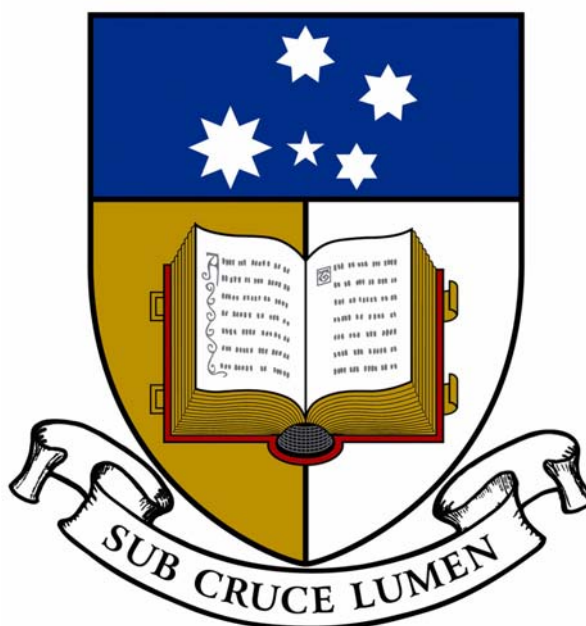


Synthesis of Rare Sugars and Novel Sugar Derivatives from 1,2-Dioxines

A thesis submitted for the
degree of Doctor of Philosophy

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Abstract

1,2-Dioxines are a specific class of cyclic peroxide that are both prevalent in nature and important synthetic building blocks. To date, much of the chemistry involving 1,2-dioxines is concerned with cleavage of the weak peroxide bond, providing a convenient method for the incorporation of 1,4-oxygen functionality into molecules. Comparatively little attention has been directed towards transformations of the alkene unit contained within 1,2-dioxines, which is the focus of this thesis.

The synthesis of a broad range of diversely functionalised 1,2-dioxines from commonly available starting materials is presented. Subsequently, the osmium catalysed dihydroxylation of 3,6-disubstituted 1,2-dioxines was investigated, furnishing novel peroxy diols in high yield and with excellent diastereoselectivity. The peroxy diols were then reduced, affording stereospecific tetraols and higher polyols, including the rare sugar allitol. In addition, homolytic ring-opening of the 1,2-dioxanes was examined, providing a new route to polyhydroxylated furanoses, highlighted by the synthesis of the natural keto-sugar psