDITION (1MNC):

The reaction of carbohydrate based unsaturated lactols with N-methyl-hydroxylamine results in intramolecular nitrone cycloaddition to give carbocycles.

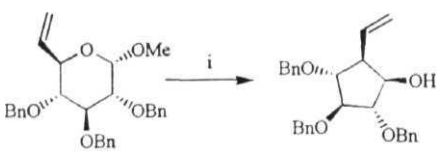


Scheme 25. *Reagents and conditions:* i) vinylmagnesium bromide, THF; ii) $NaIO_4$, aq MeOH; iii) Me(H)NOH.HCl, $NaHCO_3$, aq EtOH, reflux; iv) Ac_2O, Py; v) $Pd(OH)_2/C$, H_2, EtOH. CH_3COOH.

The D-ribose derived acetonide 109 on Gngnard addition followed by oxidative glycol cleavage afforded 110. which on treatment with N-methylhydroxylamine underwent IMNC reaction to give the isoxazolidine **111**. Acetylation and hydrogenation of **111** provided the differentially protected cyclopentane 112 (Scheme 25). A similar strategy has been used for synthesizing functionalized cyclohexanes from D-mannose.[41]

RING CONTRACTION:

Recently, Taguchi has reported the synthesis of functionalized, enantiomerically pure carbocycles through ring contraction of sugars. Thus, the olefinic sugar 113 on reaction with dicyclopentadienyldi-n-butylzirconium and boron trifluoride etherate gave the densely functionalized cyclopentane **114**, presumably through the intermediacy of a zircanocycle (Scheme 26).[42]



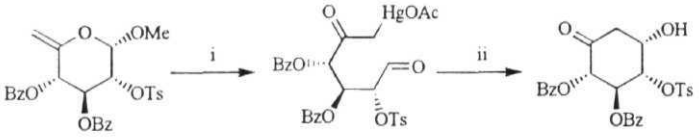
113 114

Scheme 26. *Reagents and conditions:* i) $Cp_2Zr(n\text{-}Bu)_2$, $BF_3{:}OEt_2$, THF

This strategy is also applicable to the synthesis of highly functionalized cyclobutane derivatives. All the ring contracted products were found to contain the vinyl and hydroxyl groups in a "cis" relationship to one another.

CVCLIZATIONS INVOLVING ORGANOMETALLIC INTERMEDIATES:

An excellent strategy for the synthesis of 2-deoxyinososes from carbohydrates *via* the intermediacy of mercury containing compounds has been published by Ferrier. Initially. mercury(II) chloride was employed for this purpose, but the mercury containing intermediate was observed to give undesirable side products owing to the acidic nature of mercury(II) chloride Finally, in a typical example. mercuric acetate was found to be efficient in converting the 6-deoxy-hex-5-enopyranose derivative 115 to the 2-deoxyinososc **117** *via* the organomercury intermediate **116** (Scheme 27) This methodology has been successfully applied to numerous unsaturated sugars[43]



115 116 117

Scheme 27. *Reagents and conditions:* i) $Hg(OAc)_2$, aq acetone, acetic acid, reflux, ii) H_2S, benzene, 10 min

FROM SUGARS TO PSEUDO-SUGARS:

A family of compounds closely related to sugars are pseudo-sugars, in which the ring oxygen atom of a monosaccharide is replaced by a methylene group.[44] Both 5- and 6-membered pseudo-sugars are known, but the cyclopentane derivatives are relatively uncommon. Pseudo-sugars do not exhibit any characteristic reactions of a true sugar, such as mutarotation. formation of osazones or hydrazones, due to the lack of a free anomeric hydroxyl functionality. Owing to their structural resemblance to true sugars. pseudo-sugars can be expected to replace sugars in

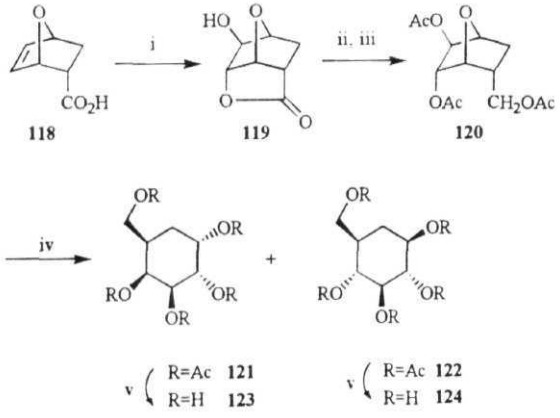
biological systems. The above idea was proved not to be far-fetched, with the discovery that pseudo-α-DL-glucopyranose inhibited both D-glucose stimulated release of insulin and islet glucokinase activity.[43] Pseudo-D-glucose, pseudo-D-galactose and pseudo-D-fructose have been suggested as replacements for their sugar counterparts as non-nutritive sweeteners.[46] Pseudo-sugars and some related carbocyclic compounds are components of some antibiotics (validamycins) and enzyme inhibitors (adiposins)[4] and pseudo-α-D-galactopyranose was found in the fermentation broth of sp. MA-4145, as an antibiotic.[48] Amino pseudo-sugars and complex substances containing them have chemotherapeuuc potential as glycosidase inhibitors. For example, the antibiotic validamycin, which is a potent α-glucosidase inhibitor, contains the amino pseudo-sugar validamine. N-[2-Hydroxy-1 - hydroxymethyl]ethyl validamine (AO-128), is under clinical trials for the treatment of diabetes.[49] Based on the assumption made regarding the mechanism of inhibition of sucrase by acarbose, it was expected that pseudo-oligosaccharides bonded by an imino linkage could be strong inhibitors of the hydrolase of the corresponding normal oligosaccharides.[50] Carba-trehalosamine was found to be as biologically active as normal trehalosamines, suggesting that replacement of a true sugar with a pseudo-sugar in biologically active oligosaccharides may not result in complete loss of activity.[51]

Synthesis of racemic pseudo-sugars was initiated by McCasland and co-workers through their syntheses of pseudo-α-DL-talopyranose, pseudo-P-DL-glucopyranose and pseudo-α-DL-galactopyranose.[52] The Diels-Alder adduct of furan and acrylic acid, *endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid was exploited as the precursor for the synthesis of various racemic pseudo-sugars. Decreased biological activity of racemic pseudo-sugars, when compared to enantiomerically pure pseudo-sugars necessitated the synthesis of pseudo-sugars in

their optically pure forms Resolution of the Diels-Alder adduct of furan and acrylic acid opened the avenue for the synthesis of enantiopure pseudo-sugars

Out of the 32 possible pseudo-sugars, fifteen have been synthesized from various chiral sources, such as antipodes of the Diels-Alder adduct of furan and acrylic acid, quebrachitol and true sugars. A brief summary of the different approaches employed towards the synthesis of pseudo-sugars is presented in the following pages

Four carbasugars, pseudo-β-D-glucopyranose, pseudo-α-D-glucopyranose, pseudo-α-L-glucopyranose and pseudo-α-D-galactopyranose have been synthesized

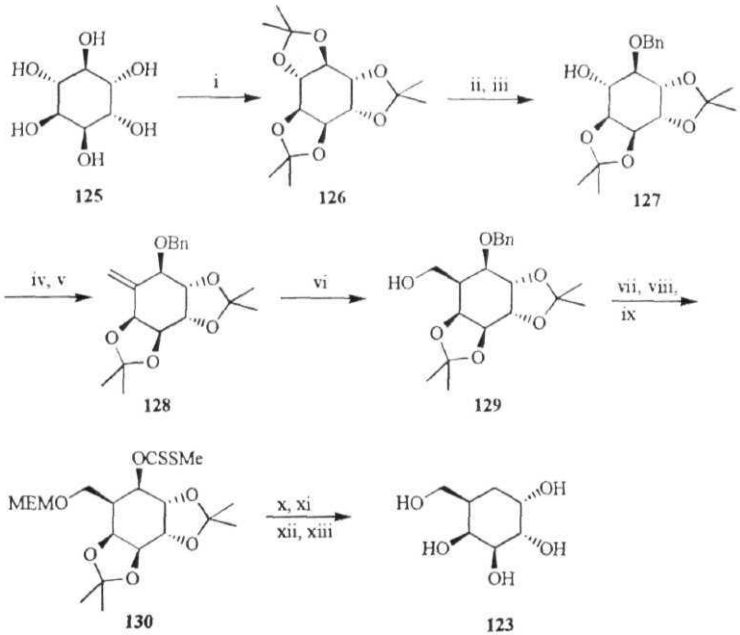


Scheme 28. *Reagents and conditions:* i) 90% formic acid, 35% H_2O_2; ii) $LiAlH_4$, THF, iii) Ac_2O, Py; iv) AcOH, Ac_2O, H_2SO_4; v) NaOMe, MeOH.

from the antipodes of the Diels-Alder adduct of furan and acrylic acid. In 1985, Ogawa and co-workers reported a synthetic approach for the preparation of pseudo-β-D-glucopyranose and pseudo-α-D-galactopyranose from (-)-*endo*-7-oxabicyclo-

[2 2 l]hept-5-ene-2-carboxylic acid **(118)**, obtained from its racemate by resolution with chiral α-methylbenzylamine. Treatment of **118** with formic acid and hydrogen peroxide gave the hydroxylactone **119** which on reduction with $LiAlH_4$ and acetylation gave the triacetate **120.** The crude triacetate on acetolysis afforded a mixture of fully acetylated pseudo-α-D-galactopyranose **121** and pseudo-p-D-glucopyranose **122,** which, without purification, on deacetylation yielded the corresponding pseudo-sugars **123** and **124** (Scheme 28).[53]

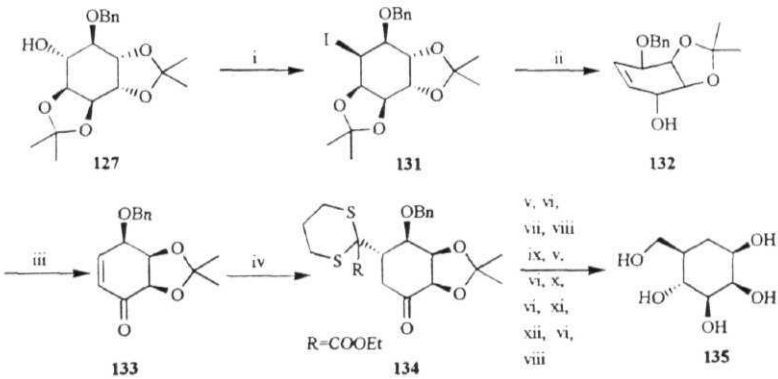
An elegant synthesis of pseudo-a-D-galactopyranose and pseudo-P-D-mannopyranose has been executed by Paulsen and co-workers from quebrachitol. L-Chiro-inositol (125), obtained from quebrachitol, on isopropylidenation with 2,2-dimethoxypropane gave **126**. Selective removal of the 3,4-*O*-protecting group in **126** and preferential benzylation provided **127.** Oxidation of **127** with DMSO-oxalyl chloride, followed by Wittig reaction with methylenetriphenylphosphorane furnished **128,** which on hydroboration-oxidation, gave **129.** Protection of the free 7-OH group, debenzylation and S-methyldithionocarbonate formation yielded **130.** The thionocarbonate **130** on deoxygenation with tri-n-butyltin hydride followed by a series of routine transformations gave pseudo-a-D-galactopyranose (123) (Scheme 29).



Scheme 29. *Reagents and conditions:* i) 2,2-dimethoxypropane, DMF. 60°; ii) 95% acetic acid; iii) BnBr, tetraethylammonium iodide. 20% NaOH. CH_2Cl_2; iv) DMSO, oxalyl chloride, CH_2Cl_2; v) methyltriphenyl phosphonium bromide, n-BuLi, THF; vi) BH_3:THF, THF. -50°, then H_2O_2, NaOH; vii) (2-methoxyethoxy)methyl chloride, diisopropylethylamine, CH_2Cl_2; viii) 10% Pd/C, H_2, MeOH; ix) Imidazole. NaH. CS_2. THF. MeI; x) Bu_3SnH, toluene; xi) 1M HCl, MeOH; xii) Ac_2O, Py; xiii) NaOMe, MeOH

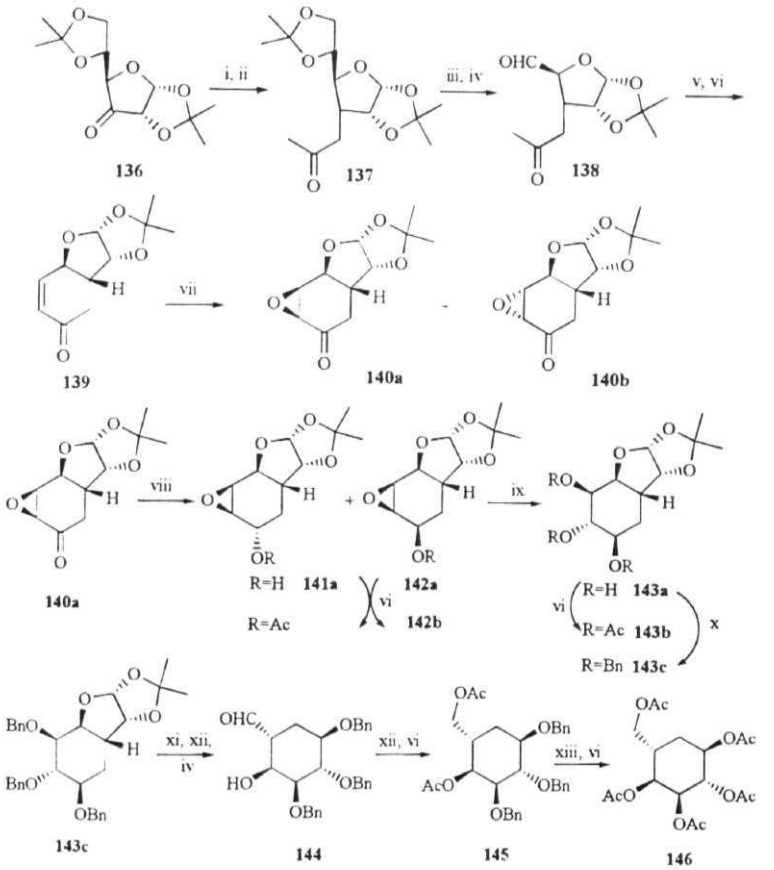
In a synthesis of pseudo-β-D-mannopyranose (135). 127 was halogenated with triphenylphosphine, iodine and imidazole to afford **131** Reduction of 131 using $LiAlH_4$ gave two endocyclic alkenes 132 and di-*O*-isopropylidenecyclohexenetetrol. The enone 133 obtained by oxidation of 132 was subjected to 1,4-addition of ethyl 2-

lithio-1,3-dithiane-2-carboxylate to furnish **134.** $LiAlH_4$ reduction of **134** and subsequent functional group manipulation yielded pseudo-p-D-mannopyranose **(135)** (Scheme 30).[54]



Scheme 30. *Reagents and conditions:* i) Imidazole, triphenylphosphine, iodine, toluene, ii) $LiAlH_4$, ether, **iii)** DMSO, oxalyl chloride, diisopropylethylamine, CH_2Cl_2; iv) ethyl 1,3-dithiane-2-carboxylate, LDA, THF; v) $LiAlH_4$, THF; vi) Ac_2O, Py; vii) HgO, $HgCl_2$, $NaBH_4$, CH_3CN; **viii)** NaOMe, MeOH; ix) $NaIO_4$, H_2O; x) $NaBH_4$; xi) acetic acid, triflouroacetic acid; xii) 10% Pd/C, H_2, MeOH.

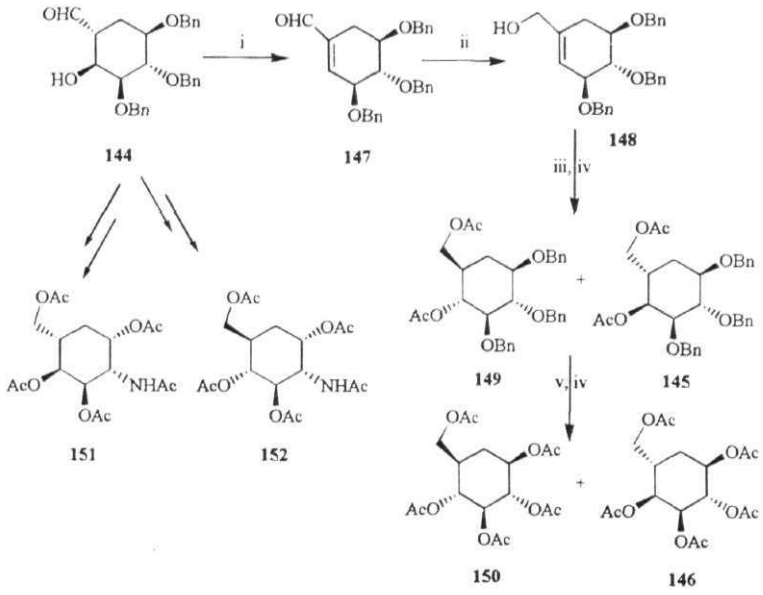
Suami and Tadano have published syntheses of pentaacetates of pseudo-α-L-altropyranose and pseudo-β-D-glucopyranose from D-glucose *via* 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose **(136)** Wittig olefination of 136 with acetylmethylenetriphenylphosphorane followed by hydrogenation of the resulting alkene gave 137, which on selective hydrolysis of the 5,6-*O*-isopropylidene group and oxidation with periodic acid afforded the aldehyde 138. After some experimentation, 138 was cyclized with DBU and the resulting aldol was dehydrated



Scheme 31. *Reagents and conditions;* i) $Ph_3P{=}CHCOCH_3$, benzene; ii) Raney Ni; iii) 60% aq AcOH; iv) aq $NaIO_4$; v) DBU, benzene, reflux; vi) Ac_2O, Py; vii)35% H_2O_2, alkaline MeOH; viii) $NaBH_4$, ethanol; ix) aq. 2-methoxyethanol, NaOAc, reflux; x) NaH. BnBr, DMF; xi) 80% aq. AcOH, dioxane, reflux; xii) $NaBH_4$, MeOH, 0°; xiii) Na. liq NH_3

with acetic anhydride and pyndine to the enone **139**. Epoxidation of **139** proceeded stereoselectively to yield the p-epoxy ketone **140a** as the major product along with traces of the α-epoxy ketone **140b** $LiAlH_4$ reduction followed by acetylation converted the β-epoxy ketone 140a to a mixture of epimers **141b** and **142b** in the ratio 5:1. Epoxide ring opening of the alcohols **141a** and **142a** in aq 2-methoxyethanol in the presence of sodium acetate provided the triol 143a, as the only product. The tnbenzyl derivative **143c** on a series of functional group adjustments gave the aldehyde **144,** which on successive sodium borohydnde reduction and acetylation provided the fully protected pseudo-α-L-altropyranose derivative **145. Debenzylation** of **145** followed by acetylation furnished pseudo-a-L-altropyranose pentaacetate **146** (Scheme 31).

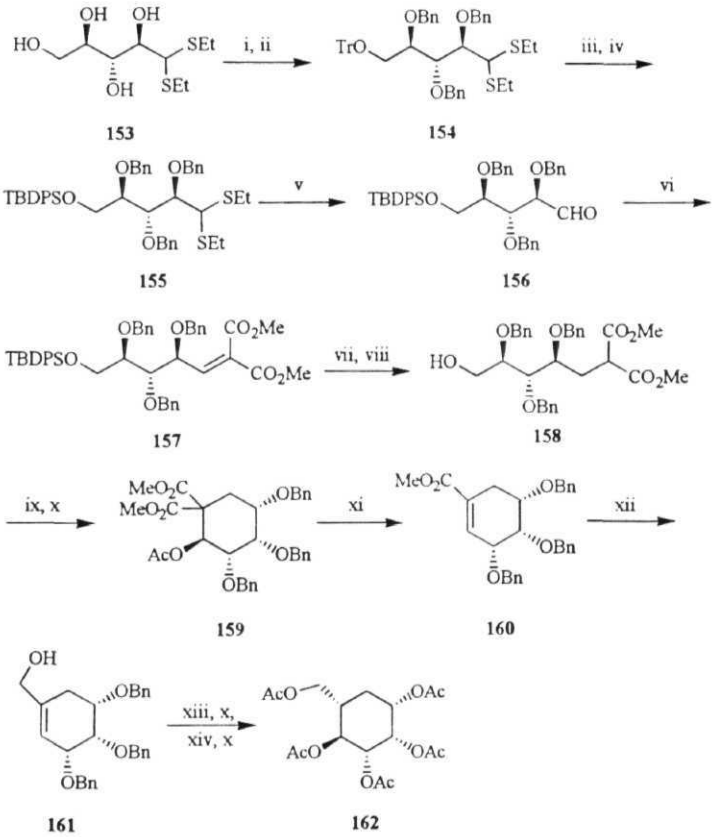
Synthesis of pseudo-β-D-glucopyranosepentaacetate **150** was accomplished as follows. Treatment of the aldehyde **144** with methanesulfonyl chloride in pyndine afforded the a,p-unsaturated aldehyde **147,** which on $NaBH_4$ reduction gave **148. Hydroboration-oxidation** of **148** occurred predominantly from the a-face and subsequent acetylation furnished the pseudo-β-D-glucopyranose derivative **149** accompanied by **145.** Conversion of **149** to the pentaacetate of pseudo-β-D-glucopyranose **150** was accomplished by successive hydrogenolysis and acetylation (Scheme 32). The chiral synthon **144** was modified further to synthesize pseudo-2-amino-2-deoxy-β-L-altropyranose **(151)** and pseudo-2-amino-2-deoxy-α-D-glucopyranose **(152)**.[55]



Scheme 32. *Reagents and conditions:* i) MsCl, Py; ii) $NaBH_4$; iii) BH_3:THF, 0°, 35% H_2O_2 in alkaline solution; iv) Ac_2O, Py; v) 10% Pd/C, H_2, MeOH.

Suami and Tadano employed the Knoevenagel reaction as a key step in the syntheses of the pentaacetates of pseudo-P-L-mannopyranose, pseudo-p-L-glucopyranose, pseudo-α-D-altropyranose and pseudo-α-L-mannopyranose from different sugars and these are presented in the following paragraphs.[56]

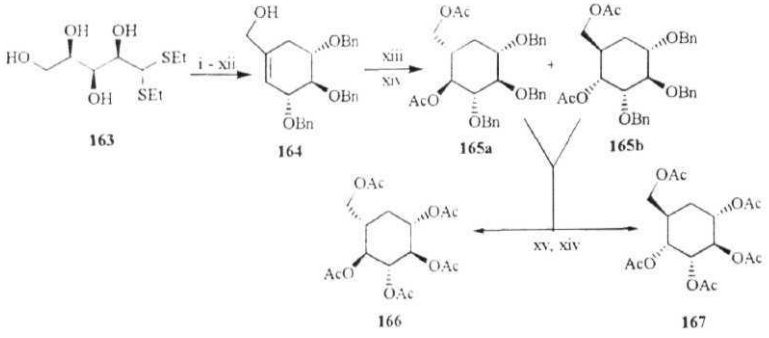
The known D-ribose diethyldithioacetal **153** on successive tritylation and benzylation gave 154. Deprotection of the trityl group with *p*-TsOH and subsequent silylation with t-butyldiphenylchlorosilane afforded **155**.



Scheme 33. *Reagents and conditions:* i) TrCl, Py, DMAP; ii) NaH, BnBr; iii) *p*-TsOH H_2O, MeOH, ethyl acetate, iv) TBDPSC1. imidazole, DMF; v) $HgCl_2$, $CaCO_3$, CH_3CN, H_2O; vi) dimethyl malonate, Py, Et_3N, Ac_2O; vii) TBAF; viii) Raney Ni; ix) PCC; x) Ac_2O, Py; xi) DMSO, H_2O, NaCl, 120-170°; xii) $LiAlH_4$, THF; xiii) BH_3:THF, 35% aq. H_2O_2 in 3M NaOH; xiv) Pd/C, acetic acid, H_2, MeOH.

The parent aldehyde group of **156** was regenerated by dethioacetahzation of **155** with mercuric chloride in aqueous acetonitrile Knoevenagel condensation of 156 with dimethyl malonatc gave, after desilylation and hydrogenation of the double bond . the intermediate **158** The primary alcohol **158** was oxidized **with** PCC and aldol cyclization occurred on treatment of the resultant aldehyde **with** acetic anhydride and pyridine to give the **cyclohexanc 159** as a single diastereomer Decarboxylation of **159 with** concomitant β-elimination of the acetate gave **160.** which was reduced to the alcohol **161** with $LiAlH_4$ Hydroboration-oxidation of the alkene **161.** followed by a sequence of standard reactions afforded pseudo-p-L-mannopyranose pentaacetate **162** (Scheme **33).**

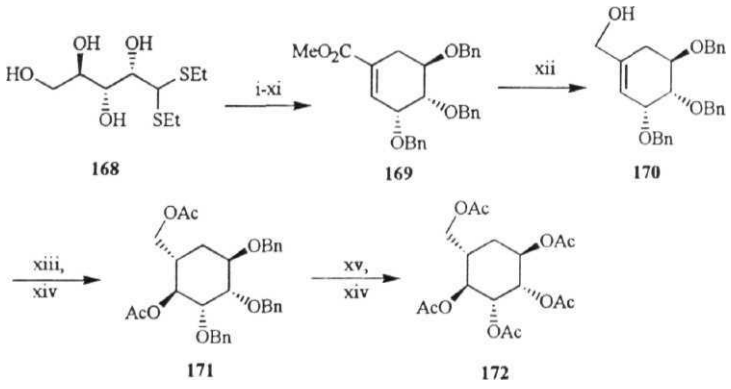
Pentaacetates of pseudo-β-L-glucopyranose **166** and pseudo-α-D-altropyranose **167 have** been synthesized from D-xylose diethyldithioacetal, obtained from D-xylose



Scheme 34. *Reagents and conditions* **i-xii)** as **in** Scheme 33; xiii) BH_3:THF, 35% aq H_2O_2 **in** 3M NaOH; xiv) Ac_2O, Py; xv) Pd/C, acetic acid, H_2, MeOH

D-xylose diethyl dithioacetal **163** was converted to **164** following the same sequence of reactions as for the conversion of **153** to **161.** A mixture of compounds **165a** and **165b** was obtained from **164** by hydroboration and oxidative workup followed by acetylation. On subjecting the mixture of acetates **165a** and 165b to debenzylation and acetylation, the pentaacetates of pseudo-β-L-glucopyranose **166** and pseudo-α-D-altropyranose **167** were obtained (Scheme 34).

Transformation of D-arabinose diethyldithioacetal **168** to **169** was achieved in 11 steps, following the same reaction sequence as described earlier. Reduction of **169** with DIBAL-H gave **170,** which on stereospecific hydroboration-oxidation and subsequent acetylation provided **171** as the sole product. Functional group manipulations on **171** gave pseudo-α-L-mannopyranose pentaacetate **172** (Scheme 35).

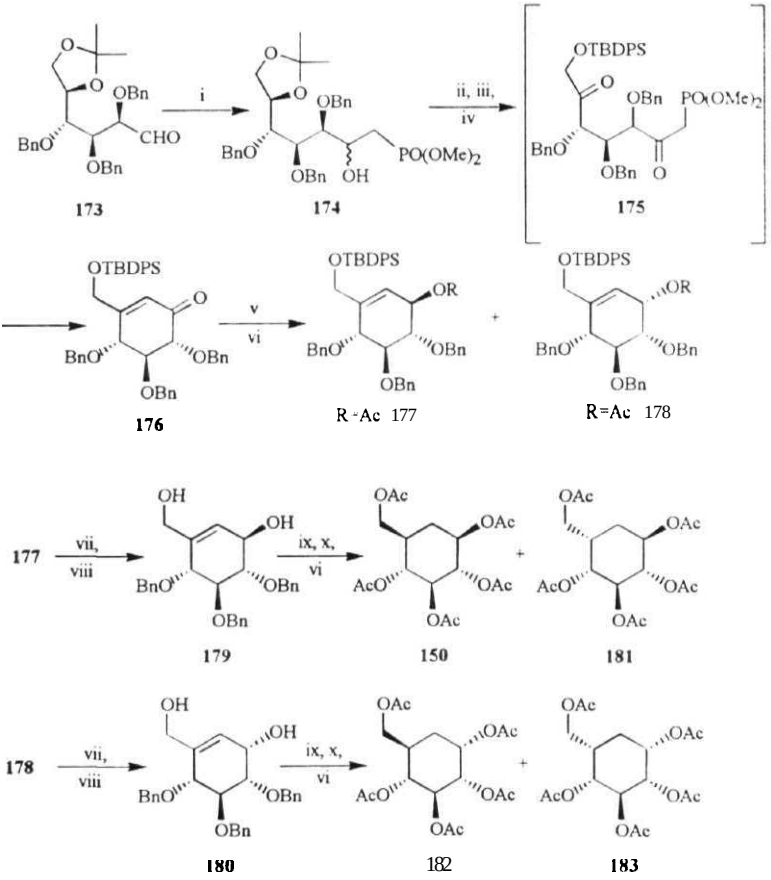


Scheme 35. *Reagents and conditions:* **i-xi)** as **in** Scheme 33; **xii) DIBAL-H,** CH_2Cl_2; **xiii)** BH_3:THF, **35% aq.** H_2O_2 **in 3M NaOH; xiv)** Ac_2O, **Py; xv)** Pd/C, **acetic acid,** H_2, MeOH.

Application of this methodology to D-erythrose resulted in the formation of pseudo-β-L-arabinofuranose

As a part of his continuous synthetic efforts towards pseudo-sugars. Paulsen has published the synthesis of pseudo-β-D-glucopyranose. pseudo-α-D-glucopyranose. pseudo-α-L-idopyranose and pseudo-β-L-idopyranose.

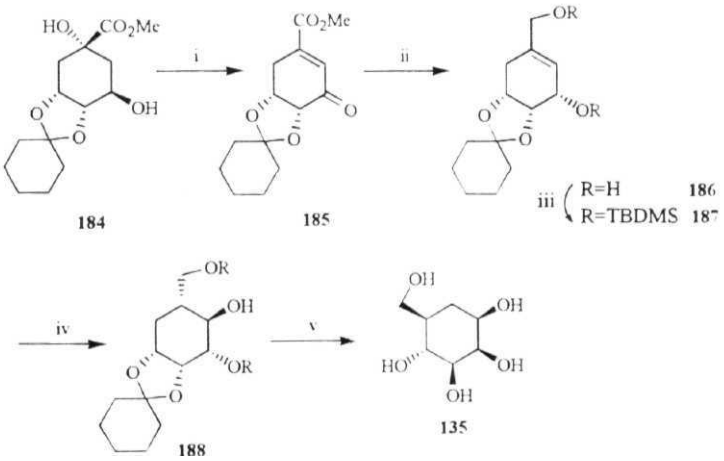
After suitable protection of D-glucose diethyldithioacetal. the thioacetal group was converted to aldehyde **173** in the presence of $HgCl_2$ and HgO Reaction of **173** with the lithium salt of dimethyl methylphosphonate **gave** a diastereomeric mixture of the adduct **174** After acid **hydrolysis** of the isopropylidene group. the primary hydroxyl group was **selectively** protected as its silyl ether and the silyl ether was oxidized with DMSO-$(COCl)_2$ to give **175** which spontaneously cyclized in the presence of diisopropylethylamine to **yield** the enone **176** Sodium borohydride reduction of **176** and subsequent acetylation provided **177** and **178** in the ratio **1.6:1.** Desilylation of the silyl ether and deacetylation of 177 and **178** with NaOMe afforded **179** and **180.** respectively On hydrogenation with Raney nickel and debenzylation. **179** yielded a mixture of products. pseudo-α-L-idopyranose and pseudo-β-D-glucopyranose which were converted to their pentaacetates **181** and **150.** respectively A similar reaction sequence on **180** gave pseudo-α-D-glucopyranose and pseudo-β-L-idopyranose pentaacetates **182** and **183** (Scheme 36) [57]



Scheme **36.** *Reagents and conditions:* i) $LiCH_2PO(OMe)_2$, THF; ii) 95% AcOH, 60°, iii) Imidazole, TBDPSC1, DMF; iv) DMSO, $(COCl)_2$, diisopropylethylarnine, CH_2Cl_2; v) $NaBH_4$, EtOH; vi) Ac_2O, Py; vii) TBAF. THF, viii) NaOMe, MeOH; ix) Raney Ni, dioxanc, 4h, rt, x) 10% Pd/C, H_2.

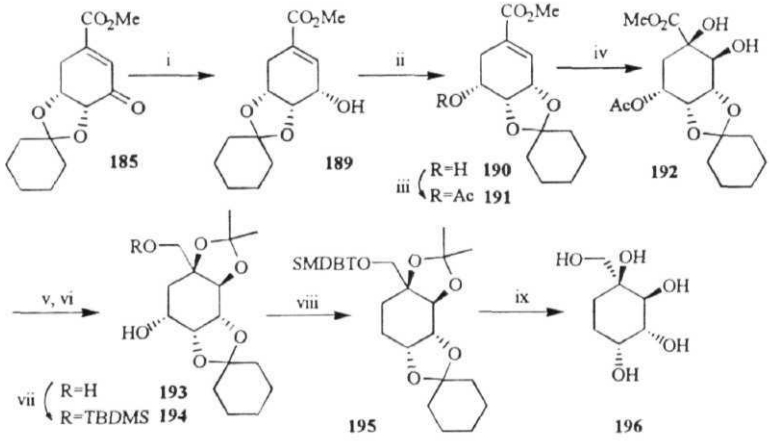
An elegant **synthesis** of pseudo-p-D-mannopyranose and pseudo-P-D-fructopyranose from quinic acid has been developed by Shing

The known hydroxy-ester **184. available** from quinic acid in 2 steps. **underwent** oxidation and concomitant β-elimination on reaction with PCC **and** pyridine to give the enone **185.** The enone **185** was converted to the diol **186** by reduction with DIBAL-H and the diol unit in **186** was protected as the disilyl ether **187** Hydroboration of the alkene **187** from the less hindered P-face and subsequent oxidation resulted **in** the exclusive formation of **188.** which on protecting group cleavage gave pseudo-P-D-mannopyranose **(135)** (Scheme 37).

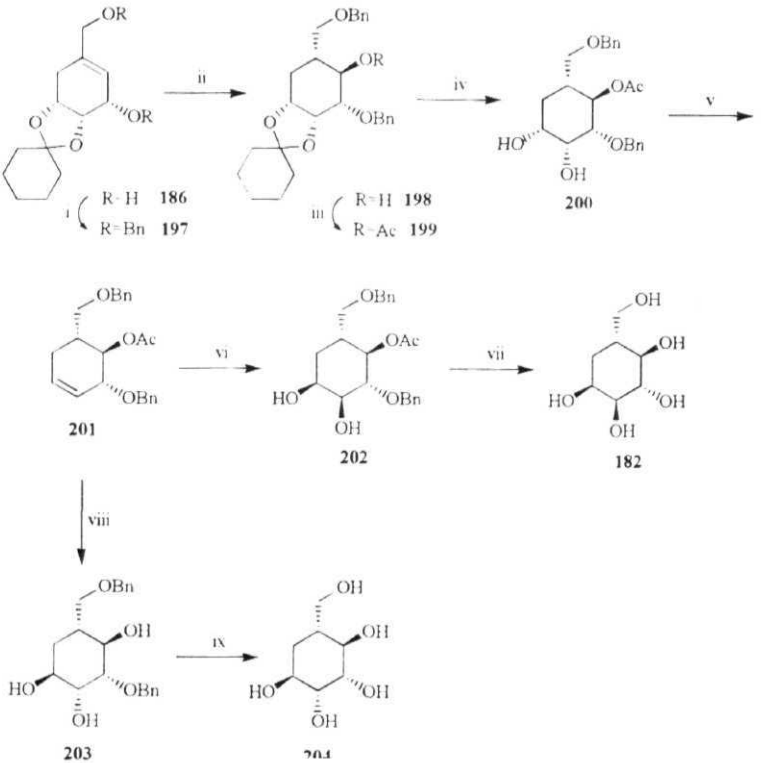


Scheme 37. *Reagents and conditions* i) PCC. 3Å molecular sieves. Py. CH_2Cl_2; ii) DIBAL-H. toluene. 0. **iii)** TBDMSC1. imidazole. DMAP. CH_2Cl_2; **iv)** 9-BBN. THF. 3M NaOH. H_2O_2; v) 50% aq. TFA. rt

For the synthesis of pseudo-P-D-fructopyranose, **185** was chosen as starting material. $NaBH_4$ reduction of **185** occurred from the less hindered P-face to give **189.** Equilibration of **189** under thermodynamic conditions afforded **190,** which on acetylation gave **191** Stereocontrolled *cis*-hydroxylation of the alkene **191** occurred from the less hindered P-face to afford the diol **192.** Acetonation of **192** with 2-methoxypropene followed by DIBAL-H reduction yielded the diol **193** Selective protection of the primary hydroxyl group in **193** as the silyl ether **194** and subsequent deoxygenation afforded **195,** which after a series of standard reactions gave pseudo-p-D-fructopyranose **(196)** (Scheme 38).[58]



Scheme 38. *Reagents and conditions:* i) $NaBH_4$; ii) acetone, *p*-TsOH; iii) Ac_2O, Py, DMAP, CH_2Cl_2; iv) OsO_4, trimethylamine-N-oxide, Py, H_2O, t-BuOH; v) 2-methoxypropene, rac-camphor-10-sulphonic acid, CH_2Cl_2; vi) DIBAL-H, THF, 0°; vii) TBDMSCI, imidazole, DMAP, CH_2Cl_2; viii) phenyl chlorothioformate, Py, DMAP, CH_2Cl_2; then n-Bu_3SnH, AIBN, toluene, reflux; ix) 50% aq. TFA, rt.



Scheme 39. *Reagents and conditions* i) NaH. BnBr. n-Bu_4NI. THF; ii) 9-BBN. THF. rt. then H_2O_2 (94%). NaOH. iii) Ac_2O. Py. DMAP. CH_2Cl_2. iv) CF_3CO_2H. CH_2Cl_2. V) 1.1 -thiocarbonyldiimidazole. toluene. reflux. then $P(OMe)_3$. reflux; vi) OsO_4. trimethylamine-N-oxide. Py. H_2O. t-BuOH; vii) NaOMe. MeOH. then Rh/C. H_2. EtOH. viii) HCO_2H. H_2O_2. reflux. then NaOH. THF. reflux. ix) $Pd(OH)_2$. H_2. EtOH

can be readily obtained from quinic acid was used as a common starting material for both the pseudo-sugars. The hydroxyl groups in **186** were protected as their benzyl ethers to give **197**, which on stereocontrolled hydroboration from the p-face afforded the alcohol **198.** After protecting the alcohol **198** as its acetate 199, the cyclohexylidene group was removed under acidic conditions, to give the diol 200. The diol unit in 200 was deoxygenated under Corey-Winter conditions to furnish the alkene **201** which on osmium tetroxide hydroxylation gave the cis diol **202** Removal of the protecting groups in **202** afforded pseudo-α-D-glucopyranose (**182**)

trans-Hydroxy lation of the alkene **201 with** formic acid and hydrogen peroxide, followed by debenzy lation of the resultant triol **203** yielded pseudo-α-D-mannopyranose **(204)** (Scheme 39).[59]

As detailed in the preceding pages, the conversion of sugars to carbocycles is a topic of current interest, as is the synthesis of pseudo-sugars. This thesis deals with the application of the oxy-Cope rearrangement as a method of ring expansion of sugars to medium nng ethers and application of the Claisen rearrangement for the conversion of sugar **derivatives** to carbocycles and thence to pseudo-sugars. The results obtained in this investigation are presented in the next chapter

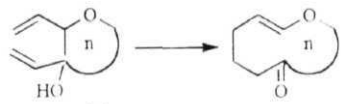
RESULTS AND DISCUSSION

RESULTS AND DISCUSSION

This chapter entitled "Results and Discussion" is divided into two parts Part I describes the work dealing with the conversion of sugars to medium ring ethers In part II. the synthesis of chiral carbocycles from carbohydrates and their further conversion to pseudo-sugars. is elaborated

PART I: SYNTHESIS OF MEDIUM RING ETHERS:

Synthesis of medium ring ethers is of topical interest due to their presence in a variety of marine natural products Typical examples are brevetoxin. laurencia metabolites. obtusenyne and diplodialides Though synthesis of medium ring compounds appears quite simple at the periphery. their synthesis is often hampered by entropy factors since formation of medium ring compounds from acyclic precursors involves loss of entropy. They also suffer from unfavorable transannular interactions. As mentioned earlier in the introduction, one of the general methods for their preparation is by forming a new bond and breaking an old bond between two side chains placed appropriately on the same ring Sigmatropic reactions fall under this category of ring expansion reactions Out of the several sigmatropic reactions available. the Cope rearrangement is one in which the parent nng of size n e.g **205** can be converted to a ring size of (n+4) e.g **206** (Scheme 40).



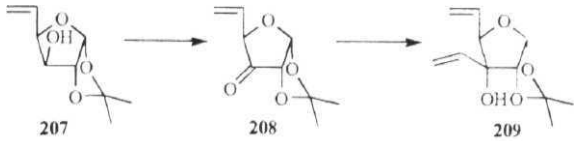
n=5,6
205 **206**

Scheme 40

The oxy-Cope rearrangement, a modified version of the Cope rearrangement, is superior to the Cope, considering the fact that the product of Cope rearrangement is in equilibrium with the starting material, whereas in the case of the oxy-Cope rearrangement the starting material is irreversibly converted into the product. The oxy-Cope rearrangement is one of the most widely used sigmatropic reactions in the synthesis of natural and unnatural compounds containing medium sized rings As a result, we envisaged using the oxy-Cope rearrangement as a suitable synthetic tool for the desired ring expansion. As only a few general methods are available for the construction of medium ring ethers in chiral form, we thought that carbohydrates would be appropriate synthons, as the inherent chirality of carbohydrates could be transferred to the products. The availability of carbohydrates in both furanose and pyranose forms make them attractive substrates, as the application of oxy-Cope rearrangement to them can provide both 9- and 10-membered rings.

PART I: A) SYNTHESIS OF CHIRAL HEXAHYDROOXONINONES FROM FURANOSES:

A careful survey of the literature for various olefinic **derivatives** of **D**-glucose in the furanose form revealed 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-eno-furanose **(207)** to be convenient starting material.[60] It was prepared from D-glucose according to the literature procedure As the substrate for the oxy-Cope rearrangement would require a **vinyl** group at C-3, we planned to oxidize the C-3 hydroxyl group and then add vinylmagnesium bromide to the resulting ulose **208,** thus generating the desired oxy-Cope system **209** (Scheme 41).



Scheme 41

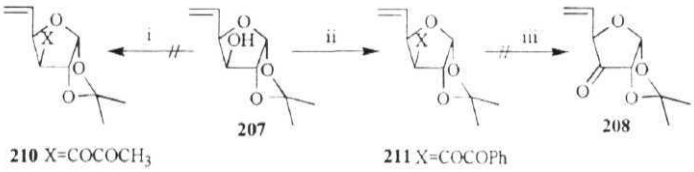
Surprisingly, standard procedures like Collins reagent/acetic anhydride: **pyridinium** chlorochromate/sodium acetate and **silver** carbonate on celite oxidations did not work on 207 to give the ulose **208** In all three cases, the starting material was recovered unchanged (Table 1) Earlier work in our laboratory had already shown that the reaction was unsuccessful with Swem s reagent as well.[61]

Table 1 : Various reaction conditions attempted for the oxidation of 207

Entry	Reaction Conditions	**Result**
1	PCC, NaOAc, CH_2Cl_2, rt, 3h	starting material recovered
2	Ag_2CO_3, celite, benzene, reflux, 14h	-do-
3	CrO_3, 2Py, Ac_2O, rt, 25 min	-do-

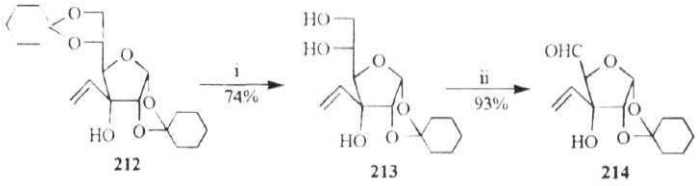
As the ulose 208 could not be obtained by direct oxidation, we decided to prepare the pyruvate ester of the C-3 hydroxyl group and then oxidize the resultant ester under photolytic conditions. To begin **with, 207** was treated with pyruvic acid and DCC in dichloromethane at room temperature However, after the usual workup, no tractable material was obtained Furanose 207 was converted to the phenylglyoxylate ester **211** on treatment with phenylglyoxyl chloride, potassium carbonate and 4-dimethylaminopyridine Absence of hydroxyl band and appearance of two carbonyl bands at 1740 and 1680 cm^{-1} in the 1R spectrum indicated formation of the phenylglyoxylate **211** The ^1H NMR spectrum showed multiplets

corresponding to aromatic protons at **7.49** and 7.92 ppm along with other signals Photolysis of **211** in benzene for 2h using a **450-W** medium-pressure Hanovia mercury lamp could not bring about the desired oxidation.[2] Only the starting material was recovered (Scheme 42).



Scheme 42. *Reagents and conditions:* i) $CH_3COCOOH$, DCC, DMAP, CH_2Cl_2, rt, 12h; ii) PhCOCOCl, DMAP, rt, 5h; iii) benzene, hv, 3h.

At this stage, faced with the difficulty of obtaining the ulose **208,** we reoriented our synthetic strategy and planned to introduce the C-3 vinyl group prior to formation of the C5-C6 double bond. Once again, literature provided a convenient precursor in the form of 1,2:5,6-di-*O*-cyclohexylidene-3-*C*-vinyl-α-D-allofuranose **(212)**, which was prepared from D-glucose by Tatchell. [3] As a first move, the 5,6-*O*-cyclohexylidene group in **212** was removed using acetic acid at 80° to give the triol **213.** There were no apparent changes in the IR spectrum of **213** when compared to that of **212,** but the ^1H NMR spectrum showed only 10 **cyclohexyl** protons as a multiplet centered around 1.62 ppm. The C NMR spectrum of **213** showed a thirteen line pattern supporting the structure of **213** The triol **213** underwent oxidative cleavage smoothly with sodium periodate to afford the aldehyde **214** in quantitative yield (Scheme 43).



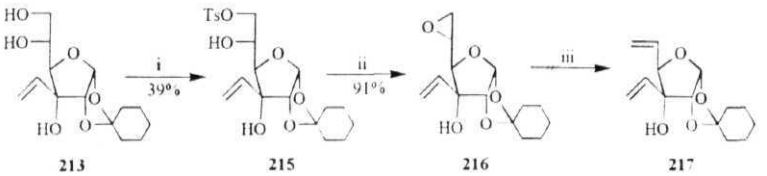
Scheme 43. *Reagents and conditions:* i) 80% AcOH. reflux. 2h; ii) $NaIO_4$, H-O, rt. 1h

Presence of the aldehyde absorption at 1720 cm ' in the IR spectrum, appearance of a singlet corresponding to the **aldehyde** proton at 9.56 ppm in the 'H **NMR** spectrum provided strong **evidence** for the formation of **214** Methylenation of the crude aldehyde **214** with methyltriphenylphosphonium iodide using n-butyllithium as a base resulted in a complex mixture Switching over to phase transfer conditions. **214** was treated **with** methyltriphenylphosphonium iodide and potassium carbonate in dioxane-water under reflux conditions. to give once more a complex mixture as indicated by tlc. No attempts were made to purify the mixture. Stirring **214** with zinc. diiodomethane and titanium(IV) tetraisopropoxide in THF[64] at room temperature for 36h led to recovery of starting material (Table 2).

Table 2: Various reaction conditions attempted for the methylenation of **214.**

Entry	Reaction Conditions	**Result**
1	Ph_3PCH_3I. n-BuLi. 0 . 4h	complex mixture
2	Ph_3PCH_3I. K_2CO_3. dioxane. water. reflux. **4h**	-do-
3	CH_2I_2. $Ti(OPr\text{-}i)_4$. **THF.** rt. 36h	starting material

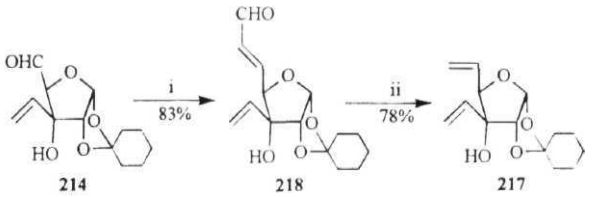
As the aldeh>de **214** was found to be either unreactive or decomposing under the aforementioned conditions. we thought of constructing the C5-C6 double bond of the diene from the triol **213** *via* its monotosylate **215** Tosylation of **213** with *p*-TsCl and pyridine in chloroform at room temperature produced the monotosylate **215** in moderate yield The structure of **215** rests on its spectral data In the IR spectrum of **215.** a band at 3000 cm^{-1} indicated the presence of aromatic groups The ^{1}H NMR spectrum of **215** showed characteristic signals for the presence of the tosyl group, such as the methyl singlet at *2* 44 ppm and two doublets at **7.33** and 7 80 ppm, respectively. corresponding to aromatic protons. Conversion of the monotosylate **215** to the epoxide **216** was **achieved** by treating **215** in methanol with a catalytic amount of sodium The H NMR spectrum of **216** was devoid of aromatic protons and doublets at 2.78 and 3.04 ppm were assigned to the epoxide protons. Satisfied with the spectral **evidence** for the formation of **216**. we set out to deoxygenate **216.** Chowdhury has reported a no\el method for the deoxygenation of oxiranes to olefins using magnesium iodide [65] Unfortunately. refluxing the epoxide **216** with magnesium iodide in diethyl ether for 3h resulted in its decomposition (Scheme 44).



213 215 216 217

Scheme **44.** *Reagents and conditions:* i) *p*-TsCl. Py. $CHCl_3$. rt, 24h; n) Na (cat amount), MeOH. rt, **3h;** m) MgI_2, ether, reflux, 3h.

The above results prompted us to condense **214** under neutral conditions with stable ylides. Wittig olefination of **214** with formylmethylene-triphenylphosphorane in toluene gave the unsaturated aldehyde **218** in good yield In the IR spectrum of **218.** the aldehyde absorption shifted to a lower **value,** to 1718 cm^{-1}, when compared to that in **214** In the ^{1}H NMR spectrum. presence of the aldehyde signal as a doublet at 9.51 ppm (J=7 8 Hz). H-5 as a doublet of doublets at 6 67 ppm (J=14.0 and 4.0 Hz) and H-6 as a multiplet at 6 33 ppm were in further support of the structure **218** A coupling constant of 14.0 Hz between H-5 and H-6 indicated the double bond stereochemistry to be trans The ^{13}C NMR spectrum of **218** displayed four olefinic resonances at 150 31. 133.72. 132 61 and 116 93 ppm Decarbonylation of **218** was effected by heating it with Wilkinson's catalyst in benzene to afford the required diene **217** in good **yield** (Scheme 45)



Scheme **45.** *Reagents and conditions:* i) $Ph_3P{=}CHCHO$, toluene. 80', 5h; ii) $(PPh_3)_3RhCl$, benzene. reflux. 2h

The IR spectrum of **217** showed absence of aldehyde absorption and the ^{1}H NMR spectrum showed no peak corresponding to the aldehyde signal and displayed six olefinic protons as multiplets at **5.37** and **5.75** ppm. The peaks at 134.84. 132.04. 118.50 and 116.07 ppm in the ^{13}C NMR spectrum of **217** were assigned to

the four olefinic carbons. Finally, microanalytical data was **in** agreement with the molecular formula $C_{14}H_{20}O_4$

We next focussed our attention on the diene **217** and conditions were sought for its ring expansion to a hexahydrooxoninone. To start with, the diene **217** was subjected to standard oxy-Cope rearrangement conditions. Heating the reaction mixture containing **217** and potassium hydride in THF at 60" gave no product. Repeating the reaction at the same temperature, but for a longer period was found to be of no **avail.** Therefore, the reaction temperature was raised However, heating the reaction mixture at 100° in 1,4-dioxane for 12h also resulted in recovery of starting material. Finally. **217** was subjected to more rigorous conditions by heating it in diglyme to 140" for 12h. Under all conditions, no rearranged product was observed and instead only starting material was recovered after usual workup (Table 3)

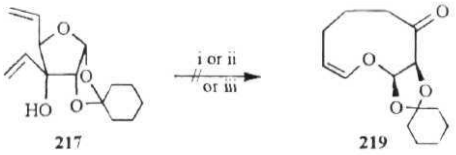
Table 3: Various reaction conditions attempted for the anionic oxy-Cope rearrangement of **217**

Entry	Reaction Conditions	Result
1	**KH,** THF, 60°, 10h	starting material recovered
2	**KH.** THF. 60°, 12h	-do-
3	**KH.** dioxane, 100°, 8h	-do-
4	KH, dioxane, 100°, 10h	-do-
5	KH, diglyme, 140°. 15h	-do-

At this point a survey of the literature regarding the oxy-Cope rearrangement conditions revealed that Macdonald reported significant improvement in yields in some oxy-Cope rearrangements on using chemically modified potassium hydride.[66] He reported that pretreating potassium hydride with iodine could remove impurities like elemental potassium and potassium superoxides and hence increase

the yields However, in our case, heating **217** with pretreated potassium hydride in THF did not bring about the desired rearrangement. The recovery of starting material was indicated by tlc and further confirmed from IR and ^{1}H NMR spectra

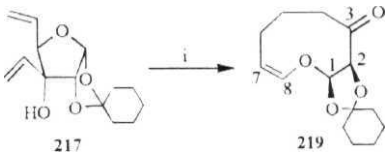
As pretreated potassium hydride was of no use, the rearrangement was tned **with** a combination of potassium hydride and 18-crown-6. as crown ethers are known to accelerate the rate of anionic oxy-Cope rearrangement.[67] Refluxing a mixture of **217** with potassium hydride and 18-crown-6 in diglyme led to recovery of starting material as indicated by IR and ^{1}H NMR spectra **Recently.** Fraser-Reid has reported that addition of tetra-n-butylammonium iodide to potassium hydride facilitates the oxy-Cope rearrangement.[68] Heating a mixture of **217.** potassium hydride and tetra-n-butylammonium iodide in THF for 10h did not lead to any rearranged product in this case as **well** (Scheme 46).



217 219

Scheme 46. *Reagents and conditions:* i) KH, I_2, THF. reflux. 4h: ii) KH. 18-C-6. diglyme. reflux. 8h: iii) KH. n-Bu_4NI, THF. reflux. **lOh**

Having failed to achieve the oxy-Cope rearrangement of **217** under anionic conditions, its thermal counterpart was attempted Fortunately, the diene **217** rearranged to the hexahydrooxoninone **219** on heating to 200-220 for 12h in a scaled tube in *o*-dichlorobenzene (Scheme 47)



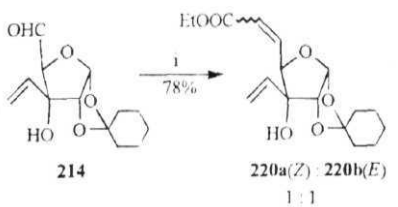
Scheme 47. *Reagents and conditions* i) *o*-dichlorobenzene (sealed tube), 200-220°, 12h.

The structure of **219** was readily apparent from its spectral and analytical data The 1R spectrum of **219** showed absence of the hydroxyl band at 3470 cm ' and presence of a carbonyl absorption at 1738 cm^{-1}, which indicated the formation of a rearranged hexahydrooxoninone. The structure of **219** was further confirmed from its H **NMR** spectrum. While the 'H NMR spectrum of **217** showed the presence of six dienylic protons which appeared as multiplets at 5.47 and 5 75 ppm, the rearranged hexahydrooxoninone **219** displayed only two protons corresponding to the enol ether double bond at 4.80 and 6 18 ppm. The ^{13}C NMR spectrum **revealed** a carbonyl signal at 206 56 ppm, the α-carbon of the enol ether double bond at 142 7 ppm and β-carbon at 113.98 ppm (Spectrum 2)

These assignments were further confirmed by 2D-homonuclear COSY. The doublet at 6 18 ppm showed a cross peak with the multiplet at 4.80 ppm. The 4.80 ppm multiplet was further coupled to a multiplet at 2.36 ppm. As the doublet at 6.18 ppm was already assigned as an olefinic proton, its coupling to only one multiplet containing single proton, proved it to be H-8 and the doublet at 4.80 ppm to be H-7. The fact that H-7 was coupled to only to the multiplet at 2.36 ppm other than to the multiplet at 6 18 ppm (H-8) showed that the multiplet at 2.36 ppm contained both the protons of H-6. The multiplet at **2.36** ppm integrated for three protons and showed cross peaks with multiplets at 4.80 ppm (H-7), 2 76 and 1 45 ppm. As the

multiplet at 2.76 ppm was assigned to be H-4 from chemical shift observations. coupling of the **multiplet** at 2.36 ppm to it meant that the third proton in the multiplet at **2.36** ppm corresponded to one of the H-5s The multiplet at 1.45 ppm displayed cross peaks with multiplets at **2.76** ppm (H-4) and 2.36 ppm (H-6 and H-5) Therefore. the multiplet at **1.45** ppm was **tentatively** assigned as H-5' due to the complexity of the spectrum in that particular region The doublets at **5.59** and 4 61 ppm showed cross peaks with one another. indicating coupling between them. and as the doublet at **5.59** ppm was assigned as H-1 from other spectral data (anomeric type proton), the multiplet at 4 61 ppm was proved to be H-2. Finally, elemental analysis showed that **217** and 219 were isomeric.

The above result encouraged us to elaborate upon the potentiality of the oxy-Cope rearrangement for the ring expansion of furanoses and in this context we set out to make different substituted dienes Wittig reaction of **214** with carbethoxymethylenetriphenylphosphorane in benzene afforded a mixture of isomers. 220a and 220b in the ratio 1:1 which were chromatographically separated (Scheme 48).



214 **220a**(*Z*) : **220b**(*E*)
1 : 1

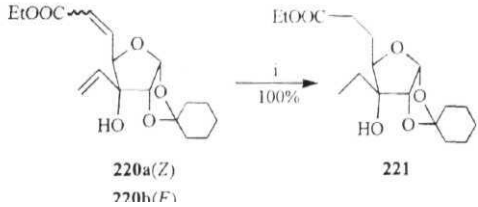
Scheme 48. *Reagents and conditions:* i) Ph_3P=CHCOOEt, **benzene, reflux, 5h.**

The 1R spectra of **220a** and **220b** showed carbonyl absorptions at 1722 and 1726 cm^{-1}, respectively. The ^1H NMR spectrum of **220a** showed **five** olefinic protons as a doublet of doublets at **5.29** ppm (J=10.7 and **1.4** Hz) and a multiplet at **5.80** ppm. The coupling constant of 10.7 Hz between H-5 and H-6 indicates a cis relationship between them. The CH_3 and CH_2 protons of the ester appeared as a triplet and a quartet at **1.30** and **4.19** ppm, respectively. In the ^{13}C NMR spectrum, the ester carbonyl resonated at 166.45 ppm and the peaks at **144**.02, **134**.46, **123.01** and 116.86 ppm were assigned to the four olefinic carbons. Microanalysis data established the molecular formula of **220a** to be $C_{17}H_{24}O_4$.

220b exhibited in its ^1H NMR spectrum five olefinic protons, with the **vinyl** group appearing as a multiplet at 5.44 ppm. H-5 as a doublet of doublets at 6.77 ppm (J=15.7 and 4.0Hz) and H-6 as a doublet of doublets at 6.02 ppm (J=15.6 and 1.4Hz). As H-5 and H-6 are coupled to each other with a J value of 15.6 Hz, the trans stereochemistry between H-5 and H-6 is established. The CH_3 and CH_2 protons of the ester appeared as a triplet and a quartet **at** 1.23 and 4.12 ppm, **respectively. In** the ^{13}C NMR spectrum of **220b,** resonance of the ester carbonyl appeared at 166.10 ppm along with 15 other lines.

Surprisingly, in the ^1H NMR spectrum of **220a, H-4** appeared as a broad singlet at 3.86 ppm in contrast to **220b** where it appeared as a multiplet at 4.44 ppm. raising doubts regarding the stereochemistry at C4. In order to establish the identity of **220a** beyond doubt, we planned to selectively reduce the C5-C6 double bonds of **220a** and **220b** and then compare the products. Stirring **220a with** magnesium turnings in methanol for 5h gave no reduced product. Only the starting material was recovered as indicated by tlc. Both double bonds of the cis ester **220a** were smoothly hydrogenated in quantitative yield by stirring with 5% Pd/C in a hydrogen atmosphere, to afford **221**. In the 1R spectrum of **220a,** the carbonyl band

appeared at 1722 cm^{-1} whereas in that of 221 it appeared at 1736 cm^{-1} Lack of olefinic signals in the ^1H NMR spectrum of **221** provided further proof for the fact that 220a had undergone complete hydrogenation Under similar conditions as those for **220a. 220b** was also completely reduced to give the same product **221** and thus proving that no epimerization had occurred in the case of **220a** (Scheme 49)



220a(Z)
220b(E)

221

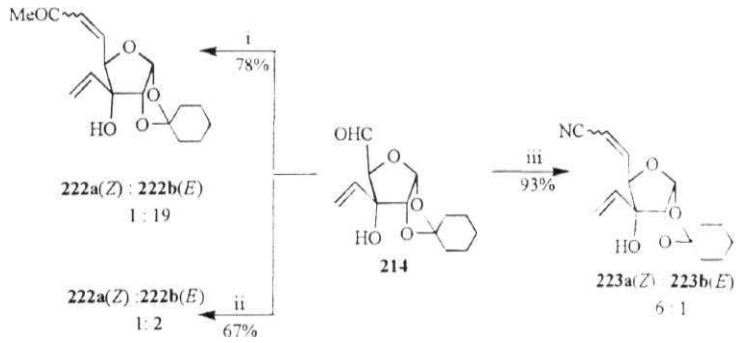
Scheme 49. *Reagents and conditions:* 5% Pd/C, H_2 (balloon). ethyl acetate, 30 min

The aldehyde **214** on refluxing in benzene with acetylmethylene-triphenylphosphorane gave a mixture of cis and trans enones **222a** and **222b** in the ratio 1 19 Separation of the isomers was effected by column chromatography In the 1R spectra of **222a** and **222b.** bands at 1697 and 1700 cm^{-1} confirmed the presence of an unsaturated carbonyl group The ^1H NMR spectrum of **222a** displayed a characteristic singlet for the acetyl methyl group at 2.27 ppm, H-5 as **a** broad doublet at 6.40 ppm (J=10 8 Hz) and H-6 as a multiplet at 5.63 ppm Similarly. **222b** also exhibited acetyl methyl. H-5 and H-6 signals as a singlet at 2 24 ppm. as **a** doublet of doublets at 6.64 ppm (J= 16.0 and **4.0** Hz) and another doublet of doublets at 6.32 ppm (J=16.0 and 1.4 Hz), respectively, in its ^1H NMR spectrum A coupling constant of 16.0 Hz between H-5 and H-6 in **222b** in contrast to the coupling constant of 10.8 Hz between the same protons in **222a** provided evidence

for their trans and cis geometries, respectively 222a and 222b showed carbonyl resonances at 199.72 and 197.87 ppm, **respectively,** in their ^{13}C NMR spectra

In order to obtain the cis isomer 222a in better **yields,** Wittig olefination of **214** with acetylmethylenetriphenylphosphorane was conducted in a polar solvent, **i.e.,** in MeOH at -78°. This gave the cis and trans isomers 222a and 222b in the ratio 1:2.

The required cis and trans nitriles, 223a and 223b were obtained in a 6:1 ratio by refluxing **214** with cyanomethylenetriphenylphosphorane in benzene They were chromatographically separated and the structures of 223a and 223b were confirmed from their spectral and analytical data The IR spectra of 223a and

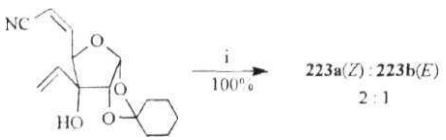


Scheme 50. *Reagents and conditions:* i) $Ph_3P=CHCOCH_3$, benzene, reflux, 5h; ii) $Ph_3P=CHCOCH_3$, MeOH, -78". 2h; iii) $Ph_3P=CHCN$, benzene, reflux, 5h.

223b showed the cyano group stretching at 2224 and 2227 cm^{-1}, respectively In the ^1H NMR spectrum of 223a. the doublet of doublets at 6 30 ppm (J=11 7 and 7 8 Hz) and the multiplet at 5 56 ppm were assigned to H-5 and H-6. **respectively**

These protons are in a cis relationship with one another In the 'H NMR spectrum of 223b. H-5 appeared as a doublet of doublets at 6 62 ppm (J=16.0 and 4 0 Hz) and H-6 as a multiplet at 5.49 ppm.(Scheme 50).

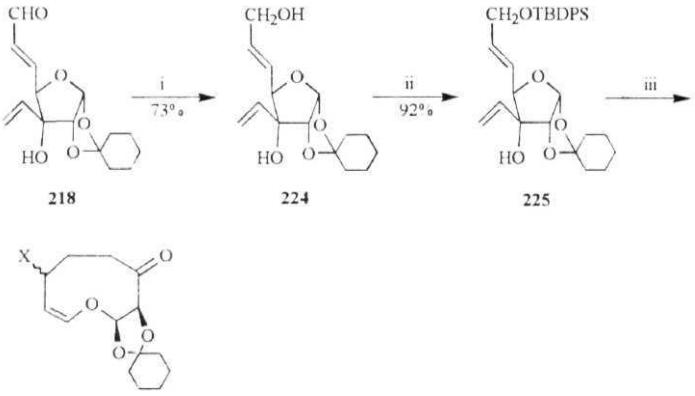
In order to obtain preparative quantities of **223b. 223a** was photolysed in benzene using diphenyl disulfide as an activator to afford a 2:1 mixture of cis and trans isomers 223a and 223b (Scheme 51)



223 a

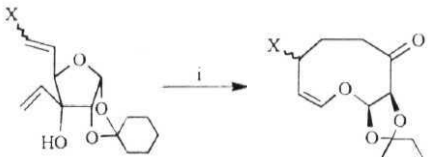
Scheme 51. *Reagents and conditions:* i) diphenyl disulfide, benzene, hv, 1h.

As the aldehyde **218** underwent slow decomposition even at room temperature, its thermal rearrangement was not attempted. Instead, it was reduced to the allyl alcohol **224** using Luche's method Thus, treatment of **218** with cerium(III) chloride heptahydrate and sodium borohydride at rt for 2h furnished the unsaturated alcohol **224** in good yield Absence of the aldehyde absorption in the IR spectrum and appearance of H-7 as a doublet at 4 12 ppm **(J=5.5** Hz) supported the structure of 224 The primary alcohol in **224** was protected as its silyl ether with t-butyldiphenylchlorosilane and imidazole to give **225** The H NMR spectrum of 225 contained the *t*-butyl signal as a singlet at 1.05 ppm and aromatic



Scheme 52. *Reagents and conditions:* i) $CeCl_3.7H_2O$, $NaBH_4$, THF, MeOH, 0°, 1h and then rt, 2h; ii) TBDPSCl, imidazole, DMF, rt, 12h; iii) KH, THF, reflux, 6h.

signals as multiplets at 7.40 and 7.22 ppm. Subjecting the **silyl** ether 225 to anionic oxy-Cope rearrangement conditions, i.e.; refluxing 225 with potassium hydride in THF resulted in recovery of starting material (Scheme 52).



Scheme 53. *Reagents and conditions* i) *o*-dichlorobenzene (sealed tube), 200-220°, 12h.

In order to illustrate the generality of this ring expansion strategy, we attempted the thermal oxy-Cope rearrangement on all the substituted dienes **220a**-223b and the results are summarized in Table 4 (Scheme 53).

Table 4: Thermal oxy-Cope rearrangement of compounds **217-223b** *(Yields based on recovered starting material.)*

Entry	Substrate	Product	**Yield** (%)
1	**217 (H)**	**219**	40
2	220a (*Z*-CO_2Et)	227	40
3	220b (*E*-CO_2Et)	No Reaction	
4	222a (*Z*-$COCH_3$)	**228**	<5
5	**222b** (*E*-$COCH_3$)	**228**	20
6	223a (Z-CN)	**229**	60
7	223b (£-CN)	**229**	5

The cis ester **220a** on heating in a sealed tube in *o*-dichlorobenzene at 200-220° for 12h gave the rearranged product 227 in 40% yield, whereas the trans isomer **220b** underwent no reaction under the same conditions. In the case of cis ketone **222a.** it rearranged to the product **228** in less than 5% yield. Fortunately, under the same set of conditions, the trans ketone **222b** gave the rearranged product 228 in 20% yield. Surprisingly, the cis nitrile 223a underwent rearrangement to give the hexahydrooxoninone **229** in **60%** yield in contrast to the trans isomer **223b** which **gave 229** in very poor yields.

The **identity** of all the rearranged products were unambiguously established from their spectral and analytical data. All ^1H NMR spectral assignments were further confirmed from 2D-COSY experiments on the rearranged products, **219.**

227, **228** and **229.** Salient features of the ^{1}H and C chemical shifts of the products are given below (Table 5).

Table 5: ^{1}H **and** ^{13}C NMR Chemical shifts of some salient protons and carbons of products 219-229

Entry	Signal	219	227	228	229
1	H-1	**5.59**	5 58	5 60	5.58
2	**H-6**	2.37	3,50	**3.58**	**3.61**
3	**H-7**	480	5 14	492	4.88
4	**H-8**	6.18	6 22	**6 34**	626
5	**C-3**	**206.56**	210 0	208 88	**203.58**
6	**C-7**	113.98	111.72	**112 47**	**115.69**
7	**C-8**	142 70	143 24	**141.38**	14465

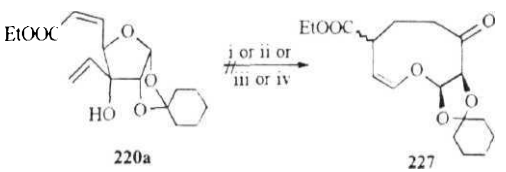
The structure of **227** was further confirmed from its homonuclear H COSY spectrum. The doublet at 6.23 ppm showed a cross peak with the multiplet at 5 14 ppm which was further coupled to the multiplet at **3.50** ppm. As the multiplet at 6.23 ppm was assigned as H-8, the multiplets at **5.14** and **3.50** ppm have to be H-7 and H-6, respectively The quartet at 4 13 ppm and the triplet at I 24 ppm showed cross peaks with one another, and they were assigned as CH_2 and CH_3 protons of the ester group, respectively. The multiplet at **3.50** ppm was coupled to multiplets at 2.36 and 1 53 ppm apart from its coupling with the multiplet at 5.14 ppm (H-7). This indicated that one of the H-5s was residing in the multiplet at 2.36 ppm whereas the other one was at 1.53 ppm This was further substantiated from the following coupling patterns. The multiplet at **2.75** ppm was assigned to be H-4 based on its chemical shift observations It showed cross peaks with multiplets at 2.36 and 1.53 ppm. Also, **the** multiplet at 2 36 ppm exhibited couplings with

multiplets at 3.50 ppm (H-6). 2 75 ppm (H-4) and 1.53 ppm Therefore. the multiplets at 1.53 and 2 36 ppm were assigned to contain H-5" and cyclohexyl protons. and H-5. respectively The doublets at 5.58 and 4.64 ppm were coupled to each other. and as the doublet at **5.58** is known to be H-1. the doublet at 4.64 ppm corresponds to H-2

The DEPT-135 spectrum of **227** exhibited fourteen lines corresponding to fourteen carbons. out of which six were CH_3 carbons. one was a CH carbon and **seven** were CH_2 carbons Finally. microanalytical data confirmed the molecular formula of **227** to be $C_{17}H_{24}O_6$

It should be noted that both isomers of the ketone **(222a** and **222b)** and the nitrile **(223a** and **223b)** give the same products on rearrangement. namely **228** and **229,** respectively The reasons for this were not investigated Finally. the stereochemistry at the substituent carbon in the products was also not established

Proceeding on the assumption that catalysis of the oxy-Cope rearrangement with metal salts would reduce the reaction temperature and increase the yields, the **oxy-Cope** rearrangement of **220a** was examined with mercury and



220a 227

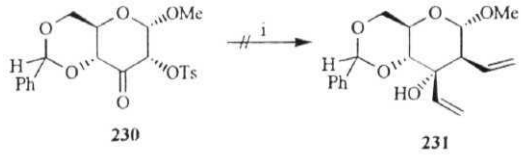
Scheme 54. *Reagents and conditions:* i) bis(benzonitrile)dichloro palladium(II). benzene rt. **12h;** ii) $Hg(COOCF_3)_2$. CH_2Cl_2. rt. **36h;** iii) $LiClO_4$. ether. rt, 36h; **iv)** $LiClO_4$. diglyme. 120°, 24h

palladium salts."' Stirring **220a** and bis(benzonitrile)dichloropalladium(II) in benzene for 12h only resulted in recovery of starting material Mercuric trifluoroacetate also failed to bring about the rearrangement on stirring with **220a** in dichloromethane for 36h Only the starting material was recovered As lithium perchlorate in diethyl ether ' has been found to accelerate the rate of Diels-Alder reactions, 1,3-sigmatropic rearrangements and 3,3-sigmatropic rearrangements. we were interested in examining the effect **of lithium** perchlorate on the rearrangement of **220a. In** our case. stirring **220a** in 5M lithium perchlorate in diethyl ether proved to be of no use. as after the usual workup. only starting material was recovered. Increasing the reaction temperature by heating **220a** and lithium perchlorate in diglyme led only to decomposition (Scheme 54)

Thus we have been successful in our attempts to synthesize functionalized 9-membered ethers from furanoses. Various sugar derived substituted dienes have been prepared and the oxy-Cope rearrangement of these substrates has been realized for the first time The resultant functionalized 9-membered ethers can be readily-manipulated to 9-membered lactones and other **systems.**

PART I: B) ATTEMPTS TOWARDS THE SYNTHESIS OF OXECANONES FROM PYRANOSES:

Encouraged by the success in ring expanding furanoses to 9-membered ring ethers, the same oxy-Cope rearrangement protocol was sought to be extended to pyranoses. For construction of the 1,5 diene unit in pyranoses, initially we chose the known methyl 4,6-*O*-benzylidene-2-*O*-(*p*-toluenesulfonyl)-α-D-*ribo*-hexopyranosid-3-ulose **(230)** as starting material and this was prepared from D-glucose according to the literature procedure [71] Based on the known reaction of α-chlorocycloalkanones with excess vinylmagnesium bromide leading to 1,2-divinylcycloalkanols,[72] it was hoped that vinylmagnesium bromide would also add to **230** in a similar fashion, generating the diene unit in one step. Contrary to our expectations, refluxing **230** with excess vinylmagnesium bromide in **THF** gave no characterizable product (Scheme 55).



230 **231**

Scheme 55. *Reagents and conditions* i) vinylmagnesium bromide, THF, reflux, 5h

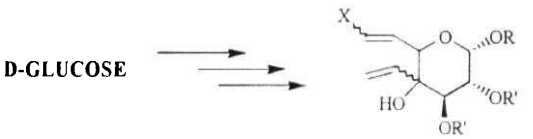
Working on the assumption that the failure of the above reaction was due to the absence of an α-chloroketone moiety, we sought to incorporate it into the pyranose template. A recent report on the conversion of epoxides to α-chloroketones[73] under the conditions of Swern oxidation prompted us to examine this reaction on the epoxy sugar **232**. Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-

mannopyranoside (**232**), was prepared according to the literature procedure [74] For epoxide opening cum oxidation, a mixture of **232**, DMSO, oxalyl chloride, triethylamine and methanol was stirred at -60° for 30 min However, after the usual vvorkup, onlv starting material was obtained as indicated bv tlc (Scheme 56)

232 **233**

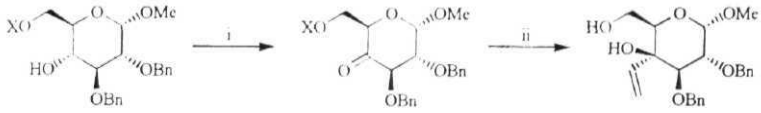
Scheme 56. *Reagents and conditions:* i) DMSO. **oxalyl** chloride. CH_2Cl_2, MeOH, -60°, 30 min, then Et_3N, -60° to rt.

At this stage, we changed our strategy and planned to introduce the diene unit as outlined below.



For this purpose the known alcohol, methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (**234**) was identified as a suitable precursor. ' Oxidation of **234** with PCC gave the corresponding ulose **235** in moderate yield. Absence of the hydroxyl absorption and presence of the carbonyl absorption at 1724 cm^{-1} in the IR spectrum of **235** indicated that the oxidation had indeed taken place. As a next step, reaction of excess vinylmagnesium bromide with **235** was thought to be logical, as it was anticipated that addition of the vinyl group to the ketone at C-4 and cleavage of

the benzoate ester would occur in a single step, leading to **236**, which could be converted to the desired diene. The experimental results were found to be different. Refluxing **235** with excess vinylmagnesium bromide in THF afforded a complex mixture. Repeating the same sequence of reactions commencing with methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (**237**)[71] was also of no avail (Scheme 57),



234 X-COPh
237 X=$COCH_3$

235 X-COPh
238 X=$COCH_3$

236

Scheme 57. *Reagents and conditions:* i) PCC, benzene, reflux, 2h; ii) vinylmagnesium bromide, THF, reflux, 24h

As the alcohol **236** could not be prepared either from **234** or from **237**, methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (239) was arrived at as yet another starting material and was prepared according to literature procedure [72]. Addition of vinylmagnesium bromide to **239** resulted in recovery of starting material. When the attempt to introduce the C-4 vinyl group directly failed, the strategy was altered towards introducing an ethynyl group at C-4 and then partially hydrogenating the triple bond to the double bond. At room temperature, Grignard reaction of **239** with a large excess of ethynylmagnesium bromide gave an epimeric mixture of alcohols **240**. No attempts were made to separate the mixture, because if the oxy-Cope rearrangement were to take place, the C-4 carbon would lose its chirality and become a carbonyl group. The IR spectrum of **240** contained no carbonyl absorption and exhibited a strong acetylenic band at

3298 cm^{-1}, which was confirmed from its ^{13}C NMR spectrum which displayed two acetylenic resonances at 144.01 and 143.60 ppm. Its ^{1}H NMR spectrum contained two singlets at 2 26 and 2.39 ppm corresponding to two acetylenic protons All further reactions were conducted on the epimeric mixture of alcohols.

Initially, a partial reduction of the triple bond in **240** was attempted utilizing the standard semi-hydrogenation reagent. Lindlar's **catalyst.** Stirring **240** with Lindlar's catalyst under hydrogen atmosphere at balloon pressure in a mixture of hexane and benzene **gave** back the starting material Partial hydrogenation of **240** was then tried at a higher pressure, at 40 psi, in a Parr apparatus for 8h **However.** only the starting material was recovered Increasing the pressure further to 55 psi was also of no use We then turned our attention towards Pdc. a complex reducing agent, prepared from sodium hydride, palladium acetate and *t*-amyl alcohol as reported in the literature [78] Attempts to semi-hydrogenate **240** by stirring it with

Table 6: Various conditions attempted for semi-hydrogenation of **240**

Entry	Reaction Conditions	Result
1	Lindlar's catalyst, H_2, balloon pressure, 8h	starting material recovered
2	Lindlar's catalyst, H_2, 40 psi, 8h	-do-
3	Lindlar's catalyst, H_2, 55 psi, 4h	-do-
4	Pdc. H_2, balloon pressure, 48h	-do-
5	Pdc, H_2, 40 psi, 6h	-do-
6	Pdc, H_2, 50 psi, 4h	-do-

Pdc and quinoline in a hydrogen atmosphere at balloon pressure failed to give the product. As a next move, the reaction was performed in a Parr apparatus at 40 psi

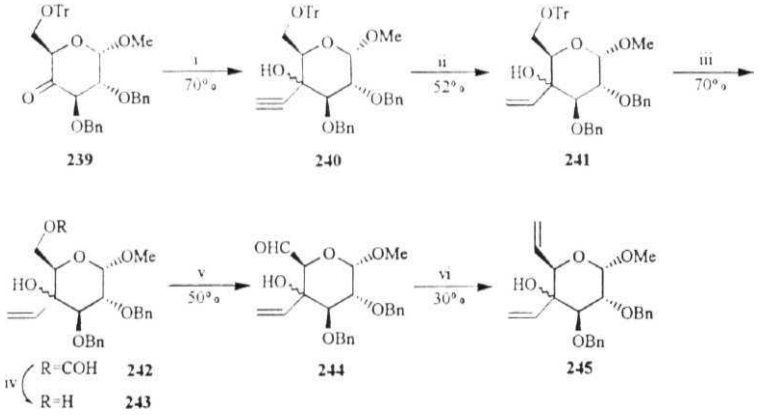
Discouragingly, no hydrogenation was observed **Finally,** the experiment was repeated at 50 psi for 4h In all cases, only the starting material was recovered as shown in Table 6

To our relief, the alcohols **240** could be partially hydrogenated in moderate **yield** on **refluxing** with $LiAlH_4$ in THF to afford the alcohols **241** The structure of **241** follows from its spectral data The acetylenic C-H band was absent in the 1R spectrum and two multiplets at 5 46 and 5 91 ppm integrating to a total of three olefinic protons were present in the ^1H NMR spectrum The ^{13}C NMR spectrum displayed four resonances corresponding to olefinic carbons at **144 17. 143.85,** 117.17 and 116.40 ppm Hydrolysis of the trityl ether[7] in **241** was achieved under acidic conditions with formic acid in ether to furnish the diol **243.** accompanied by varying amounts of the C-6 formate **242** This was in turn converted to the diol **243** on treatment with a catalytic amount of sodium in methanol. The structures of **242** and **243** were established from their spectral data Simplification of the ^1H NMR spectra of **242** and **243** in the aromatic region and reduction in the number of aromatic protons when compared to the aromatic protons in **241** provided evidence for cleavage of the trityl ether This was further confirmed from their ^{13}C NMR spectra, which displayed lesser number of aromatic resonances than that of **241** A carbonyl bond at 1726 cm^{-1} was present in the IR spectrum of **242** in addition to the other bands Furthermore, the formyl proton signal as a singlet at 8 03 ppm in the ^1H NMR spectrum and the formyl carbon at 160.66 ppm in the ^{13}C NMR spectrum substantiate the structure of **242**

Initially, the diol **243** was subjected to oxidation with DMSO-trifluoroacetic anhydride and N,N-diisopropylethylamine in dichloromethane. Under these conditions, no reaction took place as indicated by the IR spectrum Oxidation of **243** with PCC in dichloromethane gave the aldehyde **244.** but in poor yields. An

aldehyde absorption appeared at 1730 cm^{-1} in the IR spectrum In the ^1H NMR spectrum. the aldehyde proton appeared as a singlet at 9.58 ppm. Alternatively. the aldehyde 244 was obtained in good yield from the alcohol 243 on oxidation with Dess-Martin periodinane in dtchloromethane.

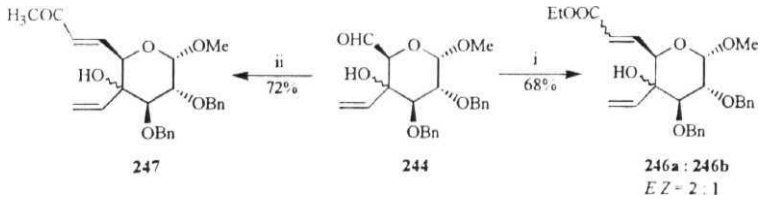
Condensation of the aldehyde 244 with methylenetriphenylphosphorane. obtained by stirring methyltriphenylphosphonium iodide with sodamide in ether for 30 min. welded the diene 245 in moderate yield (Scheme 58). Absence of the



Scheme 58. *Reagents and conditions:* i) ethynylmagnesium bromide, THF, rt, 4h; ii) $LiAlH_4$, THF, reflux, 6h; iii) formic acid, ether. rt, 1h; iv) NaOMe, MeOH, rt. 6h. v) Dess-Martin periodinane. CH_2Cl_2. rt, 3h; vi) Ph_3PCH_3I, sodamide, ether, rt, 30 min

aldehyde absorption in the IR spectrum and presence of six protons in the olefinic region as multiplets at 5 31 (4 protons) and 5 84 ppm (2 protons) in the ^1H NMR spectrum provide proof for the formation of diene **245**

Olefination of **244** with the stable ylide, carbethoxymethylenetriphenylphosphorane in benzene gave the cis and trans carbethoxy substituted dienes **246a** and **246b** in the ratio 1:2, and these were chromatographically separated. The gross structures of dienes **246a** and **246b** were based on their IR and ^{1}H NMR spectral data. The IR spectra of **246a** and **246b** showed carbonyl absorptions at 1718 cm^{-1}, characteristic of an a, P-unsaturated ester group. In the ^{1}H NMR spectrum of **246b.** the characteristic ethyl ester triplet and quartet were found at 1.27 and 4.18 ppm. **respectively.** H-7 appeared as a doublet at 6.14 ppm (J=15.7 Hz), which implies trans stereochemistry between H-6 and H-7. In the ^{13}C NMR spectrum of **246b.** absorptions at 166.12 and 14.21 ppm were attributed to the unsaturated ester carbonyl and ester methyl carbons. Four olefinic carbons resonated at 141.57, 138.46, 123.23 and 118.0 ppm in the ^{13}C NMR spectrum.



Scheme 59. *Reagents and conditions* 1) Ph_3P=CHCOOEt, benzene, reflux. **4h;** 11) Ph_3P=$CHCOCH_3$, benzene, reflux. 4h.

The trans ketone **247** was obtained as the major isomer from the aldehyde **244** on refluxing with acetylmethylenetriphenylphosphorane in benzene (Scheme 59). The IR spectrum of **247** showed a carbonyl absorption at 1722 cm^1. In the ^{1}H NMR spectrum of the trans ketone **247,** a singlet at **2.22** ppm. a doublet of doublets at **6.33** ppm(J=15.7 and 1.65 Hz) and a multiplet at **6.76 (J=15.7 and 4.4** Hz) ppm were assigned to acetyl methyl. H-7 and H-6 protons, **respectively.** A coupling

constant of 15.7 Hz between H-6 and H-7 indicates their trans stereochemistry The ^{13}C NMR spectrum of **247** displayed the carbonyl resonance at 198.04 ppm along with other lines.

After the successful preparation of the different dienes **245-247.** we turned our attention towards their oxy-Cope rearrangement to 10-membered ring compounds In this context, we first attempted the anionic oxy-Cope rearrangement of **245-247.**

According to the standard procedure, the diene **245** was heated to 120° for 24h with potassium hydride in diglyme Discouragingly, the reaction mixture after usual workup, contained only a complex mixture. As **245** gave a complex mixture under the above conditions, the same reaction was repeated at a slightly lower temperature of 110°. As this decrease was of no avail, the reaction was conducted at a still lower temperature, **60°,** and for 10h. In both the cases, a complex mixture was obtained as indicated by tlc.

Changing the substrate from **245** to **246a,** we investigated suitable conditions for its rearrangement. The rearrangement of 246a was first attempted at 100°. and only for 4h. The results of this experiment were not any different from the earlier mentioned results, as again only a complex mixture was obtained. Decreasing the temperature to 80° and increasing the reaction time to 12h did not prove to be any better. Conducting the reaction at 60° for 10h also resulted in a complex mixture.

Similarly, heating **246b** with potassium hydride in dioxane to 100° for 5h and or in THF to its reflux temperature also resulted in a complex mixture. In the case of **247,** rearrangement was tried at 120° and for 6h to afford only complex mixture. All these results are summarized in Table 7.

Table 7: Various reaction conditions attempted for anionic oxy-Cope rearrangement of compounds 245-247

Entry	Substrate	Reaction Conditions	Result
1	245	KH. dielvmc. 120°. 24h	decomposition
2	245	KH. toluene. 110°. 24h	-do-
3	245	KH. THF. 60 . 10h	-do-
4	246a	KH. dielvmc. 100°. 4h	-do-
5	246a	KH. dioxane. 80°. 12h	-do-
6	246a	KH. THF. 60°. 10h	-do-
7	246b	KH. diglyme. 120°. 6h	-do-
8	246b	KH. dioxane. 100°. 5h	-do-
9	247	KH. THF. 60°. 12h	-do-

We next attempted our rearrangements in the presence of tetra-n-butylammonium iodide along with potassium hydride. Conducting the oxy-Cope rearrangement of 245 with potassium hydride and tetra-n-butylammonium iodide in THF at 60° for 1 Oh gave discouraging results Under identical conditions. 246b

Table 8: Various reaction conditions attempted for anionic oxy-Cope rearrangement of compounds 245-247 with KH and n-Bu_4NI

Entry	Substrate	Reaction Conditions	Result
1	245	KH. n-Bu_4NI. THF. 60". 10h	decomposition
2	246b	KH. n-Bu_4NI. THF, 60°, 10h	-do-
3	247	KH. n-Bu_4NI. diglyme, 80°. 2h	-do-

displayed a similar decomposition pattern In the case of 247. the reaction was done at 80" and for a shorter time period. 2h No product was obtained In this study also.

the same fate as earlier awaited the substrates **245-247.** as all of them gave complex mixtures as indicated by tlc (Table 8)

As compounds **245-247** seemed to decompose **extensively** under anionic oxy-Cope rearrangement conditions, we decided to try its thermal counterpart Heating **245** in a sealed tube in *o*-dichlorobenzene at 180° for 12h afforded starting material as the major component along **with** slight decomposition. The temperature was then increased to 200° and the reaction mixture was heated for 6h. In this case also, most of the starting material was recovered Finally. subjecting **245** to **very** harsh conditions by heating it to 240-260 for 1h, resulted in **extensive** decomposition

Table 9: Various reaction conditions attempted for thermal oxy-Cope rearrangement of compounds **245-246b**

Entry	Substrate	Reaction Conditions	**Result**
1	**245**	*o*-dichlorobenzene, 180°, 12h	recovered unchanged
2	**245**	*o*-dichlorobenzene, 200°, 6h	recovered unchanged
3	**245**	*o*-dichlorobenzene, 240-260°, 1h	extensive decomposition
4	**246a**	*o*-dichlorobenzene, 180°, 12h	recovered unchanged
5	**246b**	*o*-dichlorobenzene, 220°, 5h	complex mixture

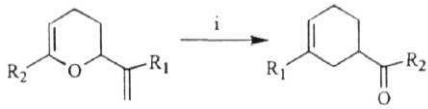
In the case of **246a** also, most of the starting material was recovered on heating at 180° for 12h. **246b,** on heating at 220° for 5h, after usual workup gave a complex mixture. Attempts to purify the mixture were unfruitful (Table 9).

In conclusion, different pyranose dienes were prepared and their oxy-Cope rearrangements attempted. The pyranose derived dienes failed to rearrange under all the conditions that were examined. Under mild conditions, no reaction took place

and under forcing conditions, extensive decomposition was observed The reasons for this are not immediately apparent, although the conditions examined included those which were similar to that employed for the successful rearrangement of furanosides

PART II: SYNTHESIS OF PSEUDO-SUGARS FROM SUGARS *VIA* CHIRAL CARBOCYCLES:

Synthesis of cyclopentane and cyclohexane rings is a topic of everlasting interest to many organic chemists This interest is due to the ubiquitous presence of these rings in various natural and unnatural products As already pointed out in the introduction, carbohydrates have been extensively utilized in the preparation of these **systems.** Our interest in the reactions of glycals and other unsaturated sugars prompted us to explore the possibility of applying the Claisen rearrangement for the conversion of sugar derivatives to carbocycles A perusal of the literature revealed that Büchi had reported the conversion of 3,4-dihydro-2H-pyranyl ethylenes **248** to cyclohexenecarbaldehydes **249** (Scheme 60).[8]



248 **249**

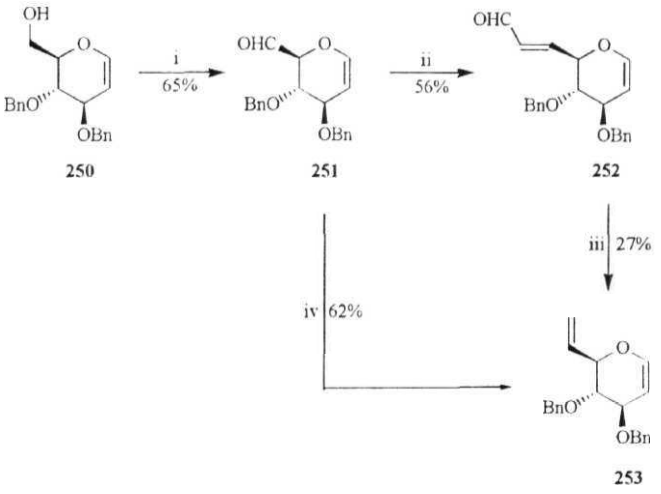
Rl=H, R_2=H R_1=H, R_2=H

R_1=CH_3, R_2=CH_3 R_1=CH_3, R_2=CH_3

Scheme 60. *Reagents and conditions:* FVP, 400°. hexane

We envisioned that application of a similar strategy to carbohydrates would provide chiral carbocycles. At this point, we recognized glycals as the best starting materials for fabrication of the allyl vinyl ether unit, as they possess an inbuilt vinyl ether moiety, and only need construction of the allyl functionality. Our strategy was to prepare various substituted allyl vinyl ethers and to rearrange them into chiral carbocycles *via* the Claisen rearrangement.

The known 1,5-anhydro-3,4-di-*O*-benzyl-D-*arabino*-hex-1-enitol **(250)** was chosen as precursor for the preparation of a suitable substrate required for the Claisen rearrangement [81] The alcohol 250 was oxidized with PDC to yield the **aldehyde 251** and the crude aldehyde was used for the next step without purification Wittig reaction of **251** with methyltriphenylphosphonium iodide using n-butyllithium as a base, resulted in a complex mixture We then planned to prepare the allyl **vinyl** ether **253** from aldehyde **251** ***via*** the unsaturated aldehyde **252** Condensation of **251** with formylmethylenetriphenylphosphorane afforded the trans unsaturated aldehyde **252** in moderate yield The IR spectrum of **252** showed an aldehyde absorption



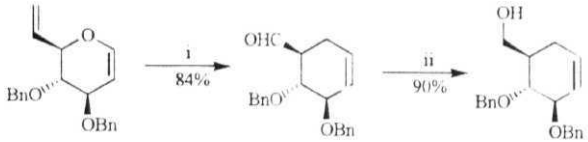
Scheme 61. *Reagents and conditions:* i) PDC. 4A molecular sieves, CH_2Cl_2. rt. 10h; ii) $Ph_3P{=}CHCHO$. toluene. 80'. 2h. iii) $(PPh_3)_3RhCl$. benzene. reflux. 4h; **iv)** Ph_3PCH_3I. $NaNH_2$. ether, n. 30 min

at 1730 cm^{-1} and the ^1H NMR spectrum showed the formyl proton as a doublet at 9.48 ppm (J=7.8 Hz). Decarbonylation of the unsaturated aldehyde with Wilkinson's catalyst in refluxing benzene furnished the allyl vinyl ether **253** in very poor yields Spectral data in support of the structure of **253** include IR, 'H NMR and "C NMR spectra. The aldehyde absorption was absent in the IR spectrum and five olefinic protons were present as a doublet at 6 44 ppm (J=6 0 Hz) and two multiplets at 5 39 and 6.04 ppm in the ^1H NMR spectrum. Presence of the C6-C7 double bond in **253** was further confirmed from its ^{13}C NMR spectrum which displayed resonances at 125.95 and **138.42** ppm in addition to the enol ether resonances. Microanalytical data authenticated the molecular formula of **253** as $C_{21}H_{22}O_3$.

Low yields of the allyl vinyl ether **253** from the above experiment forced us to look for an alternative to **achieve** the same. Wittig methylenation of **251** was attempted without the presence of base in the reaction mixture. Treating **251** with methylenetriphenylphosphorane, obtained by stirring methyltriphenylphosphonium iodide and sodamide in ether at rt for 6h, furnished **253** in moderate yield (Scheme 61).

In order to rearrange the allyl vinyl ether **253,** it was heated in a sealed tube in N,N-diethylaniline to 220° for 8h. However, after usual workup, only a complex mixture was obtained.

Claisen rearrangement of **253** was achieved by heating it in *o*-dichlorobenzene in a sealed tube at 240° for 1h to give the rearranged product **254** in good yields. The aldehyde **254** was found to epimerize on standing at room temperature. Owing to its sensitivity, no attempts were made to purify **254** and the crude aldehyde was subjected to sodium borohydride reduction to afford the alcohol **255** in good yield (Scheme 62).



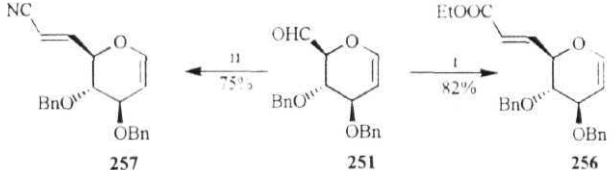
Scheme 62. *Reagents and conditions* i) *o*-dichlorobenzene (scaled tube), 240". 1h; ii) $NaBH_4$, THF, 0". 10 min

The alcohol **255** was **completely** characterized by its spectral and analytical data. Absence of the aldehyde absorption and presence of a strong hydroxyl absorption at 3445 cm^{-1} indicated that reduction had taken place This was further supported by the ^1H NMR spectrum of **255** which showed the absence of proton signals corresponding to **253,** and the presence of only two olefinic protons as a multiplet at 5.76 ppm. Apart from aromatic carbons, the ^{13}C NMR spectrum of **255** displayed 9 lines in keeping with its structure.

In order to generalize the above strategy and to illustrate the potential of the Claisen rearrangement in the synthesis of chiral cyclohexenes, synthesis of the substituted dienes **256** and **257** was undertaken

Heating **251** with carbethoxymethylenetriphenylphosphorane in benzene for **5h** resulted in formation of the trans ester **256** as the major isomer **In** the IR spectrum of **256**, the carbonyl absorption appeared at 1722 cm^{-1}. In the ^1H NMR spectrum of **256.** CH_3 and CH_2 protons of the ester appeared as a triplet and quartet at 1.28 and 4.18 ppm. respectively H-6 appeared as a doublet of doublets at 7 13 ppm (J=15.8 and 4.0 Hz) and H-7 appeared as a doublet at **6.13** ppm **(J=15.8** Hz). indicating trans stereochemistry between H-6 and H-7. The ^{13}C NMR spectrum of **256** displayed the carbonyl resonance at 166.07 ppm along with other lines

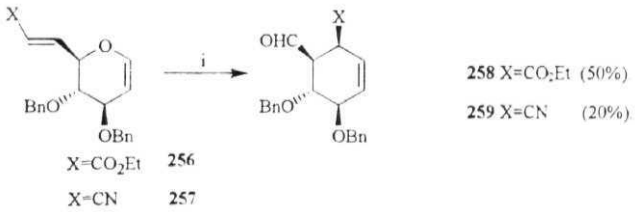
Wittig olefination of 251 with cyanomethylenetnphenylphosphorane in refluxing benzene furnished the trans **nitrite** 257 as the major product (Scheme 63). The nitrile absorption was seen at 2226 cm ' in the IR spectrum In the H **NMR** spectrum of 257, a doublet at 5 66 ppm (J= **16.4** Hz) and a doublet of doublets at 6 85 ppm **(J=16** 4 and 4.0 Hz) were assigned to H-7 and H-6 protons. respectively A coupling constant of 16 4 Hz **between** H-6 and H-7 indicates their trans stereochemistry.



Scheme 63. *Reagents and conditions:* i) Ph_3P=CHCOOEt, benzene, reflux. 5h; ii) Ph_3P=CHCN, benzene, reflux, 10h.

Having secured the substituted dienes, our attention was next focussed on the Claisen rearrangement of 256 and 257. When the ester **256** was heated in a sealed tube in *o*-dichlorobenzene to 240°, the rearranged product **258** was obtained along with some starting material In contrast to **256,** which showed only one carbonyl absorption, the IR spectrum of **258** showed two carbonyl absorptions at 1730 and 1724 c m ! In the H NMR spectrum of **258.** the ester CH_3 was seen as a triplet at 1.26 ppm and ester CH_2 as a quartet at 4 18 ppm and the number of olefinic protons was reduced to two They appeared as a doublet of triplets at 5.90 ppm (J=10.3 and 2 6 Hz) and as a doublet of doublets at 6.18 ppm (J= 10 3 and 3.1 Hz). The aldehyde proton appeared as a singlet at **9.73** ppm. The structure of **258** was thus confirmed from above observations.

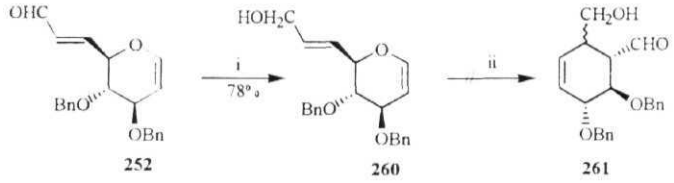
Claisen rearrangement of 257 under similar conditions as those for **256** furnished the rearranged carbocycle **259** along with recovery of starting material and some decomposition (Scheme 64) The 'H **NMR** spectrum of 259 immediately confirmed its structure. as the two olefinic protons appeared as multiplet at 5.99 ppm. The aldehyde proton appeared as a singlet at 9.61 ppm In the IR spectrum of 259. the aldehyde absorption appeared at 1730 cm^{-1} and the nitrile band at 2245 cm^{-1}. The stereochemistnes in products **258** and **259 were** assigned by analogy to the results reported by Büchi in his paper [82]



Scheme 64. *Reagents and conditions:* **i)** *o*-dichlorobenzene **(sealed** tube), **240", 1h.**

As the trans aldehyde **252** was **available,** its reduction to the corresponding allyl alcohol and its utility as yet another substrate for the Claisen rearrangement was investigated Reduction of the aldehyde with cerium(III) chloride heptahydrate and sodium borohydride occurred smoothly and the allyl alcohol **260** was obtained in good yields The gross structure of **260** was arrived at using ^{1}H NMR data In the ^{1}H NMR spectrum of **260.** H-6 and H-7 appeared together as a multiplet at 5.91 ppm The ^{13}C NMR spectrum of **260** displayed olefinic resonances at 144.52 and 127.71 ppm along with other lines

However, the allyl alcohol **260** underwent extensive decomposition on heating in a sealed tube in *o*-dichlorobenzene at 210" for 1 Oh (Scheme 65) Hence this reaction was not pursued further



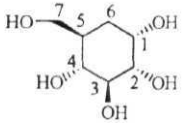
Scheme 65. *Reagents and conditions:* i) $CeCl_3.7H_2O$, $NaBH_4$, THF, MeOH. 0°, 1h; n) *o*-dichlorobenzene (sealed tube), 210°, 1()h.

Having successfully synthesized the different carbocycles **254,** 258 and 259 from carbohydrates, we wanted to use them in the synthesis of some optically pure compounds. Pseudo-sugars were identified as suitable targets, as our rearranged carbocycles meet most of the structural requirements for their conversion to pseudo-sugars.

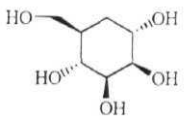
Pseudo-sugars are 2,3,4,5-tetrahydroxy-l-(hydroxymethyl) cyclohexanes in which the ring oxygen atom is replaced by a methylene group. Their structural resemblance to sugars, make them attractive targets for study in biological **systems.** Some pseudo-sugars, amino pseudo-sugars and pseudo-trisacchandes have been proven to be of medicinal importance. As stated earlier in the introduction. lot of efforts have been directed towards their enantiopure synthesis from various chiral sources, especially from sugars. However, there is a growing need for various synthetic strategies in this regard.

As pseudo-sugars in their pyranose forms are cvclohexanetetrols. our initial step towards synthesis of pseudo-sugars involved hydroxylation of the double bond

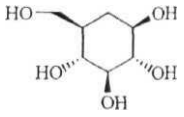
in **255** Our plan was to prepare the four pseudo-sugars. pseudo-α-D-glucopyranose. pseudo-α-D-mannopyranose. pseudo-β-D-glucopyranose and pseudo-β-D-mannopyranose, from the same precursor **255**



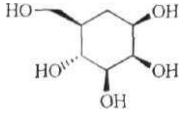
pseudo-α-D-glucopyranose



pseudo-α-D-mannopyranose



pseudo-β-D-glucopyranose

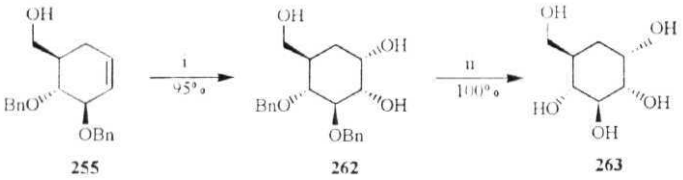


pseudo-β-D-mannopyranose

For this purpose, we wanted to hydroxylate the double bond in 255 under different conditions, in order to introduce the diol units with different stereochemistries as represented in the four pseudo-sugars mentioned above

Of the four aforementioned pseudo-sugars. we chose pseudo-α-D-glucopyranose as our initial target With a view to effect hydroxylation from the less hindered α-face. the olefin 255 was treated with osmium tetroxide. potassium hexacyanoferrate and potassium carbonate in r-butanol and water. ` Hydroxylation was smooth and the triol 262 was obtained in quantitative yield The structure of the triol 262 was supported by its spectral data The IR spectra of 255 and 262 were similar. However, in the ^{1}H NMR spectrum of 262, the olefinic protons of 255 were clearlv absent The triol 262 was hydrogenated with hydrogen and Pearlman`s

catalyst [$Pd(OH)_2/C$] at 55 psi in a Parr apparatus to give pseudo-α-D-glucopyranose (263) in **quantitative** yield (Scheme 66).



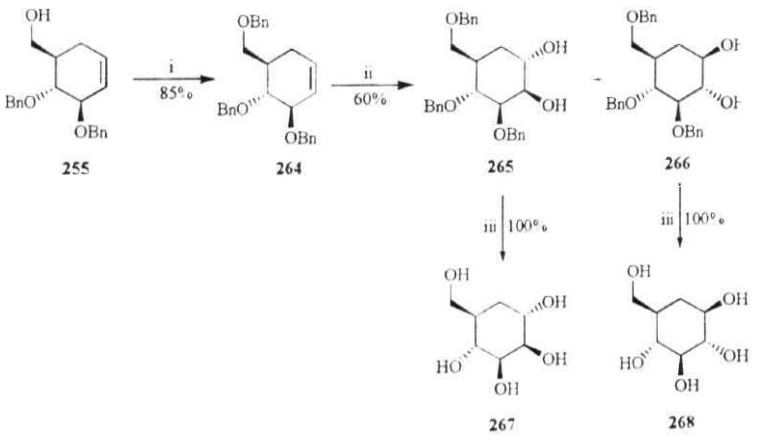
Scheme 66. *Reagents and conditions:* i) OsO_4, $K_3Fe(CN)_6$, K_2CO_3, t-BuOH, H_2O, 24h; ii) 20% $Pd(OH)_2/C$, H_2, 55 psi, 2h.

In the ^1H NMR spectrum of **263** in D_2O, no signals were present in the aromatic region, testifying to complete removal of the benzyl groups. H-6a appeared as a broad triplet at 1 32 ppm, H-6e as a multiplet at 1.72 ppm and H-1 as a multiplet at **3.93** ppm The ^{13}C NMR spectrum of **263** displayed 7 lines with C-6 and C-5 resonating at 30 26 and 38 15 ppm, respectively. The H NMR spectral data and optical rotation data of **263** were in consonance with those reported in the literature.[57]

Our next strategy involved epoxidation of the double bond in **255,** followed by hydrolysis of the epoxide under acidic or basic conditions so as to obtain a trans diol unit. At this point, it was thought better to protect the primary hydroxyl group in 255, in order to avoid its influence on epoxide opening

Conversion of the alcohol 255 to its benzyl ether **264** was straightforward Conditions for optimum yield **of 264 were** generation of the anion of **255** in **DMF** using sodium hydride, followed by quenching with benzyl bromide The structure of **264** was in accordance with its spectral and analytical data Characteristic features of the spectral data include absence of the hydroxyl absorption in the IR spectrum

and appearance of both the olefinic protons as a multiplet at 5.76 ppm and increase in the number of aromatic protons from ten in 255 to fifteen in **264** in the ^1H NMR spectrum A 16 line ^{13}C NMR spectrum further supported the structure of **264** The tribenzyl ether **264** smoothK underwent a sequence of epoxidation and ring opening on stirring first with *m*-CPBA in water and then with 10% H_2SO_4 to yield a mixture of partially benzylated pseudo-α-D-mannopyranose **265** and pseudo-P-D-glucopyranose **266** in good yield. Purification and separation of the mixture was effected by preparative tlc, which afforded 265 and 266 in pure form, whose identities were confirmed from their spectral data **265** and 266 exhibited strong hydroxyl stretches at 3425 and 3420 cm^{-1}, **respectively,** in their IR spectra The ^1H NMR spectra of **265** and **266** possessed neither olefinic nor epoxide protons



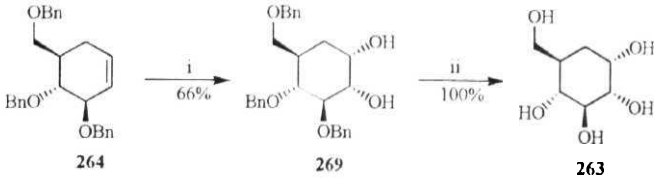
Scheme 67. *Reagents and conditions:* i) NaH. DMF. BnBr. rt. **10h;** ii) *m*- CPBA. H_2O. then 10% H_2SO_4. 48h; in) 20% $Pd(OH)_2/C$. H_2. 55 psi. **2h**

The ^{13}C NMR spectra *of* protected pseudo-sugars 265 and 266 displayed fourteen lines each Debenzylation of 265 and 266 was achieved by subjecting them to hydrogenolysis to yield pseudo-a-D-mannopyranose (267) and pseudo-P-D-glucopyranose (268) respectively. in quantitative yields (Scheme 67)

The structures of 267 and 268 were confirmed from their H NMR analysis in D_2O The ^1H NMR spectra of 267 and 268 showed no trace of aromatic protons In the case of 267, a multiplet at 1 66 ppm and a quartet at 3.96 ppm (J=? 2 Hz) were assigned to H-6 and H-1. respectively. H-6a and H-6e appeared as multiplet and doublet of triplets at 1.11 and 1.84 ppm. respectively and H-l was present in the multiplet at 3 48 ppm in the 'H NMR spectrum of 268 The ^{13}C NMR spectra of both 267 and 268 exhibited a seven line pattern Optical rotation data of 267 and 268 were in agreement with the values reported in the literature

After the efficacious syntheses of three pseudo-sugars 263. 267 and 268 out of the four as planned earlier. we next focussed our attention on the synthesis of pseudo-p-D-mannopyranose, the only remaining pseudo-sugar in our series

Synthesis of pseudo-p-D-mannopyranose from 264 requires the installation of a cis diol unit on the same face as the 3-benzyloxy group Woodward's cis hydroxylation protocol of the tnbenzyl ether 264 was thought to be best suited for this purpose, since this process in most cases results in an overall syn hydroxylation from the more hindered face. Woodward's hydroxylation*[5] of the tnbenzyl ether 264 with silver acetate, iodine and aqueous acetic acid gave a mixture of regiomeric monoacetates which were deacetylated with sodium methoxide in methanol to yield the diol 269 as the sole product The H and "C NMR spectra of 269 displayed no olefinic signals and the 'H NMR spectrum of 269 differed significantly from that of the starting material 264. No efforts were made to establish the stereochemistry of the newly introduced hydroxyl groups in 269 at this stage.



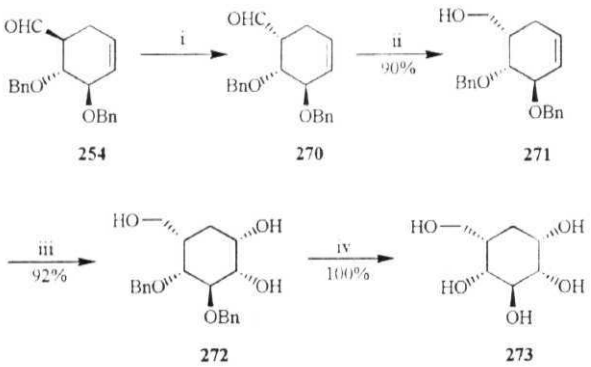
Scheme 68. *Reagents and conditions:* i) a) AgOAc, I_2, aq CH_3COOH, 90-95°, 3h; b) Na (cat amount), MeOH, 15h. ii) 20% $Pd(OH)_2/C$, H_2, 55 psi, 2h.

The diol 269 on hydrogenolysis with Pearlman's catalyst in a hydrogen atmosphere at 55 psi furnished pseudo-α-D-glucopyranose (263) instead of the anticipated pseudo-p-D-mannopyranose (Scheme 68) The identity of 263 in this instance was unambiguously established by its comparison with the sample prepared earlier from 255.

From the above result, it was realized that the Woodward's hydroxylation in this case gave an overall *syn*-hydroxylation from the less hindered a-face with good selectivity in contrast to its usual mode of *syn*-hydroxylation from the more hindered face

As mentioned earlier. 254 on standing gave the epimeric aldehyde **270** Reduction of 270 could be readily achieved by treating with sodium borohydndc in THF Thus, alcohol 271 was obtained in almost quantitative yield The ^1H NMR spectrum of 271 showed the absence of the aldehydic proton and the presence of two olefinic signals as a multiplet at 5.85 ppm Stereospecific introduction of the cis diol unit was achieved *via* osmium tetroxide hydroxylation of alcohol 271 to yield the triol **272** The structure of 272 was assigned from its IR. ^1H and ^{13}C NMR spectral data. The IR spectrum of 272 showed a strong hydroxyl absorption at 3412 cm^1. Similarly, in the 'H NMR spectrum, no signals corresponding to the olefin were

observed The ^{13}C NMR spectrum of **272** contained 16 lines. The triol 272 was hydrogenolysed with Pearlman's catalyst in a H_2 atmosphere to yield pseudo-P-L-idopyranose (273) in quantitative yield (Scheme 69).



Scheme 69. *Reagents and conditions:* i) standing at rt; ii) $NaBH_4$, THF, <2; 10 min; iii) OsO_4, $K_3Fe(CN)_6$, K_2CO_3, t-BuOH, H_2O, 24h, iv) 20% $Pd(OH)_2/C$, H_2, 55 psi, 2h.

The ^1H NMR spectrum of **273** was devoid of aromatic signals and H-6 appeared as a multiplet at 1.59 ppm. The H NMR spectral data and the optical rotation data of **273** were in agreement with those reported.[57]

The Claisen rearrangement has been used for the first time in the conversion of carbohydrates to chiral carbocycles. The above methodology has been extended to unveil a simple and convenient procedure for the synthesis of pseudo-sugars Four different pseudo-sugars. pseudo-α-D-glucopyranose, pseudo-β-D-glucopyranose, pseudo-α-D-mannopyranose and pseudo-β-L-idopyranose were arrived at in few steps from the single carbocycle **254.**

In the course of this work, it has been shown that the oxy-Copc and Claisen rearrangements can be used profitably on sugar substrates for the construction of highly functionalized 9-membered ring ethers and cyelohexenes. **respectively.**

EXPERIMENTAL

EXPERIMENTAL DETAILS

All reagents were purified by appropriate methods just before use Solvents were dried using appropriate drying agents **Solvents** used for chromatography were of commercial grade and were **fractionally** distilled before use. All organic extracts were dried o\er $MgSO_4$. Column **chromatography** was performed using **ACME** silica gel (100-200 mesh) and eluted with appropriate mixtures of hexane and ethyl acetate Thin layer chromatography (tlc) was performed on home made plates coated with ACME silica gel GF 254 (with 13% calcium sulphate as binder) and were **visualised** by shining UV light or exposing to iodine vapours Melting points were determined on a SUPERFIT melting point apparatus and arc uncorrected Optical rotations were measured on a SHIMADZU polarimeter at 25°. Infrared spectra were recorded on a JASCO FT-IR 5300 instrument ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER AF 200 NMR Spectrometer operating at 4.7 Tesla magnetic field strength in chloroform-d, with tetramethylsilane (TMS) as internal standard. unless otherwise mentioned DEPT and 2D NMR data were processed using standard software provided with **the** instrument The ^{1}H NMR spectral data are listed as follows signals are reported in parts per million (ppm) downfield of TMS. signal multiplicity is denoted as s = singlet. d = doublet. dd = doublet of a doublet. t = triplet. dt = doublet of a triplet. q = quartet, br = broad and m = multiplet. number of protons integrated for and assignments; coupling constant (J) measured in Hertz. wherever possible Elemental analyses were obtained using PERKIN-ELMER model 240C-CHN **analvser.**

FURANOSES:

5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (207) was prepared from 1,2-*O*-isopropylidene-α-D-glucofuranose according to literature procedure.[90]

Attempted oxidation of **5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose** (207):

CrO_3.2Py/ Ac_2O/ CH_2Cl_2: To a stirred solution of pyridine (0.65 ml. 8 mmol) in dichloromethane (2 ml) was added chromium trioxide (400 mg, 4 mmol) After 15 min, a solution of 207 (186 mg, 1 mmol) in dichloromethane (4 ml) was added To the resultant tarry deposit, acetic anhydride (0 37 ml. 4 mmol) was added The reaction mixture was stirred at room temperature for 10 min It was then filtered through a short column of silica gel using ethyl acetate The residue after solvent evaporation contained only starting material.

PCC/ NaOAc/ CH_2Cl_2: A solution of the alcohol 207 (50 mg, 0 27 mmol) in dichloromethane (1 ml) was added to a stirred suspension of pyridinium chlorochromate (87 mg, 0.40 mmol) and sodium acetate (5 mg) in dichloromethane (1.5 ml). After 3h, the reaction mixture was diluted with ether (20 ml) and filtered through a short column of florisil. The ether solution was concentrated The crude concentrate showed no carbonyl band in the 1R spectrum.

Silver carbonate on **celite:** To a stirred suspension of **silver** carbonate on celite (1.53 g, 5.55 mmol) in benzene (20 ml) was added the alcohol 207 (50 mg. 0 27 mmol) in benzene (1 ml). The reaction mixture was heated under reflux for 14h No reaction was observed as indicated by tlc **analysis.**

Attempted preparation of **5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-pyruvyl-α-D-*xylo*-hex-5-enofuranose** (210):

To a stirred solution of the alcohol **207** (186 mg.].() mmol) in dichloromethane (4 ml) at 0° was added a solution of pyruvic acid (105 mg. 1.2 mmol) in dichloromethane (2 ml) followed by DCC (79 mg. 1 .2 mmol) and DMAP (122 mg. 1.0 mmol) After stirring overnight at room temperature. the reaction mixture was poured into water (25 ml). the layers separated and the aqueous phase extracted with dichloromethane (3 x 20 ml) The combined organic **layers** were washed with aqueous sodium bicarbonate and dried. The reaction mixture was concentrated and chromatographed on a silica gel column No tractable material was obtained.

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-phenylglyoxyl-α-D-*xylo*-hex-5-enofuranose **(211):**

To a stirred solution of the alcohol 207 (250 mg. 1.34 mmol) in dichloromethane (5 ml) at 0° were added sequentially phenylglyoxyl chloride (271 mg. 1.61 mmol) and DMAP (409 mg. 3 35 mmol) The reaction mixture was stirred for 1h at 0° and for 5h at room temperature The reaction mixture was quenched with aqueous potassium carbonate and extracted with dichloromethane (3 x 20 ml). The dichloromethane solution was dried and concentrated The residue after purification by column chromatography gave the ester **211** (125 mg. 29%) as a colourless syrup

IR (neat) : 3000.2950. 1740. 1680. 1600. 1170. 1020. 740 cm ⁻¹.

^{1}H NMR: δ **1.28** (s. 3H. CH_3). 1 49 (s. 3H. CH_3). 4.64–4.66 (d. 1H. H-2. J=3.9 Hz). 4.75-4.85 (m. **1H.** H-4). **5.16-5.49** (m. **1H.** H-3). 5.71-5.98 (m.

5H, H-1, H-5 and $CH=CH_2$). 7.32-7.65 (m, 3H. ArH). 7.87-7.96 (m, 2H, ArH)

Attempted photolysis of the phenylglyoxylate **211**:

A solution of the phenylglyoxylate 211 (32 mg. 0 1 mmol) in deoxygenated benzene (20 ml) was photolyzed for 3h with a 450-W. medium pressure. Hanovia mercury lamp The solvent was then evaporated under reduced pressure Tlc analysis at this stage showed recovery of starting material

1,2:5,6-Di-*O*-cyclohexylidene-3-*C*-vinyl-α-D-allofuranose **(212)** was prepared as reported in the literature[63]

1,2-*O*-Cyclohexylidene-3-*C*-vinyl-α-D-allofuranose (213):

The reaction mixture containing alcohol 212 (800 mg, 2.18 mmol) and aqueous acetic acid (6 67 ml, 75% v/v) was heated to 80° for 2h. The reaction mixture was allowed to cool to room temperature and acetic acid was removed under reduced pressure. The residue was purified by column chromatography to furnish the triol 213 (463 mg, 74%) as a white solid.

M.p: 78° (ether/hexane).

$[\alpha]^{25}_D$= +31.4° (c 1.0, $CHCl_3$).

IR (KBr): 3449,2937,2876, 1128, 1010.931 cm^{-1}.

^1H NMR: 5 1 35-1 88 (m, 10H, cyclohexyl). 3.09 (s. 1H, OH). 3.65-3.87 (m, 4H, H-4. H-5. H-6 and H-6'), 4.22-4 24 (d. 1H, H-2, J=4.0 Hz), 5.36-6.00 (m, 4H, H-1 and $CH=CH_2$)

^{13}C NMR: 134.48, 116 54, 113 84, 103.26, 83 03. 80 51, 79.54. 70 53, 64.16, 36.04. 24 83, 23.91,23 51 ppm

Anal Calcd for $C_{14}H_{22}O_6$: C:58.72; H 7.74

Found C:58.65;H:7.75.

1,2-*O*-Cyclohexylidene-3-*C*-vinyl-α-D-*ribo*-pentodialdo-1,4-furanose (214):

A solution of sodium metapenodate (214 mg. 1 mmol) in water (5 ml) was added dropwise to a stirred solution of the triol 213 (286 mg. 1 mmol) in water (6 ml) at room temperature After 1h. water was removed under reduced pressure The residue was diluted with chloroform and filtered The filtrate after solvent evaporation was chromatographed on a silica gel column to yield 214 (236 mg. 93%) as a colourless syrup.

$[\alpha]^{25}_D$= +24.4° (c 0.59. $CHCl_3$)

IR(neat): 3450. 2980. 1720. 1356. 1010, 722 cm^{-1}

^1HNMR : δ 1.25-1.80 (m. 10H. cyclohexyl). 3.20 (s. 1H. OH). 4.27-4.29 (d 1H. H-2. J=3.8 Hz). 4.33 (s. 1H, H-4). 5.30-5.85 (m. 3H. CH=CH$_2$). 5.97-5.99 (d. 1H. H-1, J=3 8 Hz), 9.56 (s, 1H. CHO)

Attempted methylenation of the aldehyde 214:

Ph_3PCH_3I, n-BuLi, THF, 0°: To a stirred suspension of methyltriphenylphosphonium iodide (889 mg. 2.20 mmol) in THF (15 ml) at 0° was added a 1M solution ofn-butyllithium in hexane (2 ml. 2 mmol) The slurry was stirred at 0 for 15 min after which the aldehyde 214 (254 mg. 1 mmol) was added in THF (4 ml) and the mixture was stirred at 0° for 4h. The reaction was quenched with saturated ammonium chloride (4 ml) and the mixture was allowed to warm to room temperature The reaction mixture was diluted with ether (100 ml) and washed with water. The ether layer was dried and concentrated Tlc of the crude mixture was very complex No characterizable product was isolated from this mixture

Ph_3PCH_3I, K_2CO_3, dioxane-water, reflux: The reaction mixture containing methyltriphenylphosphonium iodide (125 mg. 0.31 mmol). potassium carbonate (55 mg, 0.40 mmol), aldehyde 214 (80 mg. 0.30 mmol) and water (1 drop) in dioxane (0 31 ml) was heated under reflux for 4h. The mixture was then filtered and the solvent evaporated under reduced pressure Tlc analysis of the reaction mixture at this stage showed the presence of a complex mixture. No attempts were made to purify this mixture.

CH_2I_2, Zn-Ti(OPr-*i*)$_4$, THF, rt, 36h: To a stirred suspension of zinc dust (206 mg, 3 15 mmol) in THF (3 ml) was added diiodomethane (468 mg. 1 75 mmol). After 30 min. a 1M solution of Ti(*i*-OPr)$_4$ (99 mg. 0.35 mmol) in THF was added and stirred at room temperature for 30 min. A solution of the aldehyde 214 (89 mg. 0.35 mmol) in THF (2 ml) was then added and stirred at room temperature for 36 h. The reaction mixture was diluted with hexane, poured into 1N HC1 (10 ml), and extracted with hexane (3 × 10 ml). The organic extracts were washed with brine, dried and concentrated Tlc of the reaction mixture showed that no reaction had taken place

1,2-*O*-Cyclohexylidene-6-*O*-(*p*-toluenesulfonyl)-3-*C*-vinyl-α-D-allofuranose (215):

To a stirred solution of the triol 213 (100 mg, 0.35 mmol) in pyridine (0.5 ml) at 0° was added *p*-toluenesulfonyl chloride (73 mg, 0 38 mmol) in chloroform (2 ml). The reaction mixture was stirred at room temperature for 24h, then quenched with water (1 ml) and diluted with chloroform (30 ml) The organic layer was washed with water, brine, dried and concentrated. The residue was purified by

chromatography on a silica gel column to afford 215 (60 mg. 39%) as a colourless syrup.

IR (neat) : 3514.2937. 1599, 1359, 1176, 1020, 850 cm ^{1}

^{1}H NMR : 6 1.25-1.80 (m. 10H. cyclohexyl). 2.44 (s. 3H, CH_3), 2.97 (s, 1H, OH). 3.72-4.30 (m. 6H. H-2. H-4. H-5 and H-6). 5.29-5.89 (m, 6H. H-1. CH=CH$_2$. CH$_2$Ph), 7.31-7.35 (d. 2H, ArH), 7.77-7.82 (d. 2H. ArH)

5,6-Anhydro-1,2-*O*-cyclohexylidene-3-*C*-vinyl-α-D-allofuranose (216):

Sodium (catalytic amount) was added to the tosylate 215 (60 mg. 0.14 mmol) in nietlianol (2 ml) and the reaction mixture was allowed to stand at room temperature for 3h. Methanol was evaporated under reduced pressure and the residue was partitioned between dichloromethane and water. The organic layer was dried and concentrated The crude product was purified by column chromatography to furnish 216 (33 mg. 91%) as a colourless syrup

^{1}H NMR : 6 1 22-1.81 (m. 10H, cyclohexyl), 2.77-2.78 (d, 2H, H-6, J=3.3 Hz), 2.87 (s, 1H, OH), 3.01-3.07 (m, 1H, H-5), 3.75-3.77 (d, 1H, H-4, J=4 8 Hz). 4.23-4.25 (d, 1H. H-2. J=4.0 Hz), 5.30-5.94 (m, 4H, H-1 and CH=CH$_2$)

Attempted deoxygenation of the epoxide 216:

To a solution of the epoxide 216 (67 mg. 0.25 mmol) in benzene (4 ml) was added a freshly prepared colourless solution of magnesium iodide in diethyl ether (1.4 ml, 0.5 mmol) (prepared by refluxing 200 mg of magnesium and 1 0 g of iodine in diethyl ether (10 ml) for 2h]. The reaction mixture was refluxed for 3h. Tlc analysis at this stage showed a complex mixture

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-enodialdo-1,4-furanose (218):

The aldehyde 214 (200 mg, 0.79 mmol) was dissolved in toluene (10 ml) and formylmethylenetriphenylphosphorane (240 mg, 0.79 mmol) was added to the stirred solution. The reaction mixture was heated at 80° for 5h, after which it was cooled and the solvent evaporated in vacuum. The residue was purified by column chromatography to furnish the aldehyde **218** (172 mg, 78%) as a pale yellow syrup

$[\alpha]_D^{25}$= +41.4° (c 1.45, $CHCl_3$).

IR(neat) : 3470, 2935, 1718, 1624, 1124, 711 cm^{-1}.

^{1}HNMR: 5 1.21-1 81 (m. 10H, cyclohexyl). 3.08 (s, 1H, OH). 4.27-4 29 (d. 1H. H-2, J=3 8 Hz), 456-454 (dd. 1H, H-4, J=3 8 and 1.3 Hz). 5.23-5.70 (m, 3H, C<u>H</u>=C<u>H</u>$_2$). 5.88-5.90 (d, 1H, H-1, J=3.6 Hz). 6.26-6.40 (m, 1H, H-6), 6.60-6.73 (dd. 1H, H-5, J=14.0 Hz and J=4.0 Hz). 9.51-9.54 (d, 1H, CHO, J=7.8 Hz)

^{13}C NMR : 193.12, 150.31, 133 72, 13261. 116.93, 113.98, 10331. 8281. 81.19, 36 13, 24.77, 23.90, 23 49 ppm.

Anal Calcd for $C_{15}H_{20}O_5$: C:64.27; H:7.19

Found: C:64.35; H:7 22.

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hex-5-enofuranose (217):

To a stirred solution of the unsaturated aldehyde 218 (280 mg, 1 mmol) in deoxygenated benzene (15 ml) was added tris(triphenylphosphine)rhodium(l) chloride (1.50 g, 1.6 mmol). The reaction mixture was heated under reflux for 2h and the solvent was evaporated. The residue was purified by column chromatography to give 217 (222 mg, 82%) as a white solid.

M.p 90-92° (hexane)

$[\alpha]^{25}_{D}$= +53.0° (c 0.35, $CHCl_3$).

IR (KBr) : 3466, 2932. 1275, 1122. 923. 734 cm^{-1}.

^{1}H NMR : 5 1 40-1.88 (m. 10H. cyclohexyl). 2.82 (s. 1H. OH). 4.26-4.28 (d. 1H. H-2. J=3.8 Hz). 4 31 (br s. 1H. H-4). 5.23-5.51 (m. 4H. 2 *x* $CH=C\underline{H}_2$). 5.67-5.83 (m. 2H. 2 x $C\underline{H}=CH_2$). 5.86-5 88 (d. 1H. H-1. J=3.8 Hz)

^{13}C NMR : 134.84, 132.04, 118.50, 116.07, 113.53, 103.23. 83.30. 82.99. 80.75, 36.23, 24.97, 24.03, 23.63 ppm

Anal Calcd for $C_{14}H_{20}O_4$: C:66.64; H:7.99.

Found: C:66.54; H7.93.

General procedure for attempted anionic oxy-Cope rearrangement of 217:

To a stirred suspension of potassium hydride (35% suspension in oil, washed with hexane to remove oil) (5 eq.) in the desired solvent was added the diene 217 (1 eq.) in the same solvent and the stirring was continued for the desired period at the specified temperature The reaction mixture was quenched with absolute ethanol at -78°. The reaction mixture was diluted with ether. washed with water. brine and dried The residue after solvent evaporation was analysed by tlc and IR

Following the above procedure, heating the reaction mixture containing 217 and potassium hydride in i) THF to 60° for 10h and ii) THF to 60° for 12h yielded the starting material. Similarly, heating the reaction mixture containing 217 and potassium hydnde at increased temperatures in i) dioxane to 100" for 8h. ii) dioxane to 100° for 10h and iii) diglyme to 140° for 15h. also afforded only starting material.

Attempted anionic oxy-Cope rearrangement of **217** with **KH/I_2**:

To a stirred suspension of mineral oil free potassium hydride (20 mg. 0.5 mmol) in THF (1 ml) was added iodine (13 mg. 0.05 mmol) in THF (0 5 ml) To the resultant suspension, the diene 217 (25 mg, 0.1 mmol) was added in THF (0.5 ml). After refluxing for 4h. the reaction mixture was worked up as described above. Tlc, 1R and 'H NMR spectra of the crude material indicated the presence of the starting compound.

Attempted anionic oxy-Cope rearrangement of 217 with **KH/18-C-6**:

The diene 217 (25 mg, 0.1 mmol) and 18-C-6 (132 mg. 0 5 mmol) in diglyme (5 ml) were added to a stirred suspension of mineral oil free potassium hydride (20 mg, 0.5 mmol) in THF (1 ml). The reaction mixture was refluxed for Xh and worked up as usual Recovery of starting material was indicated by tlc and was further confirmed from IR and ^{1}H NMR spectral data

Attempted anionic oxy-Cope rearrangement of 217 with **KH/n-Bu_4NI**:

To a stirred suspension of mineral oil free potassium hydride (20 mg. 0.5 mmol) in THF (1 ml) was added the diene 217 (25 mg. 0.1 mmol) and tetra-n-butylammonium iodide (185 mg, 0.5 mmol) in THF (4 ml) After refluxing for 10h, the reaction mixture was worked up as usual. No rearranged product was obtained as indicated by tlc and spectral data

Reaction of the aldehyde 214 with carbethoxymethylenetriphenyl phosphorane:

A solution of the aldehyde 214 (254 mg, 1 mmol) in benzene (5 ml) was heated to reflux in the presence of carbethoxymethylenetriphenylphosphorane (383 mg, 1.1 mmol) for 4h. The solvent was evaporated under reduced pressure and the

residue was chromatographed on a silica gel column to yield the cis ester 220a (127 mg) as a white solid and the trans ester 220b (126 mg) as a light yellow syrup which solidified on standing (overall yield 78%).

Ethyl **1,2-*O*-cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(Z)-eno**-furanuronate (220a):

M.p. 84-88 (hexane/ethyl acetate)

$[\alpha]^{25}_D$= -71.2° (c 1.0, $CHCl_3$).

IR (KBr): 3485. 2943. 1722, 1660. 1190, 935 cm'.

^{1}H NMR: 5 1.26-1 33. (t. 3H. $CH_2\underline{CH_3}$). 1.40-1.90 (m. 10H. cyclohexyl), 3.85-3.86 (br s. 1H. H-4). 4 14-4 24 (q. 2H. $\underline{CH_2}CH_3$), 4.29-4.31 (d. 1H, H-2. J=3.8 Hz), 5.26-5.32 (dd. 1H. H-6. J=10.7 and 1.4 Hz). 5.47-6.12 (m. 5H. H-1, H-5 and $\underline{CH}=\underline{CH_2}$).

^{13}C NMR: 166 45. 144 02. 134 36. 123.01, 116.85. 113.58, 103.54. 83.32, 83.08. 60.79, 36.26, 36.12, 24.92, 23.95. 23.53, 14.09 ppm.

Anal Calcd for $C_{17}H_{24}O_6$ C:62.94; H 7 46

Found C:62.90; H:7.45.

Ethyl **1,2-*O*-cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-eno**-furanuronate (220b):

M.p: 56-58° (hexane/ethyl acetate)

$[\alpha]^{25}_D$= +56.9° (c 0.45, $CHCl_3$)

IR (KBr): 3485.2943. 1720. 1662, 1178, 939 cm^{-1}

^{1}H NMR: 8 1 20-1 26 (t. 3H. $CH_2\underline{CH_3}$), 1.40-1.86 (m. 10H. cyclohexyl). 3.09 (br s. 1H. OH). 4 07-4 18 (q. 2H. $\underline{CH_2}CH_3$). 4.22-4.24 (d. 1H. H-2, J=3.6 Hz). 443-4.45 (m. 1H. H-4). 5.18-5.69 (m. 3H. $\underline{CH}=\underline{CH_2}$),

5.82-5.84 (d, 1H, H-1, J=3.8 Hz), 5.98-6.07 (dd, 1H, H-6, J=15.6 and 1.4 Hz), 6.72-6.82 (dd, 1H, H-5, J=15.7 and 4.0 Hz).

^{13}C NMR : 166.10. 141.23. 134 14, 122.68, 116 64. 113 77, 103.30, 83 01, 81.43. 81.00, 60.30, 36.20, 24.82, 23.92, 23.51, 14 13.

Anal. Calcd for $C_{13}H_{24}O_6$: C62 94; H:7.46.

Found: C:62.85; H:7.45.

Attempted selective reduction of the conjugated double bond in 220a:

A mixture of the cis ester 220a (32 mg, 0.1 mmol) and magnesium turnings (24 mg, 1 mmol) in methanol (1 ml) was stirred at room temperature for 5h The reaction was quenched by adding 3N HC1 to dissolve excess magnesium and the reaction mixture was extracted with ether (2 × 5 ml). The combined organic extracts were washed with brine and dried. Evaporation of the solvent afforded only starting material as indicated by tlc and IR.

Ethyl **1,2-*O*-cyclohexylidene-5,6-dideoxy-3-*C*-ethyl-α-D-*ribo*-heptofuranuronate** (221):

5% Pd/C (9 mg) was added to a solution of the cis ester 220a (30 mg, 0.09 mmol) in deoxygenated ethyl acetate (2 ml). The reaction mixture was stirred in a H; atmosphere (balloon) for 30min. The catalyst was removed by filtration and the filtrate was concentrated to yield 221 (30 mg)in quantitative yield as a colourless syrup, which crystallized on standing.

M.p: 64° (hexane).

$[\alpha]^{25}_D$= -91.7° (c 0.6, $CHCl_3$).

IR(neat) : 3518,2937, 1736, 1371, 1109, 1012,943 cm^{-1}.

^{1}H NMR δ 0.96-1.03 (t. 3H. $CH_2\underline{CH_3}$). 1.21-1.28 (t, 3H. $COOCH_2\underline{CH_3}$), 1.33-1.82 (m. 12H. H-5 and cyclohexyl), 2.41-2.57 (m, 4H, $\underline{CH_2}CH_3$ and H-6), 3.69-3.76 (q. 1H. H-4). 4.07-4.18 (q. 2H. $COO\underline{CH_2}CH_3$), 4.27-4.29 (d. 1H. H-2. J=4.0 Hz). 5.70-5.72 (d. 1H. H-1, J=4.0 Hz).

^{13}C NMR 173.21, 11269. 103 04. 81.76, 79.79. 78.91, 60.34, 36.07, 31.39, 24.89, 23.92. 23.54, 23.24, 23.07. 14.21, 7.24 ppm.

Anal. Calcd for $C_{17}H_{28}O_6$: C 62.17; H 8 59.

Found: C:62.25; H:8.64.

Ethyl **1,2-*O*-cyclohexylidene-5,6-dideoxy-3-C-ethyl-α-D-*ribo*-heptofuranuronate** (221):

Repeating the above procedure with the trans ester 220b (30 mg, 0.09 mmol). with the same quantity of 5% Pd/C also furnished 221 (30 mg) in quantitative yield

Reaction of the aldehyde 214 with acetylmethylenetriphenylphosphorane:

To a stirred solution of 214 (254 mg. 1 mmol), in benzene (11 ml) was added acetylmethylenetriphenylphosphorane (350 mg, 1.1 mmol) and the resultant solution heated under reflux After 4h. the reaction mixture was worked up as described for **220** Chromatographic purification over a column of silica gel gave the cis ketone 222a (11 mg) as colourless solid and the trans ketone 222b (218 mg) as a colourless solid (overall yield 78%)

1,2-*O*-Cyclohexylidene-5,6,8-trideoxy-3-*C*-vinyl-α-D-*ribo*-oct-5(Z)-enofuranos-7-ulose (222a):

M.p: 72° (hexane/ethyl acetate)

$[\alpha]^{25}_D$= -157.1° (c 0.07, $CHCl_3$).

IR (KBr) : 3470, 2935, 1697, 1624, 1124, 925 cm^{-1}.

^1H NMR: 5 1.40-1.90 (m, 10H, cyclohexyl), 2.27 (s, 3H, COCHj). 2.95 (s, 1H, OH). 4.29-4.31 (d, 1H, H-2, J=3 8 Hz), 4.43 (br s, 1H, H-4), 5.25-6.00 (m. 5H. H-1, H-6 and CH=CH_2), 6.37-6.43 (m, 1H, H-5, J=10.8 Hz).

^{13}C NMR : 199 72. 142 60, 134.83, 13021, 116.87, 113.66, 103.60. 83 24, 36.29. 36.09, 30.77, 24.94, 23.95, 23.54 ppm.

Anal. Calcd for $C_{15}H_{22}O_5$: C:65.29; H:7 53.

Found C:65.32;H:7.55.

1,2-*O*-Cyclohexylidene-5,6,8-trideoxy-3-*C*-vinyl-α-D-*ribo*-oct-5(E)-eno furanos-**7-ulose** (222b):

M.p: 98° (hexane/ethyl acetate).

$[\alpha]^{25}_D$= +79 6° (c 0.47, $CHCl_3$).

IR (KBr) : 3531, 2999. 2930, 1700, 1624, 1024, 727 cm^{-1}.

^1H NMR : 5 1.40-1 83 (m, 10H, cyclohexyl), 2.24 (s, 3H, COCHj), 2 95 (s, 1H, OH), 4 28-4 30 (d, 1H, H-2, J=3.7 Hz), 4 48-4.51 (m, 1H, H-4), 5.26-5.69 (m, 3H, CH=CH_2), 5.89-5 91 (d, 1H, H-l, J=3 8 Hz), 6 28-6 36 (dd, 1H, H-6, J=16.0 and 1.4 Hz), 6 58-6.69 (dd, 1H, H-5, J=16.0 and J=4.0 Hz).

^{13}C NMR : 197 87. 140 41, 134 14, 131.44, 116 90, 114 05, 103.49, 83.05, 81 50. 81 26, 36.34, 27.37, 24.98, 24.10, 23.70 ppm.

Anal. Calcd for $C_{15}H_{22}O_5$: C 65.29; H:7 53

Found: C65.18; H:7 66.

1,2-*O*-Cyclohexylidene-5,6,8-trideoxy-3-*C*-vinyl-α-D-*ribo*-oct-5(Z)-eno furanos-**7-ulose** (222a):

A solution of **214** (200 mg, 0.79 mmol) in methanol (1.5 ml) was added to a solution of acetylmethylenetriphenylphosphorane (290 mg. 0.95 mmol) at -78". The reaction mixture was stirred at -78° for 1h and then at room temperature for 5h, after which the solvent was evaporated under reduced pressure Upon chromatographic purification over a column of silica gel. the cis ketone **222a** (55 mg) as a colourless solid and the trans ketone **222b** (100 mg) as a colourless syrup (overall yield 67%) were obtained. The spectral properties of **222a** and **222b** were identical with the earlier prepared samples.

Reaction of the aldehyde **214** with cyanomethylenetriphenylphosphorane:

To a stirred solution of **214** (165 mg. 0 65 mmol) in benzene (5 ml) was added cyanomethylenetriphenylphosphorane (294 mg. 0.97 mmol) and heated under reflux After 4h, the reaction mixture was worked up as described earlier in the case of **220.** The residue after purification by column chromatography afforded the nitrile 223a (142 mg)as a white solid and the trans nitrile **223b** (24 mg) as a colourless syrup (overall yield 93%).

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(Z)-enofuranuro-nitrile (223a):

M.p: 106° (hexane/ether).

$[\alpha]^{25}_D$= -4.6° (c 1.0. $CHCl_3$).

IR (KBr): 3433,3059. 2224, 1444, 1116, 991 cm^{-1}.

^1H NMR: 8 1.41-1.90 (m, 10H, cyclohcxyl). **3.0** (s. **1H.** OH). 4.28-4.30 (d, 1H, H-2. J=3.8 Hz), 4.73-4.77 (d. 1H. H-4, J=7.8 Hz). **5.30-5.82** (m. 4H,

$CH=CH_2$ and H-6), 5.91-5 **93** (d, 1H, H-1, J=3 8 Hz), 6.25-6.34 (dd. 1H. H-5. J=11 7 and 7.8 **Hz).**

^{13}C NMR : **147.56, 133.05,** 117.38, 115.21, 114.16, 103.72, **102.38,** 82.46. **80.95,** 36.13, 24.81, **23.95,** 23.53 ppm.

Anal, Calcd for $C_{15}H_{19}O_4N$: C64.96; H6.91, N 5.05.

Found: C:65.14; H:7 04; N:5.03.

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-enofuranuronitrile (22Jb):

$[\alpha]^{25}_D$= +64.0° (c 0 65, $CHCl_3$).

1R (neat) : 3537, 2939, 2227, 1641, 1111, 736 cm^{-1}.

^1H NMR : 5 1.36-1.80 (m, 10H, cyclohexyl), 2.97 (s, 1H, OH), 4.28-4.30 (d, 1H. H-2, J=3.8 Hz), 4.44-4.47 (m, 1H, H-4), 5.30-5.68 (m, 4H, H-6 and $CH=CH_2$), 5.88-5.90 (d, 1H, H-1, J=3.8 Hz), 6.56-6.67 (dd, 1H, H-5, J=16.0 and 4.0 Hz).

^{13}C NMR : 148.24, 133 36, 11719, 116.88, 114.16, 103 30, 100.70, 82.79. 81.22, 80.96, 36 17, 36.12, 24.75, 23.90, 23 49 ppm.

Anal. Calcd for $C_{15}H_{19}O_4N$: C64.96; H6 91; N:5.05.

Found: C65.12; H:6.97; N:5.12.

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-enofuranuronitrile (223b):

A solution of **223a** (50 mg, 0 18 mmol) and diphenyl disulphide (10 mg. 0 05 mmol) in deoxygenated benzene (25 ml) was photolvsed for 1h using a high pressure mercury lamp and Pyrex filter. The solvent was evaporated under reduced pressure and the residue was purified by column chromatographv to afford the trans

nitrile 223b (18 mg. 36%) (recovered starting material 32 mg) as a colourless syrup. The spectral properties of **223b** and **223a** obtained from this experiment were identical with those of earlier prepared samples

1,2-*O*-Cyclohexylidene-5,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-enofuranose (224):

Cenum(III) chloride heptahydrate (256 mg. 0.72 mmol) in methanol (1.9 ml) was added to a stirred solution of the unsaturated aldehyde **218** (190 mg. 0.68 mmol) in THF (0.80 ml) at 0°. To the reaction mixture. sodium borohydnde (50 mg. 1.33 mmol) was added portionwise and was stirred at 0° for 1h and at room temperature for 2h The residue was partitioned between ethyl acetate (50 ml) and water (50 ml). The aqueous layer was extracted with ethyl acetate (2 x 60 ml) and the combined organic layers were dried and evaporated The crude product was purified by chromatography to yield **224** (139 mg. 73%) as a colourless syrup.

IR (neat): 3350, 2900, 1360, 1120. **1010,** 720 cm^{-1}.

^1H NMR : 5 1.40-1.82 (m, 10H, cyclohexyl). 4.09-4.12 (d. 2H. H-7, J=5.5 Hz), 4.22-4.24 (d. 1H, H-2, J=3 8 Hz). 4.26-4.30 (m. 1H. H-4), 5.23-6.02 (m, 6H, H-1, CH=CH$_2$ H-5 and H-6)

1,2-*O*-Cyclohexylidene-5,6-dideoxy-7-*O*-(t-butyldiphenylsilyl)-3-*C*-vinyl-α-D-*ribo*-hept-5(E)-enofuranose (225):

To a stirred solution of the unsaturated alcohol **224** (150 mg. **0.53** mmol) in DMF (3 ml) at 0° was added imidazole (79 mg. **1.17** mmol) and t-butylchlorodiphenylsilane (160 mg. 0.58 mmol) The reaction mixture was stirred at 0" for lh and for 12h at room temperature. The reaction mixture was diluted with ethyl acetate (20 ml), washed with water (2 x 20 ml). dried and concentrated. The

residue on column chromatography afforded the silyl ether **225** as a colourless syrup in quantitative yield.

IR (neat) : 3425. 3072. **2932,** 1427, 1113, 740 cm^{-1}.

^1H NMR 5 1 OS (s, 9H, t-butyl), 1.40-1.85 (m, 10H, cyclohexyl), 4.20-4.22 (m, 1H, H-4), 427-429 (d, 1H, H-2, J=3.8 Hz), **5.27-5.80** (m, **6H,** $CH=CH_2$, H-5. H-6 and H-7), 5.87-5 89(d, 1H, H-1, J=4 0 Hz), **7.38-7.42 (m, 6H,** ArH), 7.69-7.74 (m, 4H, ArH)

Attempted anionic **oxy-Cope** rearrangement on **the** silyl ether 225:

To a stirred suspension of potassium hydride (36 mg, 0.89 mmol) in THF (1 ml) was added the silyl ether 225 (50 mg, 0.18 mmol) in THF (1 ml) and heated under reflux. After 6h, the reaction mixture was cooled to -78°, quenched with ethanol and extracted with ether. The ether solution was dried and concentrated Purification on **a** silica gel column gave only starting material.

General procedure for sealed tube reactions:

A solution of the diene in *o*-dichlorobenzene was heated in a sealed tube to 200-220° for 12h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was purified by column chromatography

(3'aR*,10'aS*)-3'a,8',9',10'a-Tetrahydro-spiro[cyclohexane-1,2'-[1,3]dioxolo-[4,5-b]oxoninl-10'-(7'H)-one(219):

As described above, heating the diene **217** (100 mg, 0.40 mmol) at 200-220° for 12h and purification of the reaction mixture gave the rearranged product **219** [16 mg, recovered starting material 60 mg, yield: 40% (based on recovered starting material)] as a colourless syrup.

$[\alpha]^{25}_{D}$= -36.2° (c 0.63, $CHCl_3$).

IR (neat) 2937, 1738. 1651, 1095, 1053. 754 cm^{-1}.

^1H NMR : 5 1 40-2.12 (m, 12H. H-5 and cyclohexyl). 2 36-2.37 (m, 3H, H-6 and H-5). 2.70-2.82 (m. 2H. H-4), 4.60-4.62 (d. 1H, H-2, J=4.0 Hz). 4 74-4.86 (m, 1H. H-7). 5.58-5.60 (d, 1H. H-1, J=4.0 Hz), 6.16-6.19 (d. 1H, H-8, J=5.5 Hz).

^{13}C NMR : 206.56. 142.70, 114.40, 113.98, 101.29, 84.57, 37.23, 37.02, 36.18. 35.87, 24.92, 23.93. 23.76, 23.37, 22.63 ppm.

Anal Calcd for $C_{14}H_{20}O_4$: C66.64; H:7.99.

Found; C:66 40: H8.08.

Note: For ^1H and ^{13}C NMR spectral assignment purposes, the numbering of compounds 219. 227. 228 and 229 has been done as shown on page 54 of results and discussion and not as in the systematic names given here.

Ethyl **(3'aR*,10'aS*)-3'a,7',8',9',10',10'a-hexahydro-spiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-b]oxonin]--10'-oxo-7'-carboxylate** (227):

The cis ester 220a (50 mg. 0.15 mmol) on thermal oxy-Cope rearrangement under above mentioned conditions furnished the rearranged product 227 [4 mg. recovered starting material 40 mg. yield: 40% (based on recovered starting **material)]** as a colourless syrup.

Heating the trans ester 220b (50 mg. 0 15 mmol) at 200-220° for 12h gave no rearranged product

$[\alpha]^{25}_{D}$= -1.12° (c 1.15, $CHCl_3$).

IR(neat): 2935, 1736, 1657, 1114, 1049, 760 cm^{-1}.

^{1}H NMR : δ 1.20-1.28 (t, 3H, $COOCH_2CH_3$), 1 29-1.76 (m, 11H, H-5 and cyclohexyl), 2 31-2.40 (m. 2H, H-4' and H-5), 2.72-2 78 (m, 1H. H-4), 3.44-3.56 (m, 1H, H-6), 4.06-4 19 (q, 2H, $COOCH_2CH_3$), 4 63-4.65 (d, 1H, H-2, J=4.0 Hz), 4.96-5 32 (m, 1H, H-7), 5.57-5.59 (d. 1H, H-1, J=4 0 Hz), 6 21-6 24 (d, 1H. H-8, J=5.5 Hz).

^{13}C NMR : 210.0, 173.76, 143 24. 115.12, 111.72. 101.34, 84.34, 60 82. 40.12. 37.43, 36.17, 36.06, 26 38, 24.80, 23 83, 23 73, 14 16 ppm.

Anal Calcd for $C_{17}H_{24}O_6$: C:62 94; H7.46.

Found: C62 75; H:7.43

(3'aR*,10'aS*)-3'a,8',9',10'a-Tetrahydro-spiro[cyclohexane-1,2'-[1,3]dioxolo-(4,5-bloxoninl-7'-acetyl-10'-(7'H)-one(228):

As mentioned above for the diene 217, heating the cis ketone 222a (60 mg. 0.20 mmol), in a sealed tube furnished the rearranged product 228 [1 mg. recovered starting material 40 mg, yield : < 5% (based on recovered starting material)] as a colourless syrup.

The trans ketone 222b (60 mg, 0.20 mmol), underwent oxy-Cope rearrangement to furnish 228 [6 mg, recovered starting material 30 mg, yield: 20% (based on recovered starting material)] as a colourless syrup. Its spectral properties were identical with those of the earlier prepared sample.

$[\alpha]^{25}_D$= +50.0° (c 0.1, $CHCl_3$).

IR(neat): 3452, 2937, 1740. 1712, 1369, 1114, 736 cm'.

^{1}H NMR : 5 1.39-2.75 (m, 17H, H-4. H-5, $COCH_3$ and cyclohexyl), 3.51-3.64 (m. 1H, H-6), 4.68-4.70 (d. 1H, H-2, J=4.0 Hz), 4 88-4.96 (m, 1H. H-7). 5.59-5.61 (d, 1H, H-l, J=4.0 Hz), 6.32-6.35 (d, 1H, H-8, J=5 6 Hz)

T N M R : 208 88. 208 36. 141.38, 114 08. 112.47, 101.11, 84.05, 47.64. 36 08. **35.16,** 34.34. 28.88, 25.37, 25.04, **24.01, 23.72** ppm

Anal Calcd for $C_{16}H_{22}O_5$: **C:65.29; H:7.53.**

Found: C:65.32; H 7 76

(3'aR*,10'aS*)-3'a,7',8',9',10',10'a-Hexahydro-spiro[cyclohexane-1,2'-[1,3]-dioxolo|4,5-b]oxonin]-10'-oxo-7'-carbonitrile (228):

Subjecting the cis nitrile 223a (100 mg. 0.36 mmol) to thermolysis at 200-220' for 12h yielded the rearranged product 229 |24 mg. recovered starting material 60 mg. yield: 60% (based on recovered starting material)] as a white solid

The trans nitrile 223b (100 mg. 0.36 mmol) under similar conditions as those for 223a furnished 229 [2 mg. recovered starting material 60 mg. yield: 5% (based on recovered starting material)] as a white solid Spectral features of the rearranged products obtained from 223a and 223b were identical.

M.p: 110-112° (hexane).

$[\alpha]^{25}_D$= -157.3° (c 0.1, $CHCl_3$).

IR (KBr) 3418, 2935, 2243, 1718. 1660, 1053, 760 cm^{-1}.

'H NMR : 6 1.29-1.86 (m, 14H. H-4, H-5 and cyclohexyl), 3.54-3.68 (m, 1H. H-6), 4.64-4.66 (d. 1H. H-2, J=4.0 Hz). 4 83-4.93 (m, 1H, H-7). 5.57-5.59 (d. 1H. H-1, J=4.0 Hz), 6 24-6 27 (d. 1H, H-8, J=5.5 Hz)

'TNMR: 203.58. 144.65, 120 87. 115.69, 108.48, 101.38, 85.96, 84 05. 37.39, 35.96, **35.63,** 29.67. 27.34, 25 47. 24.71, 23.78, 23.68. 22.67 ppm

Anal. Calcd for $C_{15}H_{19}O_4N$: **C:64.96; H:6.91;** N:5.05.

Found: C:65.00; H:6.93; **N:5.08.**

Attempted oxy-Cope rearrangement of 220a in the presence of bis(benzonitrile)dichloropalladium(II):

A solution of the unsaturated ester **220a** (20 mg, 0 06 mmol) and bis(benzonitrile)dichloropalladium(II) (12 mg, 0.06 mmol) in benzene (1.5 ml) was stirred at room temperature for 12h Benzene was removed in vacuum and DMSO was added to quench the complex The reaction mixture was diluted with dichloromethane, washed with water and the organic layer was dried and evaporated The residue contained only starting material as indicated by the H NMR spectrum

Attempted oxy-Cope rearrangement of 220a in the presence of mercuric trifluoroacetate:

To a stirred solution of **220a** (20 mg, 0.06 mmol) in dichloromethane (2 **ml)** was added mercuric trifluoroacetate (26 mg, 0.06 mmol). The reaction mixture was stirred at room temperature for 36h, after which solid sodium borohydnde (2 mg, 0.06 mmol) was added. The organic layer was dried and evaporated to yield recovered starting material

Attempted oxy-Cope rearrangement of 220a in the presence of lithium perchlorate:

To a stirred solution of lithium perchlorate (532 mg, 5 mmol) in ether (1 ml) was added the unsaturated ester **220a** (50 mg, 0.15 mmol) and stirred at room temperature for 36h. The reaction mixture was diluted with dichloromethane and washed with water. The organic layer was dried and on evaporation only starting material was obtained

The above experiment was conducted in diglyme (1.5 ml) and heated at 120" for 24h After the usual workup. tlc showed decomposition of **220a**

PYRANOSES:

Methyl 4,6-*O*-benzylidene-2-*O*-(*p*-toluenesulfonyl)-α-D-*ribo*-hexopyranosid-3-ulose **(230)** was prepared from D-glucose following literature procedure [71]

Attempted addition of vinylmagnesium bromide to methyl 4,6-*O*-benzylidene-2-*O*-(*p*-toluenesulfonyl)-α-D-*ribo*-hexopyranosid-3-ulose (230):

To a solution of vinylmagnesium bromide (generated from 89 mg of Mg and an excess of vinyl bromide in THF) was added the ketone **230** (400 mg. 0.92 ml) in THF (7 ml) and the contents were heated under reflux for 5h The reaction mixture was quenched with saturated ammonium chloride and partitioned between water and ether The organic layer was dried. concentrated and purified on a silica gel column No characterizable product was obtained

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside **(232)** was prepared as reported in the literature "

Attempted reaction of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-manno-pyranoside (232) with DMSO and oxalyl chloride:

To a stirred solution of DMSO (0.13 ml. 1.9 mmol) in dichloromethane (0.5 ml) at -60° was added **oxalyl** chloride (0.17 ml. 1.9 mmol) in dichloromethane (0.2 ml). After 15 minutes. the epoxide **232** (200 mg. 0.76 mmol) in dichloromethane (3 ml) and dry methanol (3µl) were added and stirred at -60° After 30 min. triethylamine **(0.53** ml. 3.8 mmol) was added and the reaction mixture was

allowed to come to room temperature The reaction mixture was diluted with dichloromethane (50 ml), washed with water, brine and dried Only a complex mixture was obtained as indicated by tlc

Methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-glucopyranoside **(234)** was prepared from methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside following reported procedure.[7]

Methyl **6-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-*xylo*-hexopyranosid-4-ulose** (235):

A solution of methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-glucopyranoside **(234)** (96 mg, 0.20 mmol) in benzene (1.5 ml) was added to a stirred suspension of pyridinium chlorochromate (73 mg, 0.34 mmol) in benzene (2 ml) After heating under reflux for 2h, the reaction mixture was cooled, diluted with ether (20 ml) and filtered through a short column of florisil. The ether solution was concentrated and purified by chromatography to give **235** (29 mg, 31%) as a colourless syrup.

IR (neat): 3063, 3032. 2926, 1724, 1602, 1275. 1097. 736 cm^{-1}.

Attempted addition **of** vinylmagnesium bromide to 235:

Vinylmagnesium bromide (generated from 15 mg of Mg and a solution of vinyl bromide in THF) was added to the ketone 235 (70 mg, 0.15 mmol) in THF (1.5 ml) and refluxed for 24h. The reaction mixture was worked up as described for **230.** Tlc analysis at this stage showed a complex mixture. No purification was attempted.

Following reported procedure, methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (237) was prepared from methyl 2,3-di-*O*-benzyl -α-D-gluco pyranoside

Methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-*xylo*-hexopyranosid-4-ulose (238):

A solution of the methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (237) (170 mg. 0.41 mmol) in benzene (3 ml) was added to a stirred suspension of pyridinium chlorochromate (150 mg. 0.70 mmol) in benzene (3 ml) After heating under reflux for 3h, the reaction mixture was worked up as described for **235** The residue was chromatographed to furnish 238 (43 mg. 25%) as a colourless syrup]R (neat) : 3032. 2928, 1724, 1740, 1099, 734 cm^{1}.

Attempted addition of vinylmagnesium bromide to 238:

To a stirred solution of vinylmagnesium bromide (generated from 45 mg of Mg and a solution of vinyl bromide in THF) was added a solution of the ketone 238 (190 mg, 0.46 mmol) in THF (4 ml). After stirring the reaction mixture at room temperature for 24h, the usual workup was done. Tlc of the crude product showed it to be a complex mixture.

Methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-α-D-glucopyranoside was oxidised to methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid -4-ulose (239) using DMSO and Ac_2O as reported in the literature.[77]

Attempted addition of vinylmagnesium bromide to 239:

Vinylmagnesium bromide (generated from 46 mg of Mg and a solution of vinyl bromide in THF) was added to the ketone 239 (120 mg. 0.19 mmol) in THF (5

ml) and refluxed for 1 Oh. The reaction mixture was then worked up as described for **230** Only starting material was recovered.

Methyl **2,3-di-*O*-benzyl-4-*C*-ethynyl-6-*O*-triphenylmethyl-α-D-gluco-** and **gala-**ctopyranosides (240):

A solution of methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (239) **(6.15** g. 10 mmol) in THF (50 ml) was added to a sUrred solution of ethynylmagnesium bromide (generated from 2 43 g of Mg. 100 mmol and excess acetylene) in THF (20 ml) at -20°. The reaction mixture was wanned to room temperature and stirred for 4h Saturated aqueous ammonium chloride was added to the reaction mixture and the solvent was evaporated under reduced pressure The residue was diluted with ether. washed with water, brine and dried. The resultant crude product was purified by chromatography to give an epimeric mixture of the alcohols 240 (4.5 g, 70%) as a colourless syrup.

IR(neat): 3474, 3298, 3061, 2935, 1450. 1053, 738 cm^{1}.

^{1}H NMR : 5 2.26(s, 1H, acetylenic). 2 39 (s. 1H. acetylenic), 3.26-4.00 (m, 8H, H-2, H-3, H-5. **H-6, OMe),** 4.56-4.94 (m, 5H, H-1 and -OCH_2Ph), **7.19-7.54** (m, 25H, ArH).

^{13}C NMR : 144.01, 143.60, 138.99, 138 36. 138.21, 128.84, 128.73, 128.44, 128.08, 127.99. 127.86, **127.26, 127.02,** 98.30, 98.17, 87.93, 87.14, 83.27, 82.49, 81.34, 81.12, 78 55. **75.78, 75.61,** 74 21, 74 06, 73.74, 73.62, 72.33, 71 22. 70 15. 64.06. 63.49. 55 34 ppm.

Attempted partial hydrogenation of the propargyl alcohols 240 with Lindlar's catalyst:

A suspension of the propargyl alcohols 240 (1 eq) and Lindlar's catalyst (0.1 eq.) in hexane:benzene (2:1) was subjected to hydrogen atmosphere (balloon) for 8h. The reaction mixture was filtered and evaporated to give back unreacted starting material Carrying out the partial hydrogenation at increased pressures. i) 40 Psi for 8h and ii) 55 Psi for 5h in a Parr hydrogenation set-up also resulted in recovery of starting material

Attempted partial hydrogenation of the propargyl alcohols 240 with Pdc:

Preparation of Pdc[7h]:

To a stirred suspension of sodium hydride (1 44 g. 60 mmol) and palladium acetate (2.24 g. 10 mmol) in THF (40 ml) at 4()° was carefully added a solution of t-amyl alcohol (1.76 g. 20 mmol) in THF (10 ml) so that the reaction temperature did not exceed 45°. After stirring for 3h at 45° . t-amyl alcohol (2 82 g. 32 mmol) was added to neutralise the remaining sodium hydride. and the mixture was allowed to come to rt The resultant non pyrophonc black suspension is Pdc

To a suspension of Pdc in THF (0.2 ml) and quinoline (0 2 ml) exposed to a hydrogen atmosphere for 30 nun. the propargyl alcohols 240 (50 mg. 0.08 mmol) was added and stirred under hydrogen atmosphere (balloon) for 48h The reaction mixture was then filtered and evaporated The residue contained only starting material The partial hydrogenation of propargyl alcohols 240 was attempted at increased pressures. in a Parr hydrogenation set up i) 40 Psi for 6h and ii) 50 Psi for 4h In both the cases after usual workup only starting material was recovered

Methyl **2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-4-*C*-vinyl-α-D-gluco-** and galacto-pyranosides **(241):**

To a stirred suspension of lithium aluminium hydride (237 mg, 6.24 mmol) in THF (4 ml) was added the alcohols **240(1** 0 g. **1.56** mmol) in THF (12 ml). After heating under reflux for 6h, the reaction mixture was cooled in ice and quenched by careful addition of saturated aqueous sodium sulfate. The salts were filtered and washed **several** times with THF. The filtrate was dried and concentrated The residue on chromatographic purification furnished **241** (520 mg, 52%) as a colourless syrup

IR (neat) 3497, 3061, 2935, 1450, 1051. 740. 700 cm^{-1}

H NMR δ 3 41-3 93 **(m,** 8H, H-2. H-3. H-5. H-6. OMe), 4.59-4.86 (m, 4H, -OCH$_2$Ph), **4.97** (s, 1H, H-1), 5.03 (s, 1H, H-1), 5.35-5.57 (m, 2H. CH=CH$_2$), 5 74-6.09 (m, 1H. CH=CH$_2$), **7.22-7.50** (m, 25H, **ArH).**

^{13}C NMR : 144.17, **143.85,** 139.27, 139 01, 138.52, 138.34, **135.02,** 128.85, **128.75,** 128.48, 128 33, 12807, 127 94, **127.86,** 12762, **127.21, 127.02,** 117.17, 116.40, 98 26. 87.66, 87.12, 83 55, **80.11,** 78.46, **77.89,** 77.39, 76.06, **75.63, 73.50,** 71.71, 71 10, **63.67, 62.99,** 55.27, 55.18 ppm.

Detritylation of methyl 2,3-di-*O*-benzyl-6-*O*-triphenylmethyl-4-*C*-vinyl-α-D-gluco- and galactopyranosides (241):

A solution of the alcohols **241** (650 mg, 1 01 mmol) and 98% formic acid (93 mg. 2 02 mmol) in ether (2.0 ml) was stirred at room temperature for 1h Formic acid and ether were evaporated under reduced pressure The residue was purified by column chromatography to yield the diols **243** (120 mg) and the corresponding C-6 formates **242** (254 mg) as colourless syrups

Methyl **2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-gluco-** and galactopyranosides (243):

IR (neat) : 3474. 3032. 2932. 1454. 1051, 738, 698 cm^{-1}

^1H NMR δ 2.90 (s. 1H. 2 x OH). 3.43-3.90 (m. 8H. H-2, H-3. H-5. H-6. OMe), 4 60-4.86 (m. 5H. H-1 and -OCH_2Ph). 5.35-5.57(m. 2H. $CH=CH_2$), 5.75-5.89 (m. 1H. $CH=CH_2$). 7.28-7.35 (m. 10H, ArH)

^{13}C NMR 143.87. 139.03, 138.36, 138 09. 128.72. 128.47, 128.34. 128.05, 127 90. 127 05. 116.91, 98.39, 79 70. 77.99. 76.06, 73.38. 71.20, 61.22, 55.42 ppm

Methyl **2,3-di-*O*-benzyl-6-*O*-formyl-4-*C*-vinyl-α-D-gluco-** and galactopyranosides (242):

IR(neat): 3539,2914. 1726. 1454. 1186. 1055.736 cm^1.

^1H NMR δ 3 40-4.25 (m. 8H. H-2. H-3. H-5, H-6, OMe), 4.61-4 84 (m, 4H, -OCH_2Ph). 4.95 (s. 1H. H-l). 5.05 (s. 1H. H-l). 5.36-5.44 (m, 2H, $CH=CH_2$). 5.99-6.10 (m, 1H. $CH=CH_2$), 7.28-7.43 (m, 10H, ArH), 8.03 (s. 1H, OCOH)

'TNMR: 160.66, 134 19. 128.67, 128 46. 127.96. 127.80, 117.36, 98.10. 83.26. 78 78, 75.69,75.54, 73.30. 71 03. 62 68, 55.11 ppm.

Methyl **2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-gluco-** and galactopyranosides (243):

A catalytic amount of sodium was added to the formates 242 (50 mg. 0.12 mmol) in methanol (1.5 ml) and the contents were allowed to stand at room temperature for 6h The solvent was removed under reduced pressure and the residue was partitioned between ethyl acetate and water The organic layer was dried and evaporated to yield 243 (33 mg. 69%) as a colourless syrup. ^1H and ^{13}C NMR spectra of 243 obtained from both the expennicnts were identical.

Attempted oxidation of 243 with DMSO and trifluoroacetic anhydride:

To a solution of DMSO (10 mg, 0 13 mmol) in dichloromethane (1 ml) at **-78°.** trifluoroacetic anhydride (21 mg, 0,10 mmol) in dichloromethane (1 ml) was slowly added and stirred for 30 nun. The alcohols **243** (27 mg, 0.07 mmol) in dichloromethane (1 ml) were then added After 1h. N. N-diisopropylethylamine (26 mg. 0 20 mmol) was added and the reaction mixture was allowed to come to room temperature The contents were diluted **with** dichloromethane (50 ml). washed with water. brine and dried The IR spectrum of the residue indicated that no oxidation had taken place

Methyl **2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-*gluco*-** and ***galacto*-hexodialdo-1,5-**pyranosides **(244):**

A solution of the alcohols **243** (200 mg, 0.50 mmol) in dichloromethane (5 ml) was added to a suspension of pyridinium chlorochromate (323 mg, 1.5 mmol) in dichloromethane (6 ml) After stirring at room temperature for 18h, the reaction mixture was filtered and the filtrate was evaporated. The resultant residue was column chromatographed to give **244** (40 mg, *20%)* as a colourless syrup.

IR (neat): 3472, 2926, 1730, 1454, 1053, 736, 700 cm^{-1}.

^1H NMR; 5 3.42 (s, 3H, OMe), 3.86-3.88 (m, 2H, H-2 and H-3), 4.12-4 13 (m, 1H, H-5), 4.61-4.90 (m, 5H, H-1 and -OCH$_2$Ph), 5.44-5.58 (m, 2H, CH=CH$_2$), 5 91-6 05 (m, 1H, CH=CH$_2$), 7.29-7.37 (m, 10H, ArH), **9.58** (s, 1H, CHO)

Methyl **2,3-di-*O*-benzyl-4-*C*-vinyl-α-D-*gluco*-** and ***galacto*-hexodialdo-1,5-**pyranosides (244):

To a stirred suspension of Dess-Martin periodinane (1.6 g. 3.75 mmol) in dichloromethane (10 ml) was added the diols 243 (500 mg. 1 25 mmol) in dichloromethane (8 ml) After stirring at room temperature for 3h. the reaction mixture was diluted with dichloromethane The dichloromethane layer was washed with aqueous sodium thiosulfate. aqueous sodium bicarbonate and water. The organic layer was dried. concentrated and purified by column chromatography to yield 244 (250 mg. 50%) as a colourless syrup. Its spectral features were identical with those of the sample prepared earlier

Methyl **2,3-di-*O*-benzyl-6,7-dideoxy-4-*C*-vinyl-α-D-gluco-** and **galacto-hept-6-**enopyranosides (245):

Sodamide (66 mg. 1.65 mmol) was added to a suspension of methyl triphenylphosphonium iodide (728 mg. 1.8 mmol) in ether (12 ml) and the mixture stirred at room temperature for 6h The thus formed methylenetriphenylphosphorane was added to a solution of the aldehydes 244 (600 mg. 1 5 mmol) in ether (15 ml). After 30 nun. the reaction mixture was quenched with saturated ammonium chloride and worked up as usual Clromatographic purification of the crude mixture on a silica gel column afforded 245 (300 mg. 50%) as a pale yellow syrup

1R (neat) : 3499. 2928. 1660. 1280. 1049. 700 cm^{-1}.

^1H NMR : 5 3.38-3 40 (s. 3H. OMe). 3.84 (m. 2H. H-2. H-3). 4 094.12 (m, 1H, H-5). 4.60-4.84 (m. 5H. H-1 and -$OC\underline{H}_2Ph$). 5.16-5.46 (m, 4H, 2 x $CH=C\underline{H}_2$). 5.69-6.08 (m. 2H. 2 x $C\underline{H}=CH_2$). 7.25-7.33 (m, 10H, ArH)

^{13}C NMR : 139.11. 138 32. 135 25. 132.81. 132 04. 128.44. 128.30. 128.05. 127 86. 118.55. 118.21, 116.84. 98.42. 83.15. 79.86. 77.20. 76.00. 75.57. 73 97. 73.43. 72.22. 55.50, 29.71 ppm.

Reaction of the aldehydes 244 with **carbethoxymethylenetriphenylphosphorane:**

To a stirred solution of the aldehydes 244 (60 mg. 0.15 mmol) in benzene (3 ml) was added carbethoxymethylenetriphenylphosphorane (63 mg, 0.18 mmol) After heating the reaction mixture under reflux for 4h. benzene was removed under reduced pressure The residue was column chromatographed to yield the cis esters 246a (9 mg) and the trans esters 246b (39 mg) (overall yield 68%) as colourless syrups

Ethyl [methyl **2,3-di-*O*-benzyl-6,7-dideoxy-4-*C*-vinyl-α-D-*gluco*-** and *galacto*-oct-6(Z)-eno-pyranosid|uronates (246a):

IR (neat): 3449. 2930. 1720, 1655, 1095, 698 cm^{-1}.

^{1}H NMR : δ 1.23-1.30 (t. 3H, $CH_2\underline{CH_3}$). 3 40 (s, 3H. OMe). 3.62-3.83 (m, 2H), 4.0-4.04 (d. 1H), 4.16-4.28 (q. 2H. $\underline{CH_2}CH_3$), 4 60-5.0 (m, 5H, H-1 and -O$\underline{CH_2}$Ph), 5.24-5.63 (m, 3H, $\underline{CH}$=$\underline{CH_2}$), 5 96-6 10 (m, 2H, H-6 and H-7).

Ethyl [methyl **2,3-di-*O*-benzyl-6,7-dideoxy-4-*C*-vinyl-α-D-*gluco*-** and ***galacto*-**oct-6(E)-eno-pyranosid]uronates (246b):

IR(neat): 3499.2930. 1718, 1662, 1280, 1049.738 cm^{-1}

^{1}HNMR : 5 1.23-1.30 (t. 3H, $CH_2\underline{CH_3}$), 3.40 (s, 3H, $\underline{OMe}$), 3.86-3.87 (m, 2H, H-2 and H-3). 4.12-4.23 (q, 2H, $\underline{CH_2}CH_3$). 4 32-4 34 (m, 1H. H-5), 4.62-4.87 (m, 5H, H-1 and -O$\underline{CH_2}$Ph), 5.38-5.56 (m, 2H, $\underline{CH}$=$\underline{CH_2}$,

J=6 8 and 17.4 Hz). 5.76-5.90 (m, 1H. CH=CH$_2$. **J=10.6** and 17 **4 Hz). 6.10-6.18** (d. 1H. **H-7,** J=15.7 Hz). 6 87-6 97 (dd. 1H. H-6. J=15.7 and 4.3 Hz). **7.31-7.34** (m. 10H. ArH).

^{13}C NMR : 166 12. 141.57. 138.46. 138.20. 137.94. 128 48. 128 33. 128.07. 127.95. 123 23. 118.0. 98 49. 79.72. 77.70. 76.09. 73.50. 70.53. 60 34. 55.68. 14.21 ppm

Methyl **2,3-di-*O*-benzyl-6,7,9-trideoxy-4-*C*-vinyl-α-D-*gluco*-** and ***galacto*-non-**6(E)-eno-pyranosid-8-uloses (247):

A solution of the aldehydes 244 (200 mg. 0.50 mmol) in benzene (5 ml) was added to acetylmethylenetriphenylphosphorane (206 mg. 0.65 mmol) in benzene (5 ml). The reaction mixture was heated under reflux for 4h. and the solvent was removed under reduced pressure. Purification of the crude material by column chromatography furnished the trans ketones 247 (158 mg. 72%) as a colourless syrup.

IR (neat): 3462. 3070. 1722. 1633. 1275. 1113. 706 cm^{-1}.

'H NMR : 5 2.22 (s. 3H. COCH$_3$). **3.41** (s. 3H. OMe). 3.77-3.98 (m. 2H H-2 and H-3). 4.32-4.34 (m. 1H, H-5), 4 58-4.87 (m. 5H. H-1 and -OCH$_2$Ph). 5.38-5.54 (m. 2H. CH=CH$_2$. **J=6.8** and **17.3** Hz). **5.75-**5.89 (m. 1H. CH=CH$_2$. **J=10.6** and 17.3 **Hz), 6.29-6.37 (dd.** 1H. **H-7.** J=15.7 and 1.6 **Hz), 6.70-6.81** (m, **1H,** H-6, **J=15.7** and 4.4 Hz), 7.31-7.34 (m. 10H. ArH)

^{13}C NMR : 19804. 140.36. 138.66. 138.18. 13792. 132 20. 12847. 128.32. 128 03. **127.96,** 117 85. 98.58. 79.67. 77.70, 76 08. 73.49. 70 74. **55.74, 27.23 ppm.**

General procedure for attempted anionic oxy-Cope rearrangement of 245, 246a, 246b and 247:

To a stirred suspension of potassium hydride (5 eq) in the desired **solvent** was added the dienes (1 eq) in the same **solvent** and the stirring was continued at the temperatures and time periods as given below. The reaction mixture was then quenched with absolute ethanol at **-78°.** The reaction mixture was diluted with ether, washed with water, brine and dried. The residue after **solvent** evaporation was **analysed** by tlc and IR

According to the general procedure, heating potassium hydride and the dienes **245** in i) THF at **60°** for 10h, ii) diglyme at 120° for 24h and iii) toluene at 110° for 24h led to decomposition. Carrying out the above reaction with **246a** in i) dioxane to 80° for 12h. ii) diglyme to 100° for 4h and iii) THF to **60°** for 10h led to decomposition. Similarly, heating potassium hydride and **246b** in i) diglyme to 120° for 6h and ii) dioxane to 100° for 5h also led to decomposition. Heating a mixture of **247** and potassium hydride in THF at 60° for 12h as described in the general procedure, gave a complex mixture which could not be purified

General procedure for attempted anionic oxy-Cope rearrangement **of 245, 246b and 247 with KH/n-Bu_4NI:**

To a stirred suspension of mineral oil free potassium hydride (5 eq) in the desired solvent was added the diene (1 eq.) and tetra-n-butylammonium iodide (5 eq.) in the same solvent After stirring for the required time, the reaction mixture was worked up in the usual manner No rearranged product could be obtained.

Carrying out the above reaction with **245** in THF at 60° for 1 Oh led to decomposition, while **246b** under similar conditions **yielded** a complex mixture The

reaction with 247 in diglyme at 80° for 2h also was not fruitful, leading to extensive decomposition.

General procedure for attempted thermal oxy-Cope rearrangement of 245, 246a and 246b:

A solution of the substrate in *o*-dichlorobenzene was heated in a sealed tube Evaporation of the solvent afforded the crude residue Heating 245 in *o*-dichlorobenzene to 180° for 12h gave the starting material as the major component along with slight decomposition. The thermal oxy-Cope rearrangements of 245 at 240-260° for 1h led to extensive decomposition, while at lower temperatures, (<200°) the starting material was recovered Heating 246a in *o*-dichlorobenzene to 180° for 12h, resulted in recovery of starting material Thermal oxy-Cope rearrangement of 246b was attempted by following the above procedure at 220 for 5h led to a complex mixture.

PSEUDO-SUGARS:

1,5-Anhydro-3,4-di-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (250) was prepared from tri-*O*-acetyl-D-glucal following literature procedure.[79]

2,6-Anhydro-3,4-di-*O*-benzyl-5-deoxy-D-*arabino*-hex-5-enose (251):

A solution of 1,5-anhydro-3,4-di-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (250) (2.4 g. 7.35 mmol) in dichloromethane (100 ml) was added to a stirred suspension of pyridinium dichromate (9.7 g. 25.73 mmol) and 4A molecular sieves (9.7 g) in dichloromethane (50 ml). After 10h. the reaction mixture was diluted with ether and filtered through a short column of silica gel. The ether solution was

concentrated and the crude aldehyde 251 was used in the next step without further purification.

Attempted Wittig reaction on **2,6-anhydro-3,4-di-*O*-benzyl-5-deoxy-D-*arabino*-hex-5-enose (251):**

To an ice cooled suspension of methyltriphenylphosphonium iodide (75 mg. 0.18 mmol) in THF (2 ml) was slowly added 1M n-BuLi (0.17 ml, 0.17 mmol) and the reaction mixture was allowed to stir at the same temperature for 30 min. The aldehyde **251** (40 mg, 0.12 mmol) in THF (1 ml) was then added and the contents were allowed to come to room temperature before quenching it with saturated ammonium chloride. The compound was extracted into ether (3 × 10 ml) and the combined organic layers were dried and evaporated. Tlc analysis showed a complex mixture.

4,8-Anhydro-5,6-di-*O*-benzyl-2,3,7-trideoxy-D-*arabino*-oct-2(E),7-dienose (252):

The aldehyde **251** (100 mg, 0 31 mmol) and formylmethylene-triphenylphosphorane (94 mg, 0.31 mmol) in toluene (4 ml) were heated to 80° for 2h. Toluene was removed under reduced pressure and the crude mixture was chromatographed on a silica gel column to give the unsaturated aldehyde 252 (60 mg, 56%) as a pale yellow syrup.

IR (neat) : 2928, 2854, 1730, 1435, 1265, 740 cm!

^{1}HNMR : 5 3.67-3.73 (m, 1H), 3.88-3.96 (m, 1H), 4.20-4.29 (m, 1H), 441-4 80 (m, 4H, -OCH$_2$Ph), 5 00-5.09 (m, 1H), 6 27-6 69 (m, 2H, H-1 and H-7), 6.80-6.90 (dd, 1H, H-6, J=16.0 Hz and 4.0 Hz), 7 30-7.37 (m. 10H, ArH), 9.44-9 48 (d, 1H, CHO, J=8 0 Hz)

1,5-Anhydro-3,4-di-*O*-benzyl-2,6,7-trideoxy-D-*arabino*-hept-1,6-dienitol (253):

To a stirred solution of the unsaturated aldehyde **252** (60 mg. 0.17 mmol) in deoxygenated benzene (5 ml) was added tns(tnphcnylphosphine)rhodium(I) chloride (252 mg. 0.27 mmol). The reaction mixture was heated under reflux for 4h and the solvent evaporated The residue was purified by column chromatography to gnc **253** (15 mg. 27%) as a pale yellow syrup

$[\alpha]^{25}_{D}$= -70.2° (c 1.3, $CHCl_3$).

IR (neat) : 3065. 2862. 1643. 1238. 1095. 696 cm^{-1}.

^{1}H NMR : 6 3.58-3.65 (dd. **1H).** 4.21-4.26 (dd. 1H). 4.30-4.40 (t. 1H). 4 61-4.92 (m. 4H). **5.29-5.48** (m. 3H). 5.94-6 14 (m, 1H), **6.40-6.45 (d.** 1H), 7.20-7.33 (m, 10H. ArH)

^{13}C NMR : 144.63. 139.90. 139.82. 134 54. 12847. 128.02, 127.81. 12771, 118.23, 100 48. 78 50. 78.11. **75.63,** 73.87, 70.74 ppm.

Anal Calcd for $C_{21}H_{22}O_3$: C78.23. H 6.88.

Found: C 78 28. H:6.85

1,5-Anhydro-3,4-di-*O*-benzyl-2,6,7-trideoxy-D-*arabino*-hept-1,6-dienitol (253):

Sodamide (135 mg. 3.39 mmol) was added to a suspension of methyl triphenylphosphonium iodide (1.5 g. **3.68** mmol) in ether (20 ml) and stirred at room temperature for 6h The resultant methylenetriphenylphosphorane was added to a solution of the aldehyde **251** (1.0 g. **3.08** mmol) in ether **(10** ml). After 30 min, the reaction mixture was quenched with saturated ammonium chloride and worked up as usual. Chromatographic purification of the crude mixture on a silica **gel** column afforded **253** (300 mg. 62%) as a pale **yellow** syrup Its spectral properties were identical to that reported earlier

Attempted Claisen rearrangement of 253 in N, N-diethylaniline:

A solution of 253 (200 mg. 0 62 mmol) in N. N-diethylaniline (3 ml) was heated to 220' in a sealed tube for 8h. The contents were cooled and diluted with ethyl acetate The organic layer was washed with 2N HC1. water. bnne and dried Tlc analysis at this stage showed a complex mixture.

(lS,2R,3R)-2,3-Dibenzyloxy-4-cyclohexenecarboxaldehyde(254):

A solution of 253 (200 mg, 0.62 mmol) in o-dichlorobenzene (4 ml) was heated to 240° in a sealed tube After 1h, the reaction mixture was cooled and the solvent was removed under reduced pressure to give the crude aldehyde 254

(3R,4R,5R)-3,4-Dibenzyloxy-5-hydroxymethylcyclohexene (255):

To an ice cooled solution of the crude aldehyde 254 (325 mg, 1.01 mmol) in THF (5 ml) was added sodium borohydride (153 mg, 4.04 mmol) in portions and the reaction mixture stirred for 10 min. The reaction mixture was quenched with 10% aqueous citric acid and the THF was removed under reduced pressure The residue was diluted with ethyl acetate It was then washed with water. brine and dried. The crude product was purified by column chromatography to yield the alcohol 255 (292 mg, 90%) as a colourless syrup.

$[\alpha]^{25}_{D}$= -27.0° (c 1.75, $CHCl_3$).

IR (neat) : 3445. 2924, 1454, 1093, 1028, 698 cm^{-1}.

^{1}H NMR : δ 1.81-2 21 (m, 3H), 2 52-2 66 (br s. 1H. OH). 3 57-3 71 (m, 3H). 4.20-4.27 (m, 1H), 4 67-5.03 (m, 4H, -OCH_2Ph). 5 74-5 78 (m, 2H), **7.30-7.48** (m, 10 H, ArH).

^{13}C NMR 138.42. 128.57, 128.48, 128.21, 127 87. 127 72. 125 95, 82.00. **81.15,** 74.30, **71.30, 65.53,** 40.62, 28.05 ppm

Anal Calcd for $C_{21}H_{24}O_3$ C77.7. H 7 46

Found: C:77.8: H 7.46.

Ethyl **4,8-anhydro-5,6-di-*O*-benzyl-2,3,7-trideoxy-D-*arabino*-oct-2(E),7-dieno**-uronate (256):

A solution of the **aldehyde** 251 (200 mg. 0.62 mmol) and carbcthox>Tncthylenetnphcnylphosphorane (258 mg. 0.74 mmol) in benzene (7 ml) was heated to reflux for 5h The solvent was removed and the residue was purified by column chromatography to yield the unsaturated ester 256 (200 mg. 82%) as a pale yellow syrup.

$[\alpha]^{25}_D$= +26.0° (c 1.9, $CHCl_3$).

IR(neat): 2928, 1722. 1188, 1111, 702, 491 cm^{-1}.

^1H NMR : 6 1.25-1.32 (t, 3H, $CH_2\underline{CH_3}$), 3.60-3.68 (m. 1H, H-4), 4.13-4.24 (q. 2H, $\underline{CH_2}CH_3$), 4 47-4.82 (m. 4H), 4.90-4.96 (m, 1H, H-2, **H-5** and $-OC\underline{H_2}Ph$), 6.09-6.17 (d, 1H. H-7, J=15.8 Hz). 6 42-6.45 (d. 1H. **H-**1, J=6.0 Hz), **7.09-7.16** (dd, 1H. **H-6, J**=4.0 and 15.8 **Hz), 7.22-7.45** (m, 10H, ArH).

^{13}C NMR : 166.07, 144.26, 143.12, 138 26, 137.68, 128 47. **128.11,** 12795. 127.70, 122.44, 10055. **75.72,** 74.82. 73 82. 70.62, 60 48. 1423 ppm

4,8-Anhydro-5,6-di-*O*-benzyl-2,3,7-trideoxy-D-*arabino*-oct-2(E),7-dienonitrile (257):

To a stirred solution of the **aldehyde** 251 (350 mg. 1.08 mmol) in benzene (12 ml) was added cyanomethylenetriphenylphosphorane (488 mg. 1.62 mmol) and the reaction mixture was maintained at 80° for 10h The usual workup and

chromatographic purification of the crude product over **a** column of silica gel gave the required unsaturated nitrile 257 (280. 75%) as a colourless syrup.

$[\alpha]^{25}_{D}$ = -5.6° (c 1 0. $CHCl_3$)

IR (neat) 3065.2868,2226, 1651, 1454, 1244, 1091, 698 cm^{-1}.

^1H NMR : 5 **3.56-3.64** (m. **1H, H-4**), 4 20-4.27 (m, 1H, H-3), 4.48-5.01 (m, 6H, H-2. **H-5** and **-OCH_2Ph**), 5.62-5.70 (d, 1H, H-7, **J=16 4** Hz), 6.42-6.45 **(d, 1H, H-1, J=6 1** Hz). 6.79-6.90 (dd, 1H, H-6, **J=4**.0 and 16.4 Hz), 7 30-7.50 (m,10H, ArH).

^{13}CNMR 149 64, 143 76, 136 21, 137 34. 128 52, 128 17, 128 08, 127.75, 100 84. 100.38 ppm.

General procedure for the Claisen rearrangement of vinyl ethers 256 **and** 257:

The vinyl ether in *o*-dichlorobenzene was heated to **240°** in **a** sealed tube for 1h. After cooling to room temperature, the solvent was removed in vacuum. **The** crude compound after purification on a silica gel column afforded the pure rearranged product.

(1S,2S,3R,4R)-Ethyl 3,4-dibenzyloxy-2-formyl-5-cyclohexenecarboxylate (258):

IR **(neat)** : 2922, 1730, 1724, 1454, 1099, 688 cm^{-1}

^1H NMR : δ 1.22-1.29 **(t, 3H, $CH_2\underline{CH_3}$)**, 3.05-3.11 (t, 1H), 3.61-3.62 (m, 1H), 3.99-4.05 (m, 1H), 4.12-4 23 (q, 2H,$\underline{CH_2}CH_3$), 4.32-4.38 (q, 1H), 4.55-4.85 (m, 4H, **-$O\underline{CH_2}Ph$**), 5.85-5 94 (dt, 1H, J=10.3 and 2.6 Hz), 6.14-6 21 **(dd, 1H, J=3 1** and 10 3 Hz), 9.73 **(s, 1H, $C\underline{H}O$)**

(1S,2S,3R,4R)-3,4-Dibenzyloxy-2-formyl-5-cyclohexnecarbonitrile (259):

I R (neat) 3032, 2926, 2245, 1730, 1454, 1070, 700 cm^{-1}.

^{1}H NMR 6 3 12-3 18 (m, 1H). 3.79-3.95 (m. 2H). 4.25 (s. 1H). 4 39-4 61 (m. 4H. -OCH$_2$Ph). 5 94-6 03(m. 1H). 7 17-7.22 (m. 1H). 7 27-7 40 (m, 10H. ArH). 9 61 (s. 1H. CHO)

1,5-Anhydro-3,4-di-*O*-benzyl-2,6,7-trideoxy-D-*arabino*-oct-1,6(E)-dienitol (260):

An ice-cooled stirred solution of the unsaturated aldehyde **252** (32 mg. 0.14 mmol) in **THF** (0 06 ml) was diluted with **0.4** M cerium(III) chloride heptahydrate in methanol (0.25 ml) and further with methanol (0.12 ml) and treated with sodium borohydnde (7 mg). After stirring further for 1h. the reaction mixture was partitioned between ethyl acetate (10 ml) and water (10 ml) The organic laser was washed with water. brine and dried The residue after solvent evaporation was purified by column chromatography to yield the alcohol 260 (25 mg. 78%) as a colourless syrup.

^{1}H NMR : 6 3.57-3.64 (m, 1H), 4.10-4.94 (m. 9H). **5.86-5.96** (m. 2H, H-6 and **H-7). 6.42-6.45** (d, 1H, H-1. J=6 1 Hz).

^{13}C NMR : 144.52. 138 70. 133 18. 128.41. 128 05. 127 71. **127.27, 100.34,** 78.16. 77.20, 75.35, 73.75. 70.69, 62.87 ppm.

Attempted Claisen rearrangement of 260:

The alcohol 260 (30 mg, 0.09 mmol) in *o*-dichlorobenzene (2 ml) was heated to 210° in a sealed tube for 10h. After cooling to room temperature. the solvent was removed in **vacuum.** Purification of the residue on a silica gel column gave no tractable material

(lS,2S,3R,4R,5R)-3,4-Dibenzyloxy-5-hydroxymethyl-l,2-cyclohexanediol(262):

To a solution of the alcohol **255** (80 mg, 0 25 mmol) in t-butyl alcohol (1 72 ml) and water (1.72 ml) were added potassium hexacyanoferrate(III) (226 mg, 0 75 mmol), potassium carbonate (95 mg, 0.75 mmol) and a solution of osmium tetroxide in t-butanol (57 µl, 0 003 mmol). The reaction mixture was stirred at room temperature for 24h. after which sodium sulphite was added and stirring continued for several hours. The pale blue solution was concentrated to dryness under reduced pressure and the residue was extracted thoroughly with ethyl acetate The solvent was removed in vacuum and the crude product was purified by column chromatography to yield the triol **262** (88 mg) in quantitative yield as a colourless syrup.

$[\alpha]^{25}_D$= +28.0° (c 0.15, $CHCl_3$).

1R (KBr) : 3408, 3030, 2926, 1454, 1089, 698 cm^{-1}.

^{1}H NMR : δ 1.40-1.80 (m, 3H), 3.40-3.88 (m, 5H), 4.04-4.10 (m, 1H), 4.72-5.04 (m, 4H, -OC$\underline{H}_2$Ph), 7.26-7.36 (m, 10H, ArH)

Pseudo-α-D-glucopyranose (263):

The triol **262** (27 mg, 0.08 mmol) in MeOH was hydrogenated at 55 Psi pressure for 2h in a Parr apparatus using 20% $Pd(OH)_2/C$ (Pearlman's catalyst, 3 mg). **The** catalyst was filtered off and the solvent was evaporated to give pure **263** as **a** colourless syrup in quantitative yield (13 mg).

$[\alpha]^{25}_D$= **+57.0°** (c 0.65, H_2O); lit $[\alpha]^{20}_D$= +70.0° (c **1.02, H_2O)**[57]

^{1}H NMR (D_2O) : 5 1.28-1 36 (br t, 1H), 1 66-1 77 (m, 2H), 3.07-3.58 (m, 5H), 3.92-3 93 (m, 1H).

^{13}C NMR (D_2O) : **74.66, 74.04,** 73.44, **68.95, 62.63,** 38 15, 30.26 ppm.

(3R,4R,5R)-5-Benzyloxymethyl-3,4-dibenzyloxycyclohexene (264):

To a stirred suspension of mineral oil free NaH (29 mg. 1 2 mmol) in DMF (3 ml) was added a solution of the alcohol **255** (324 mg. 1 mmol) in DMF (4 ml) After 30 min, benzyl bromide (0.24 ml. 2 mmol) was added and the reaction mixture was stirred for 10h After the usual workup with ethyl acetate (3 x 30 ml), and chroniatographic purification of the crude product over a column of silica gel. the required tribenzyl ether **264** (340 mg. 85%) was obtained as a colourless syrup

$[\alpha]^{25}_{D}$= +3.4° (c 1.6, $CHCl_3$).

IR (neat): 3030, 1496, 1454, 1155. 1097. 696 cm!

^{1}H NMR : 6 2.02-2.30 (m, 3H, H-5 and **H-6), 3.54-3.75** (m. **3H.** H-4 and **H-7). 4**.12-4 24 (m, **1H. H-3). 4.50-5.92** (m. **6H.** -OCH_2Ph), **5.66-5.85** (m. 2H, H-1 and H-2), 7.24-7.40 (m. 15H. ArH)

^{13}C NMR : 139.14, 138.76, 128.52, 128.34, 127.91, 127.78. 127.51, 126 17. **81.11,** 79.62, 74.29, **73.17,** 71 44, 70.64, 39.47, 28 81 ppm

Anal. Calcd for $C_{28}H_{30}O_3$: C:81 12; H:7 29.

Found: C:81 18; H7.31.

Hydroxylation of (264):

To **a** stirred dispersion of the tribenzyl ether **264** (84 mg. 0.20 mmol) in deionized water (0.45 ml), *m*-CPBA (38 mg. 0.22 mmol) was added and was stirred at room temperature for 8h 10% H_2SO_4 (0 03 ml) was then added and the mixture was stirred for a further 48h The aqueous solution was extracted with ethyl acetate (3 × 10 ml) and the combined organic layers were washed with sodium bicarbonate. water, brine and dried. The crude diol was purified by preparative tlc to afford 265 (30 mg. 36%) and **266** (22 mg. 24%) as colourless syrups

(lS,2R,3R,4R,5R)-5-Benzyloxymethyl-3,4-dibenzyloxy-l,2-cyclohexanediol **(265):**

$[\alpha]^{25}_D$= +14.3° (c 0.7, $CHCl_3$).

IR(neat) : 3425, 3065, 1454, 1267, 1055, 738 cm^{-1}

^1H NMR: 5 1.52-1.86 (m, 3H, H-5 and H-6). 3 56-3 61 (t. 2H. H-7). 3 73-3 84 (m, 2H). 3.88-4.03 (m, 2H), **4.46-4.79** (m, 6H, OCH_2Ph). 7.24-7 35 (m, 15H, ArH)

^{13}C NMR : 138.40, 128 48. 128.33, 127.84. **127.55,** 81.56. 74.12, 73.04, 72.68. 71.95, 70.56, 68.68, 37.28. 30.03 ppm.

(lR,2S,3R,4R,5R)-5-Benzyloxymethyl-3,4-dibenzyloxy-l,2-cyclohexanediol (266):

$[\alpha]^{25}_D$= +40.4° (c 0 45, $CHCl_3$).

IR(neat): 3420, 3062, 1454. 1266, 1055, 738 cm^{-1}.

^1H NMR : 6 1.50-1.84 (m, 3H, H-5 and H-6), 3 34-3.38 (m, 2H), 3.49-3 63 (m, 4H), 4.48-5 02 (m, 6H, $-OCH_2Ph$). 7 23-7 35 (m, 15H. ArH)

^{13}C NMR : 138.43, 128.62. 128.36, 127.85, 127.57. 85.78. 81.00, 75.34, 75.09, 74.11, **71.97,** 69.81, 39.50, 32.15 ppm.

General procedure for the hydrogenation of 265 and 266:

A solution of the alcohol in methanol (3 ml) was taken in a 250 ml Parr hydrogenation flask and Pearlman's catalyst (3 mg) was added Hydrogenation was carried out at 55 psi for 2h The catalyst was filtered off and the **solvent** evaporated to give the products

Pseudo-α-D-mannopyranose (267):

The alcohol **265** (10 mg. **0.02** mmol) upon hydrogenation gave pscudo-a-D-mannopyranose **(267)** (4 mg) as a colourless syrup in quantitative yield

$[\alpha]^{25}_{D}$= +1.5° (c 0.4, MeOH). lit $[\alpha]^{20}_{D}$=+1.9° (c **1.0,** MeOH)[59]

^{1}H NMR (D_2O) : **8 1** 52-1 78 (m. **3H). 3.36-3.68** (m. **4H).** 3.88-3.91 (br t. 1H). 3.94-3.98 (q. 1H).

^{13}C NMR (D_2O) : 72.59. 72.36. **70.30, 69.0,** 62.55, **38.70,** 28.28 ppm.

Pseudo-β-D-glucopyranose (268):

The alcohol **266** (10 mg. 0.02 mmol) was hydrogenated to furnish pseudo-P-D-glucop\ranose **(268)** (4 mg) as a colourless syrup in quantitative yield

$[\alpha]^{25}_{D}$= +10.0° (c 0.3, H_2O). lit $[\alpha]^{20}_{D}$=+10.9° (c 0.83, H_2O)[57]

^{1}H NMR (D_2O) :6 1.01-1 20 (m. 2H). I 37-1 64 (m. 1H), 1.79-1.89 (dt, **1H,** J=4.7 Hz). 3.05-3.16 (m, 3H), 3.32-3.64 (m, 3H).

^{13}C NMR (D_2O) : 77.12, 76.95. 72.88. 71.22, 62.42, 40.20, 31.79 ppm.

(1S,2S,3R,4R,5R)-5-Benzyloxymethyl-3,4-dibenzyloxy-1,2-cyclohexanediol (269):

To a solution of the tribenzyl ether **264** (20 mg, 0.05 mmol) in glacial acetic acid (0.2 ml) was added **silver** acetate (16 mg. 0.09 mmol) and finely powdered iodine (12 mg. 0 05 mmol) over a period of 30 min, at room temperature After 30 min. aqueous glacial acetic acid (0.02 **ml,** prepared by dilution of 2.0 ml of water up to 50 ml **with** glacia] acetic acid) was added The reaction mixture was heated to 90-95° for 3h The reaction mixture was then cooled. excess sodium chloride was added and the insoluble salts were filtered off. The precipitate was washed with ethyl acetate and the solvent was removed in vacuum. The resultant residue was taken **in**

methanol (2 ml) and sodium (catalytic amount) was added The reaction mixture was allowed to stand for 12h at room temperature The reaction mixture was neutralised by careful addition of dilute HC1 at 0°, The residue was concentrated to dryness and column chromatographed to afford the diol 269 (14 mg, 66%) as a colourless syrup

^{1}H NMR : 6 1 **60-1.67** (m. 2H). 1.90-2.02 (m. 1H), **3.47-3 60** (m, **3H), 3.70-3.83** (m. 2H). 4 06-4 09 (m. 1H). **4.47-5.03** (m. 6H. -OCH$_2$Ph), 7.27-7 35 **(m.** 15H. ArH).

^{13}C NMR 138 63. 128.69. **128.35,** 127 86. 127.57. **83.55, 81.17,** 75.25, 74.84, 74.45. 73 10. 69.80, **68.27,** 37.45, 30.53 ppm

Pseudo-α-D-glucopyranose (263):

A solution of the alcohol 269 (10 mg, 0.02 mmol) in methanol (3 ml) was taken in a 250 ml Parr hydrogenation flask and Pearlman's catalyst (3 mg) was added. Hydrogenation was carried out at 55 psi for 2h The catalyst was filtered off and the solvent was evaporated to yield pseudo-α-D-glucopyranose **(263)** (4 mg) as a colourless syrup in quantitative yield. Its spectral properties were identical with that reported earlier

Aldehyde **(254)** on standing at room temperature yielded **(1R,2R,3R)-2,3-dibenzyloxy-4-cyclohexenecarboxaldehyde (270).**

(3R,4R,5S)-3,4-Dibenzyloxy-5-hydroxymethylcyclohexene(271):

To a solution of the **aldehyde** 270 (163 mg, 0.5 mmol) in THF (3 ml) at 0° was added sodium borohydride (76 mg, **2.02** mmol) portionwise and the mixture was stirred for 10 min before quenching with 10% aqueous citric acid. THF was

then removed under reduced pressure The residue was diluted with ethyl acetate and washed with water The organic layer was dried and evaporated to give the crude alcohol. Purification by chromatography on a silica gel column gave the pure alcohol **271** (150 mg. 92%) as a colourless syrup.

^{1}H NMR : 6 **2.05-2.07** (m, **2H). 2.35-2.42 (m.** 1H), **3.40-3.63** (m. 2H). 3.81-3.87 (m. 2H). 4 48-4 60 (m. 4H, -OC$\underline{H}_2$Ph), **5.70-6.00** (m. 2H). 7.27-7.30 (m. 10H, ArH).

(1S,2S,3R,4R,5S)-3,4-Dibenzyloxy-5-hydroxymethyl-1,2-cyclohexanediol (272):

Potassium hexacyanofcrrate(III) (226 mg. 0.75 mmol), potassium carbonate (95 mg. 0 75 mmol) and a solution of osmium tetroxide in t-butyl alcohol (57 µl, 0.003 mmol) were sequentially added to a solution of the alcohol 271 (80 mg, 0.25 mmol) in t-butyl alcohol (1.72 ml) and water (1.72 ml). The reaction mixture was stirred at room temperature for 24h. Sodium sulphite was then added to the reaction mixture and was stirred for 2h. The pale blue solution was concentrated to dryness under reduced pressure and the residue was extracted thoroughly with ethyl acetate. The solvent was removed under reduced pressure and the crude product was purified on a silica gel column to furnish the triol 272 (81 mg. 92%) as a colourless syrup.

$[\alpha]^{25}_D$= +1.5° **(c 0.9, $CHCl_3$)**

1R (neat): 3412, 2932, 1454, 1072, 1028, 700 cm^{-1}.

^{1}H NMR: 5 1 59-1.64 (m, 2H), **2.03-2.21** (m, **1H), 3.61-3.64** (d. **2H,** J=6.4 **Hz),** 3.78-3 85 (m, 1H), 3.86-3.95 (m, 3H). **4.47-4.67** (m, 4H). 7.27-7.38 (m. 10H. ArH).

^{13}C NMR : 137.98. 137.14. 128.67, 128.50. **128.29,** 127.91. 127 69, 75.34, **73.22,** 72.75, 72.62, 67.90, 63.53. **37.91,** 27.11 ppm

Pseudo-β-L idopyranose (273):

A solution of the tool ***272*** *(50 mg, 0.15 mmol) in methanol (6 ml) was hydrogenated at 55 psi for 2h in a Parr apparatus using 20% Pd(OH)₂/C (Pearlman's catalyst, 6 mg) to afford* ***273*** *(25 mg) as* a colourless syrup in quantitative yield

$[\alpha]^{25}_D$= +11 5° (c 1.0, H_2O), lit. $[\alpha]^{20}_D$= +8.5° (c 1.02, H_2O)[57]

^{1}HNMR (D_2O) :5 1.48-1.69 (m, 2H), 1.86-2.08 (m, 1H), 3 46-3.63 (m, 4H), 3.80-3 84 (m, 2H)

REFERENCES

1 *Carbohydrates as Organic Raw Materials;* F. W. Litchenthaler, Ed.; VCH Publishers: Weinheim/New York, **1991**

2, *Bioactive Carbohydrates in Chemistry. Biochemistry and Biology;* J F Kennedy, C A White, Eds ; Halsted Press: New York. **1983**

? *Carbohydrates as Organic Raw Materials II;* G Descotes, Ed.; VCH Publishers: Weinheim/New York. **1993**

4 *Total Synthesis of Natural Products: The "Chiron" Approach;* S. Hanessian. Pergamon: Oxford. 1983

5 H Kunz and K Ruck. *Angew. Chem Int Ed Engi,* 1993. *32,* 336

6 Y Shimizu. H. N. Chou. H Bando. G van Duyne and J. C. Clardy, *J Am Chem Soc.,* **1986,** *108,* 514.

7 a) *Marine Natural Products;* K L, Erickson and P J Scheuer, Eds ; Academic Press: New York. 1983. *Vol5,* Ch 4, p 131 b) D J Faulkner, *Nat. Prod Rep.,* **1988.** 5, 613.

8 B M Howard. G R Schulte. W. Fenical, B Solheim and J. Clardy, *Tetrahedron,* 1980. *36,* 1747

9 a) H Niwa, K Wakamatsu and K Yamada. *Tetrahedron Lett.,* **1989**, *30,* 4543 b) H Kigoshi. H Niwa. K Yamada. T J Stout and J Clardy, *Tetrahedron Lett.* 1991, *32,* 2427.

10 T Ishida and K Wada. *J. Chem Soc. Chem Commun,* 1975, 209.

11 B M Trost and T. R Verhoeven. *J Am Chem Soc* . 1980, *102,* 4743.

12 L E Overman. T. A Blumenkopf. A S Castaneda and S Thompson, *J. Am Chem Soc,* 1986. *108.* 3516

13. K Ishihara, M Kubota. H Kunhara and H Yamamoto, *J. Org Chem.,* **1996**, *61.* 4560.

14. K. C. Nicolaou, D. G. McGarry, P. K. Somers, B. H. Kim, W. W. Ogilvie, G. Yiannikouros, C. V. C. Prasad, C. A. Veale and R. R. Hark, *J. Am. Chem. Soc.*, 1990, *112*, 6263.

15. Ring Enlargement in Organic Chemistry, M. Hesse, VCH publishers Weinheim/New York, 1991

16. A. Oku, S. Ohki, T. Yoshida and K. Kimura, *J. Chem. Soc, Chem. Commun.*, 1996, 1077

17. E. Fouque, G. Rousseau and J. Seyden-Penne, *J. Org. Chem.*, 1990, *55*, 4807

18. H. Suginome and S. Yamada, *Tetrahedron*, 1987, *43*, 3371

19. a) T. Wakamatsu, K. Akasaka and Y. Ban, *Tetrahedron Lett.*, 1977, 2751 b) T. Wakamatsu, K. Akasaka and Y. Ban../ *Org. Chem*, 1979, *44*, 2008

20. N. Hanaki, K. Ishihara, M. Kaino, Y. Naruse and H. Yamamoto, *Tetrahedron*. 1996, *52*. 7297

21. R. W. Carling, J. S. Clark and A. B. Holmes,./. *Chem. Soc, Perkin Trans. I.* 1992, 83

22. E. Vedejs and D. W. Powell,./ *Am. Chem. Soc*, 1982, *104*, 2046

23. R. C. Cookson and P. S. Ray, *Tetrahedron Lett.*, 1982, *23*, 3521

24. M. R. Kling, G. A. McNaughton-Smith and R. J. K. Taylor, *./ Chem. Soc., Chem. Commun* , 199J, 1593

25. E. Vogel, *Angew. Chem Int. Ed. Engl.*, 1962, *74*, 829

26. R. C. Gadwood and R. M. Lett, *J. Org. Chem.*, 1982, *47*, 2268.

27. R. J. Ferrier and S. Middleton, *Chem. Rev*,. 1993, *93*, 2779.

28. F. O. Andersson, B. Classon and B. Samuelsson, *J. Org. Chem.*, 1990, *55*, 4699.

29. D. R. Williams and F. D. Klingler. *J. Org. Chem.*, 1988, *53*, 2134

30. a) P R McGuirk and D B Collum, ***J. Am Chem Soc*** . **1982.** *104.* 4496 b) P R McGuirk and D B Collum. *J Org Chem* . **1984.** ***49,*** 843 c) D R Williams and S -Y. Sih. *J. Am Chem Soc* . **1984**, *106*, 2949 d) S D Burke, J E Cobb and K Takeuchi, *J. Org Chem* . **1985.** *50*, 3420 c) A B Smith III and M J. Fukui. *J. Am Chem Soc,* **1987.** *109.* 1269 f) S F Martin. M S Dappen, B Dupre and C J Murphy. *J. Org Chem* . **1987.** *52*, 3706

31 S Knapp and T G M Dhar, *J Org Chem.* **1991.** *56*, 4096

32 a) S J Angyal and B M Luttrell. *Aust J Chem* . **1970.** *23.* 1831 b) T Suami. K Tadano. S Nishivama and F W. Litchenthaler. ***J.*** *Org Chem* **1973.** *38.* 3691 c) K Tadano. Y Emori. M Avabe and T Suami. *Bull Chem Soc Jpn* , 1976. ***49,*** 1108

33. D E Kiely and H G Fletcher. Jr . *J Org Chem* . 1969. ***34,*** 1386

34 F. W Litchenthaler, *Angew Chem Int Ed Engl* . **1962.** *1*, 662

35. R V. Bonnert, J Howarth. P R Jenkins and N J Lawrence, *J. Chem Soc., Perkin Trans., I.* **1991**, 1225

36 J L Primeau, R C Anderson and B Fraser-Reid. *J. Am Chem Soc* . **1983.** *105*, 5874

37 L Pettersson. T Frejd and G Magnusson. *Tetrahedron* ***Lett.,*** **1987.** ***28.*** 2753

38 J. Marco-Contelles, C Pozuelo. M L Jimeno. L Martinez and A Martinez-Grau, *J. Org Chem.*, **1992**, *57*, 2625

39 T. V RajanBabu, *J Am Chem Soc* . **1987.** *109.* 609

40 H J Bestmann and H A Heid. ***Angew.*** *Chem Int Ed Engl.* **1971.** *10.* 336

41 T K M. Shing. D A Elsley and J G Gillhouley. *J. Chem Soc., Chem Commun,* **1989,** 1280

42 H. Ito, Y Motoki. T. Taguchi and Y. Hanzawa. *J Am Chem. Soc* . **1993.** *115.* 8835

43. R. Blattner, R J. Fcrrier and S. R. Haines. *J. Chem. Soc., Perkin. Trans.. I.* **1985**, 2413

44 T. Suami and S. Ogawa, *Adv Carbohydr Chem Biochem.,* 1990, *48.* 21.

45 I Miwa, H Hara, J. Okuda, T Suami and S. Ogawa. *Biochem. Int..* 1985, //. 809

46. S Ogawa, Y. Uematsu, S Yoshida, N Sesaki and T. Suami, *J. Carbohydr Chem.*, 1987, 6,471.

47 S Ogawa, *Yuki Gosei. Kagaku Kyokai Shi* , **1985**, *43,* 26.

48 T W Miller, B H. Anson and G. Albers-Schonberg, *Biotech. Bioeng.,* 1973. *15*, 1075.

49 S Horii, H. Fukase, T. Matsuo, Y Kameda, N Asano and K. Matsui, *J. Med. Chem..* 1986, 29, 1038.

50 N Asano, T. Yamaguchi, Y. Kameda and K Matsui, *J. Antibiot.*, 1987, *40,* 526.

51 T Tsuno, C Ikeda, K. Numata, K Tomita, M Konishi and H. Kawaguchi, *J. Antibiot.,* **1986**, *39*, 1001.

52. G E McCasland, S. Furuta and L J Durham, *J Org. Chem.,* 1966. *31.* 1516

53 S. Ogawa, Y. Iwasawa, T. Nose and T. Suami, *J. Chem. Soc. Perkin. Trans.. I.* 1985, 903.

54 H Paulsen, W. von Deyn and W Röben, *Liebigs. Ann. Chem,* 1984, 433.

55 K. Tadano, Y. Ueno, C Fukabon, Y Hotta and T. Suami, *Bull. Chem. Soc. Jpn.*, 1987, *60,* 1727

56 K Tadano, H Maeda, M. Hoshino, Y. Iimura and T Suami, *J. Org. Chem* . 1987,52, 1946

57. H Paulsen and W von Deyn, *Liebigs. Ann Chem* . 1987, 125.

58 T K M Shing and Y. Tang, *Tetrahedron.* 1991. *47,* 4571.

59. T. K. M. Shing. Y. Cui and V. Tang. *J. Chem Soc., Chem Commun*, **1991**, 756.

60 M V. Rao, unpublished results. University of Hyderabad

61 R L Whistler, C C. Wang and S Enokawa, *J Org Chcm*, **1968**, *33*. 3495

62. R. W. Binkley, *J Org Chcm.*, 1977, *42*. 1216

63. K. James, A. R Tatchell, R D Rees and R H Williams. *J. Chcm Soc (C).* 1968,2716.

64. T. Okazoe, J Hibino. K Takai and H Nozaki. *Tetrahedron Lett.*, 1985. *26,* 5581.

65. P. K. Chowdhury, *J. Chem Research (S),* **1990**, 192

66. T. L. Macdonald, K J Natalie Jr., G Prasad and J S Sawyer, *J Org Chcm.*. **1986**, *51*, 1124

67. L. A. Paquette, *Angew Chem Int Ed Engl.*, 1990, *29*, 609

68. M. Georges, T. -F. Tarn and B Fraser-Reid. *J. Org Chcm.*, 1985, *50*. 5747

69. L E. Overman, *Angew. Chem Int Ed. Engl.*, **1984**. *23*, 579

70. a) P. A Gneco, J. J Nunes and M D. Gaul, *J Am Chem Soc,* 1990. *112*, 4595. b) N. Palani and K K Balasubramanian, *Tetrahedron Lett.*, 1993. *34,* 5001.

71. K Onodera, S Hirano and N. Kashimura. *Carbohyd Res*, 1968. *6,* 276

72. T. Kato, H Kondo, M Nishino, M Tanaka, G Hata and A Miyake. *Bull Chem Soc Jpn.*, **1980**, *53,* 2958.

73. S. Raina and V, K Singh. *Tetrahedron.* 1995. *51,* 2467

74 D R Hicks and B Frascr-Reid. *Synthesis.* **1974**. 203.

75. H. C. Jarrell and W. A Szarek. *Can. J. Chem.* 1979, *57,* 924

76. R Eby, K. T. Webster and C. Schuerch. *Carbohyd Res*, 1984. *129.* 111

77. J. Yoshimura, K. Sato. N Hong, K. Kubo and H. Kodama, *Bull. Chem. Soc Jpn.*, **1982**, *55*, 938.

78. J -J Brunet and P. Caubere. *J. Org. Chem.*. **1984**, *49*. 4058.

79 M Bessodes, D Komiotis and K Antonakis, *TetrahedronLett.*, 1986. 27 579

80. G Büchi and J E Powell Jr ../ *Am. Chem Soc.* 1967. *89*. 4559

81 B Fraser-Reid, R A Alonso. G D Vite and R E McDevitt. *J. Org Chem* 1992, *57*, 573

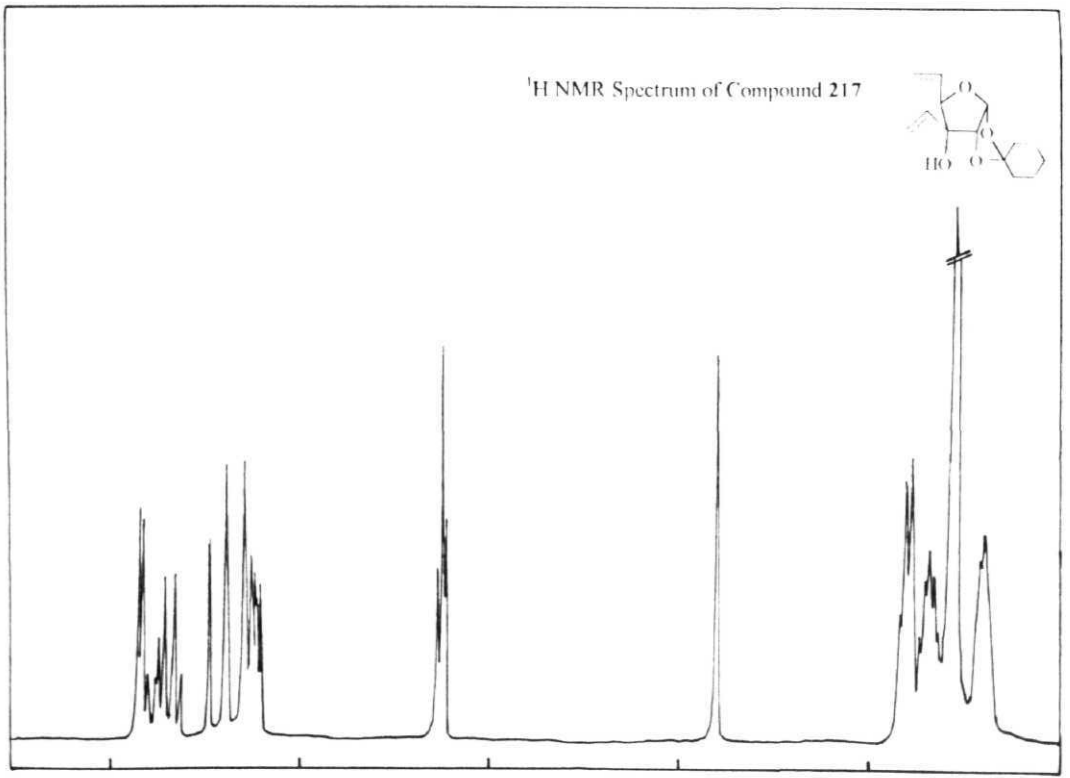
82 G Buchi and J E Powell Jr., *J Am. Chem Soc* . 1970. *92*. 3126

83. K. Yamamoto, M Minato and J Tsuji, *J Org. Chem* . 1990. *55* 766

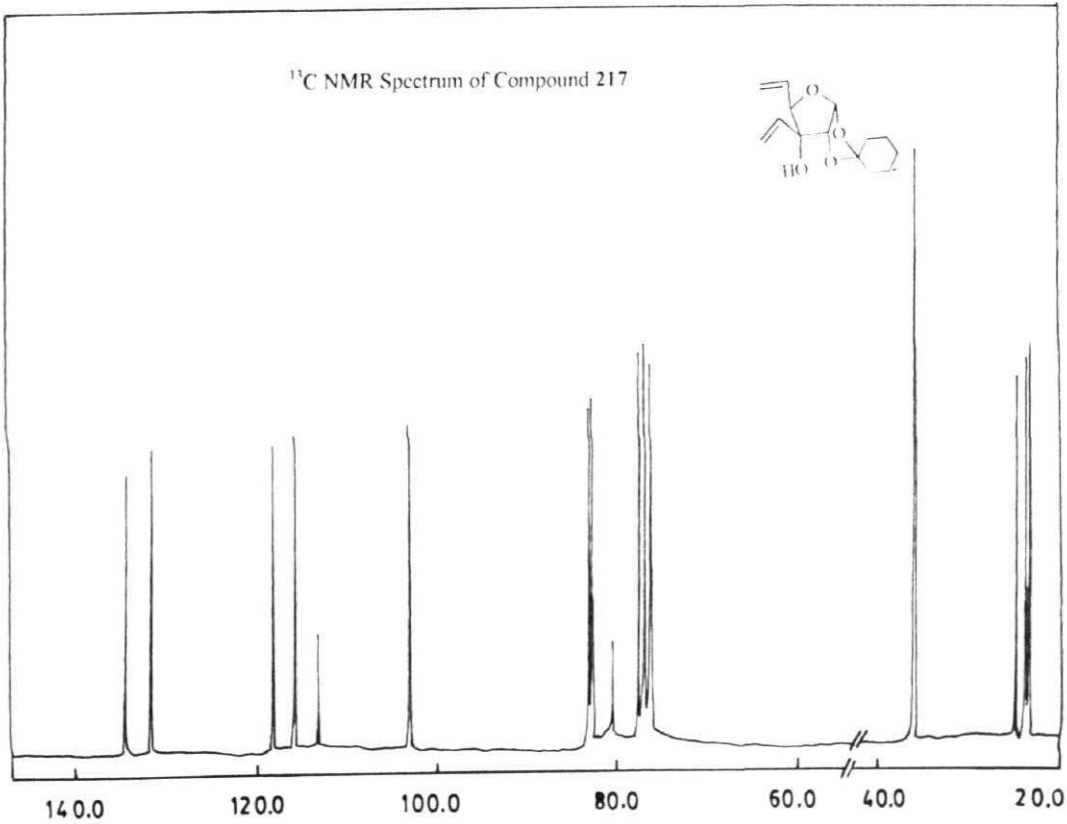
84. F. Fringuelli, R Germani, F Pizzo and G Savelli, *Synth. Com/n.*. 1989 19 1939.

85. R. B Woodward and F V. Brutcher Jr., *J Am. Chem. Soc.* 1958, *80* 209

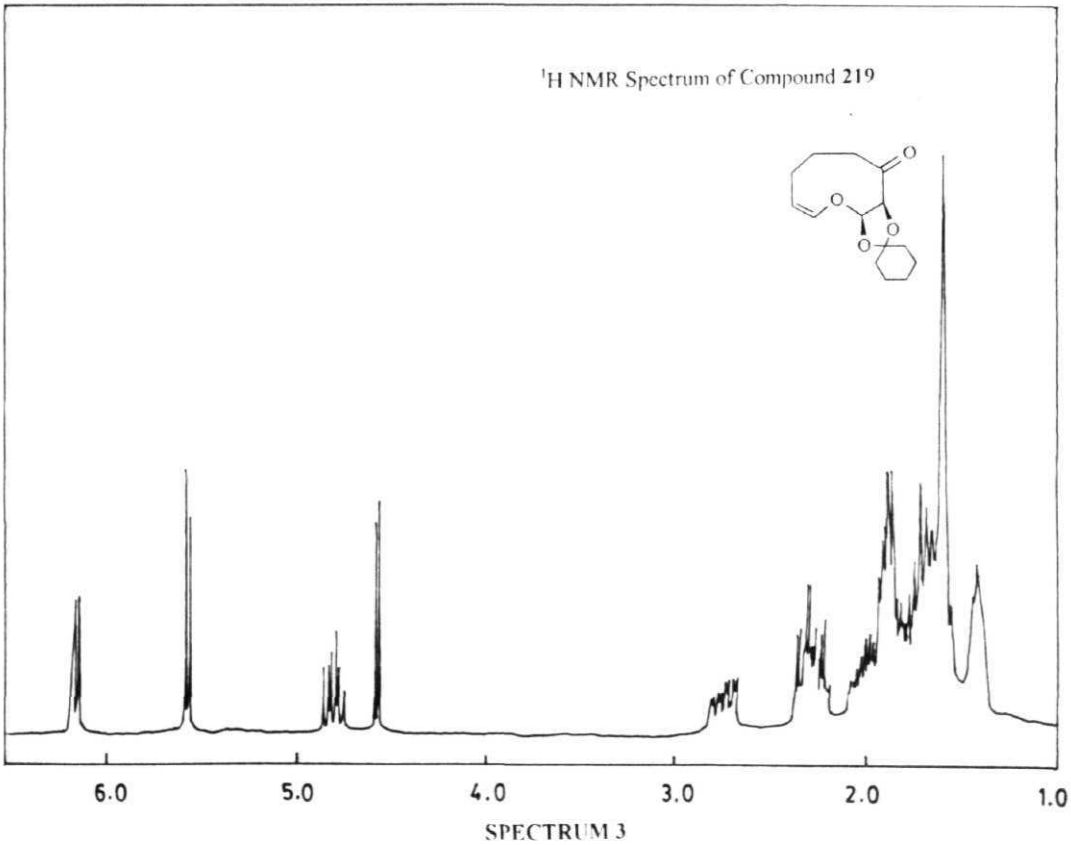
SPECTRA



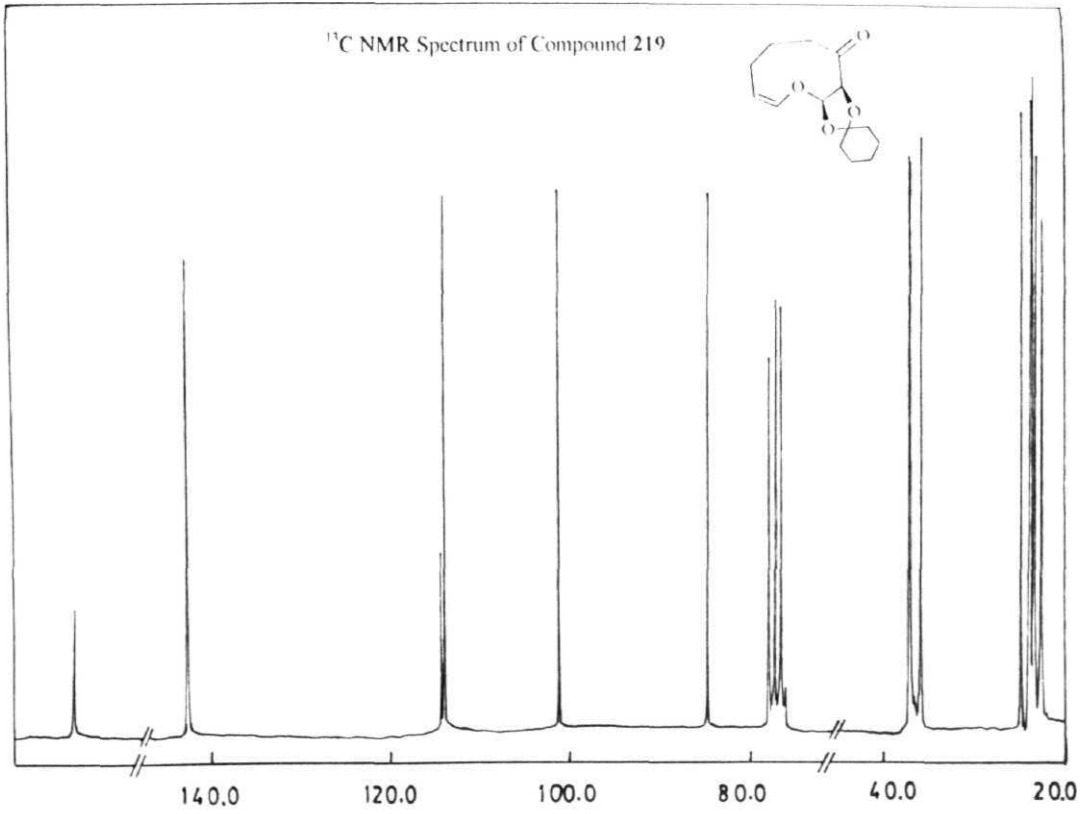
SPECTRUM 1


^{13}C NMR Spectrum of Compound 217
HO
O
O
O
140.0
120.0
100.0
80.0
60.0
40.0
20.0

SPECTRUM 2

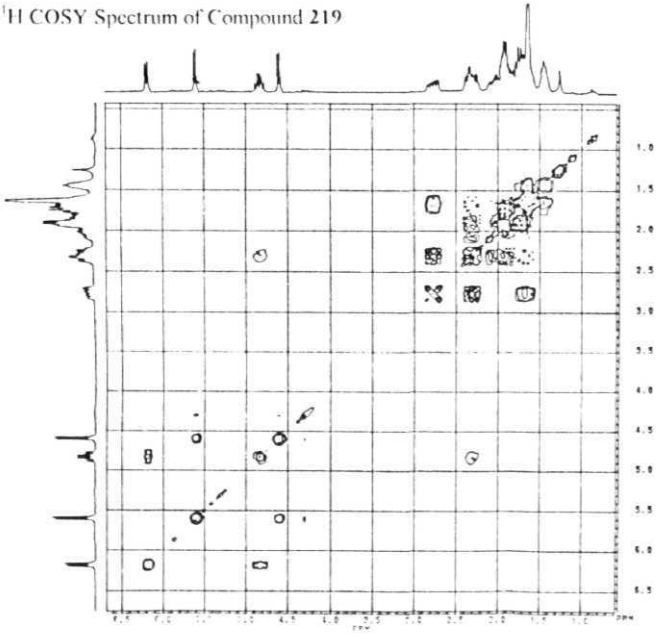


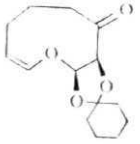
SPECTRUM 3



SPECTRUM 4

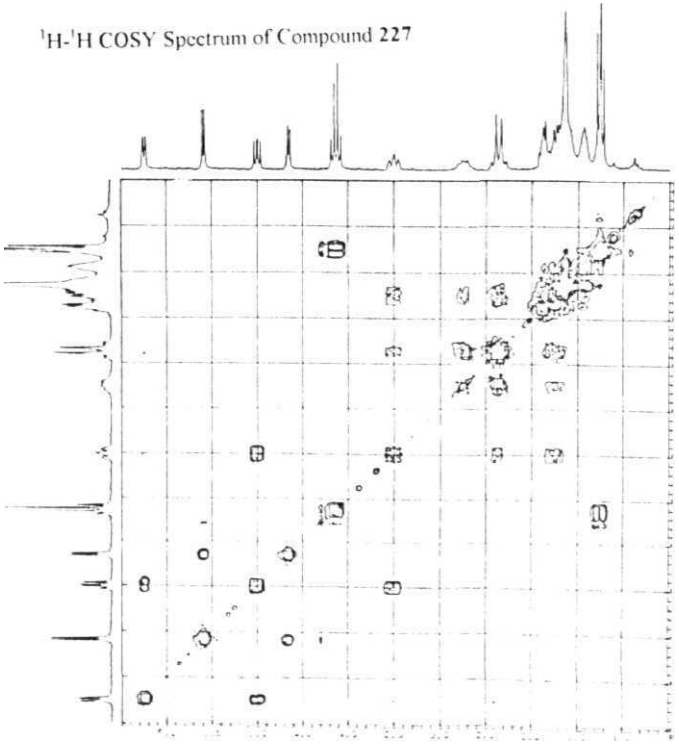
^{1}H-^{1}H COSY Spectrum of Compound 219

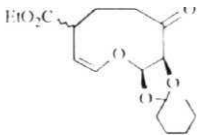




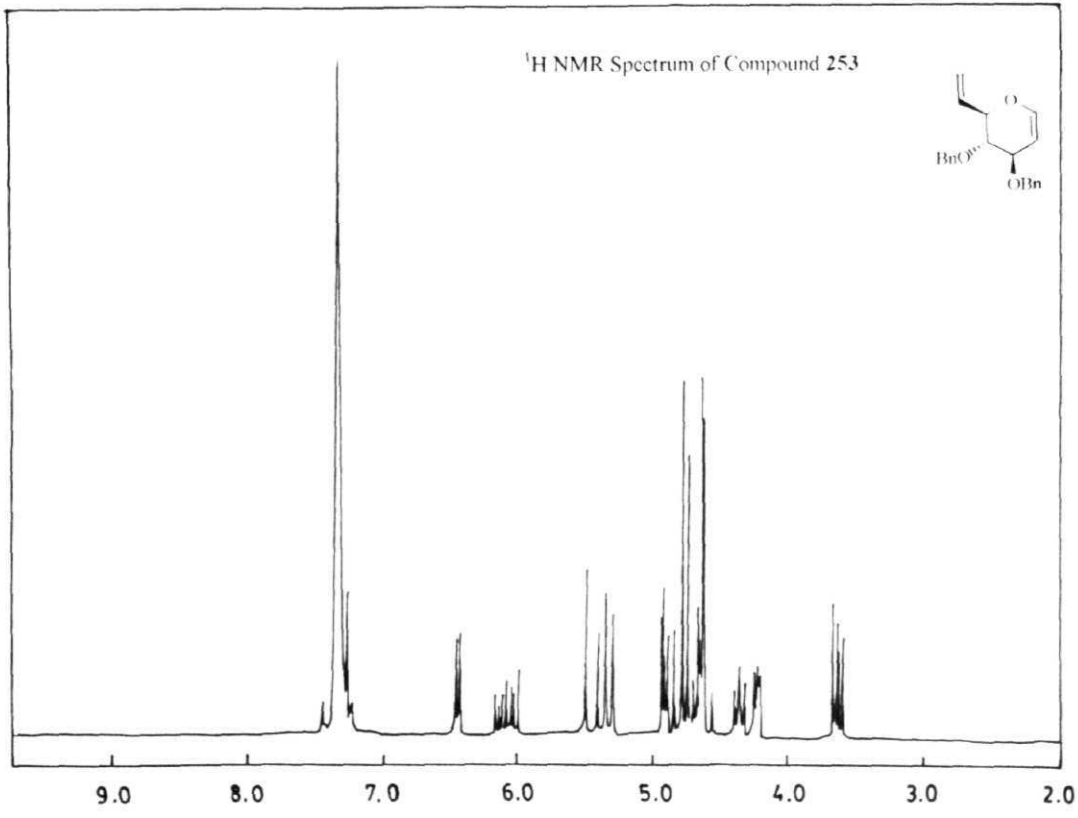
SPECTRUM 5

^{1}H-^{1}H COSY Spectrum of Compound **227**

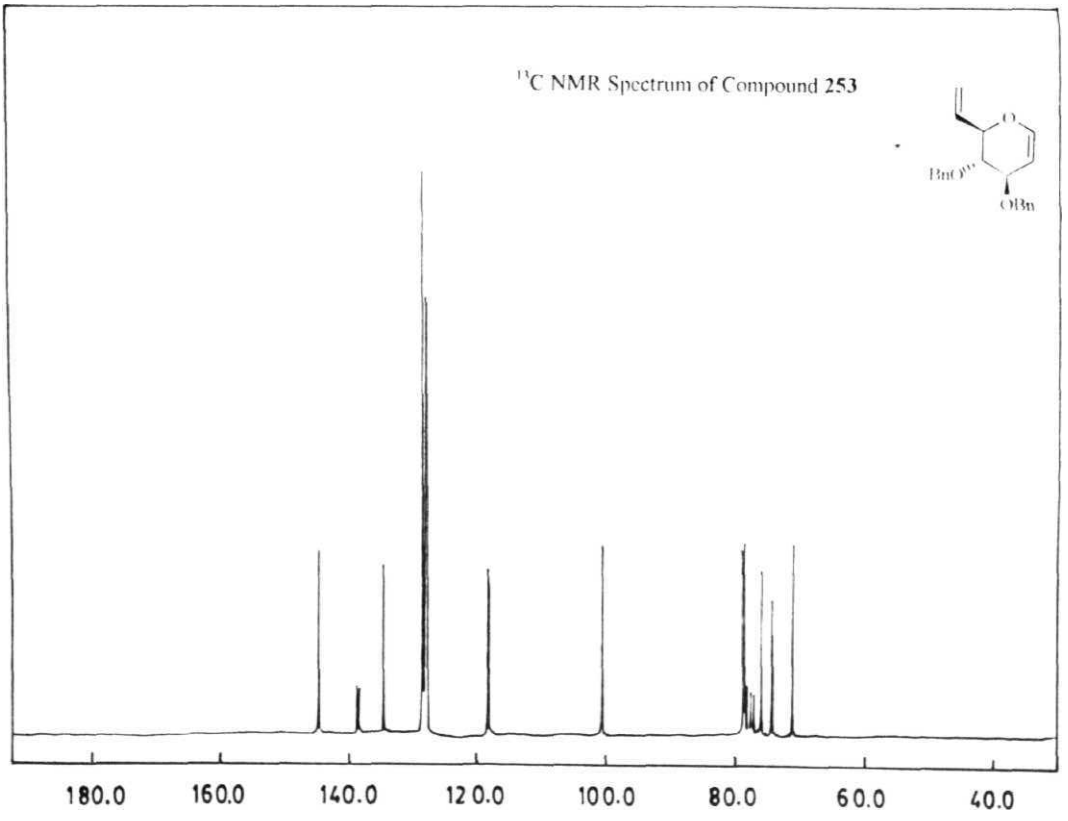




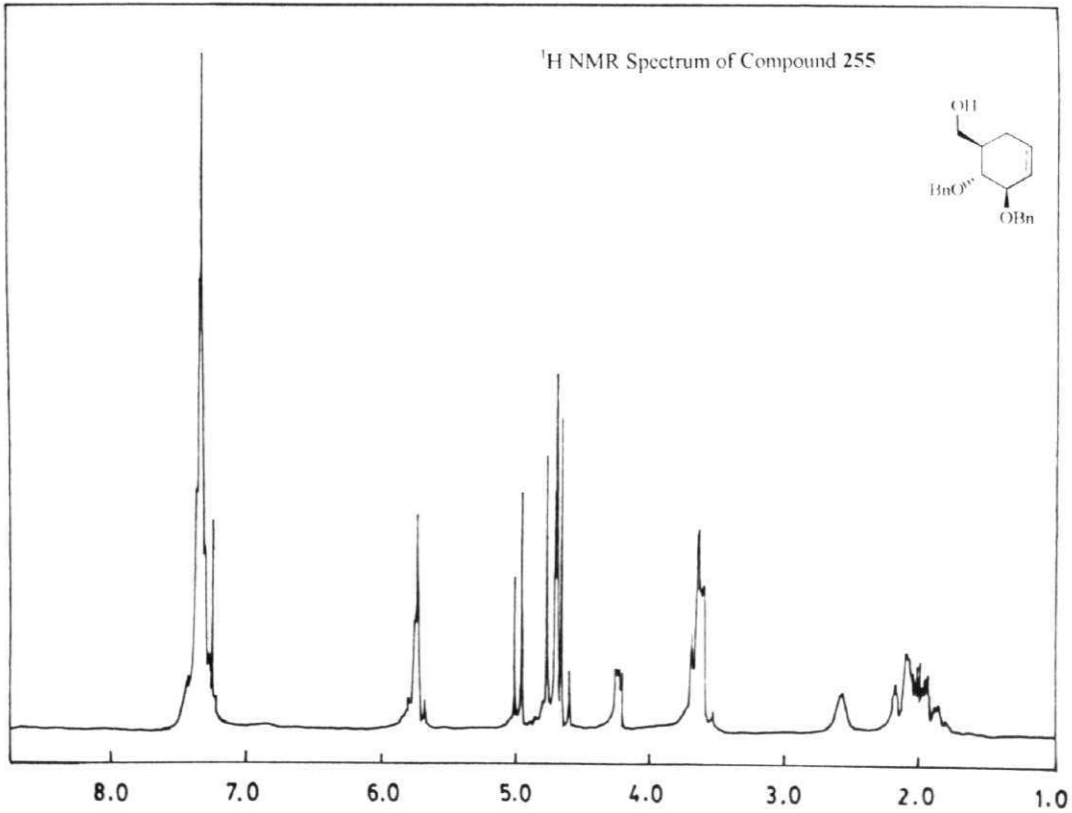
SPECTRUM 6



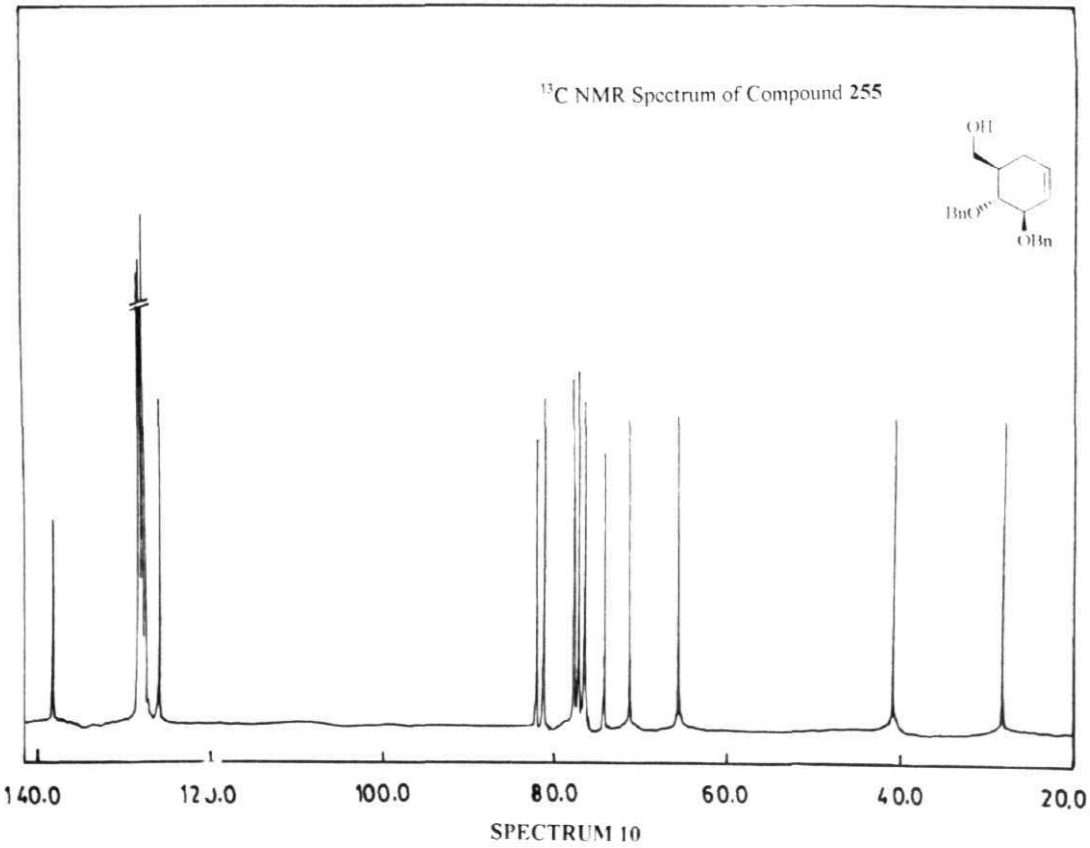
SPECTRUM 7


^{13}C NMR Spectrum of Compound 253
BnO
OBn
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0

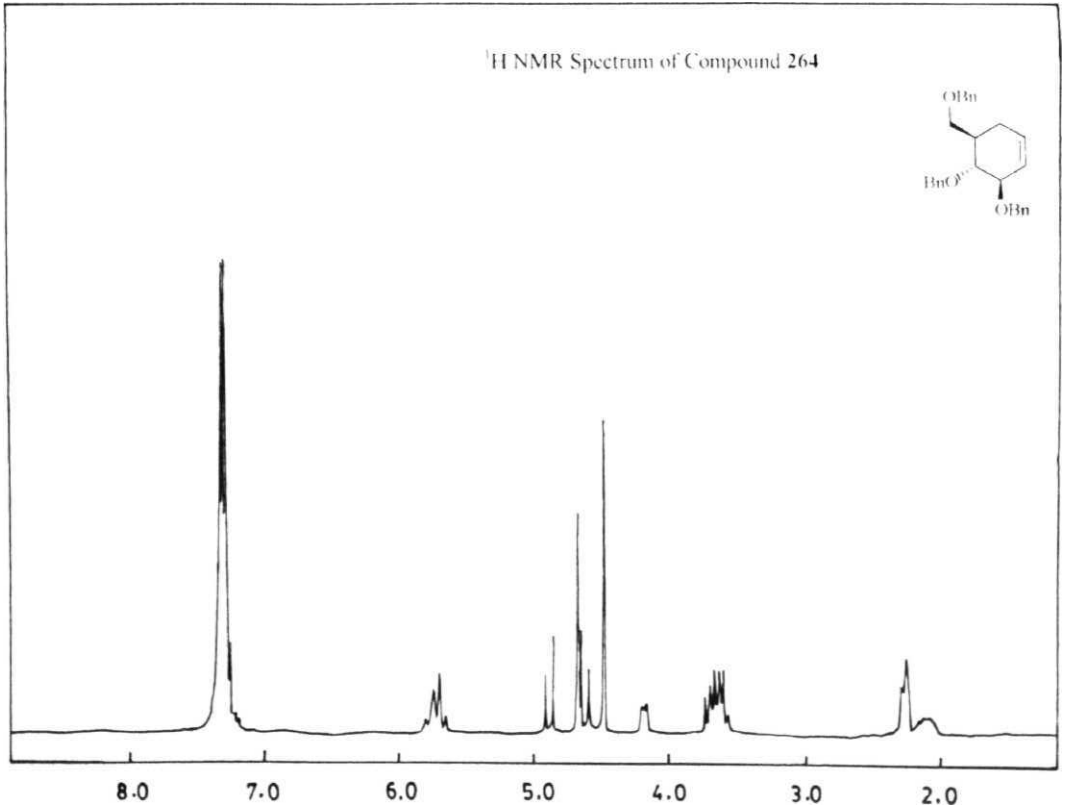
SPECTRUM 8


^{1}H NMR Spectrum of Compound 255
OH
BnO
OBn
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

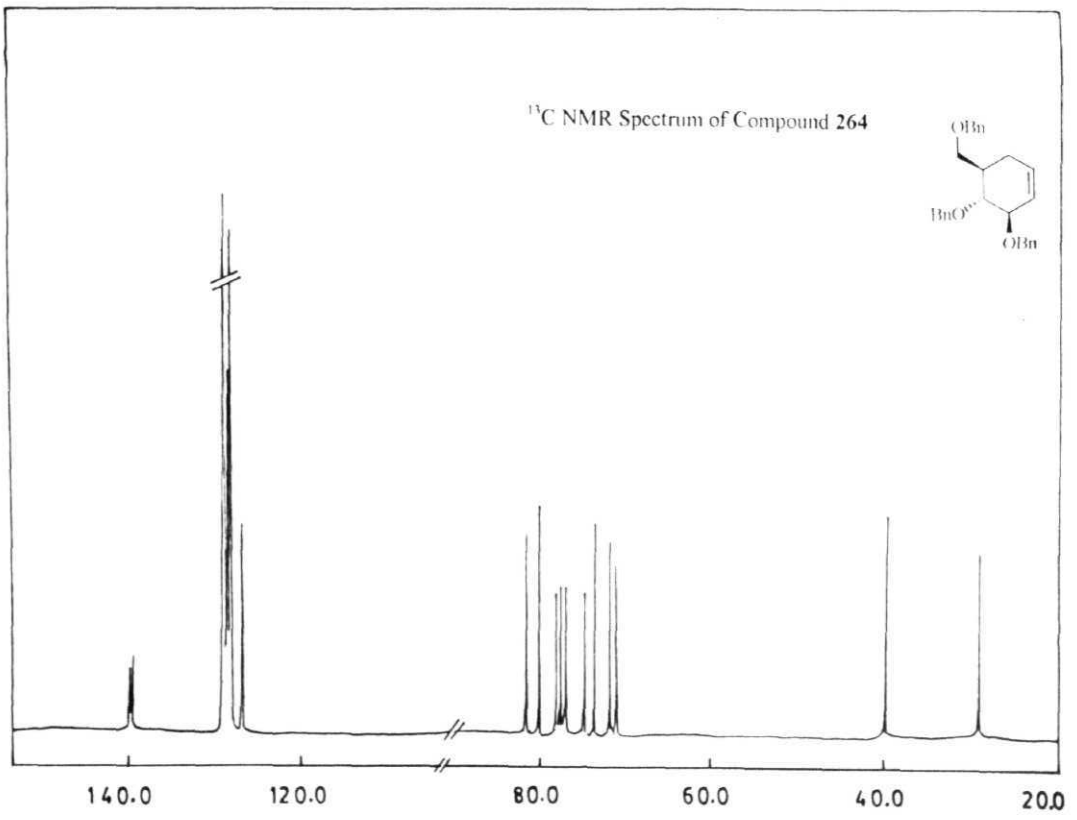
SPECTRUM 9


^{13}C NMR Spectrum of Compound 255
OH
BnO
OBn
140.0
120.0
100.0
80.0
60.0
40.0
20.0

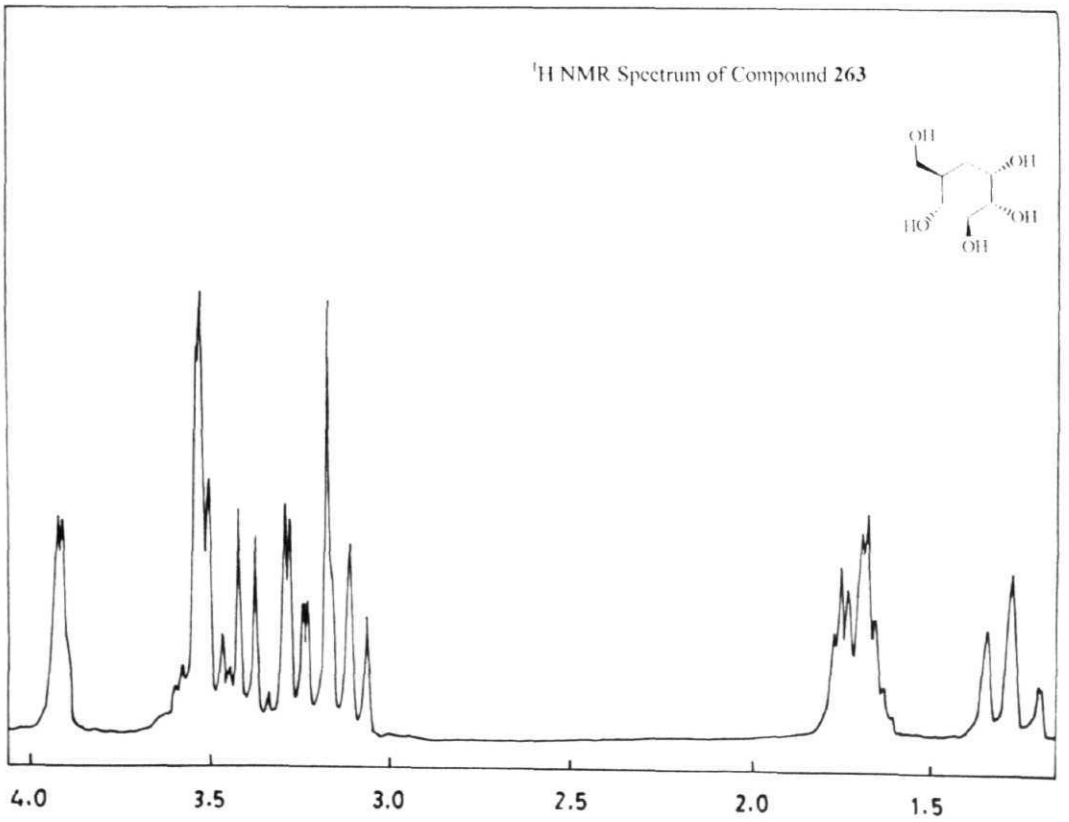
SPECTRUM 10



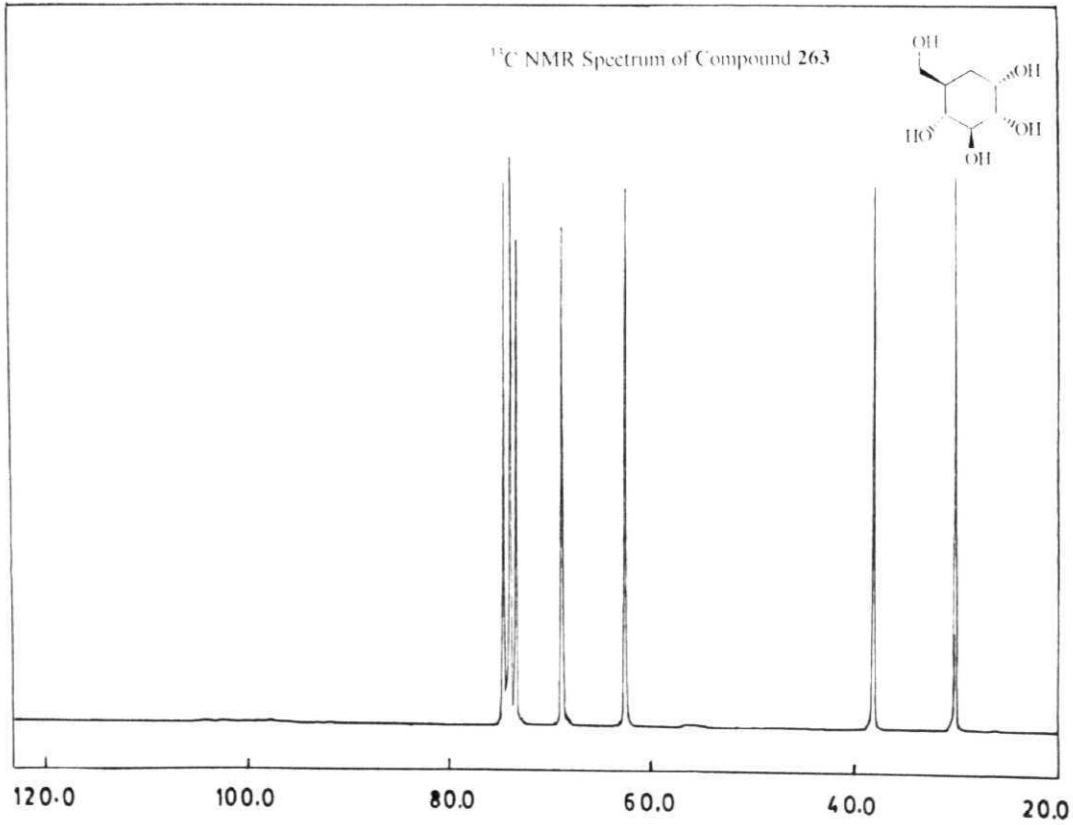
SPECTRUM 11


^{13}C NMR Spectrum of Compound 264
OBn
BnO
OBn
140.0
120.0
80.0
60.0
40.0
20.0

SPECTRUM 12



SPECTRUM 13


^{13}C NMR Spectrum of Compound 263
OH
OH
HO
OH
OH
120.0
100.0
80.0
60.0
40.0
20.0

SPECTRUM 14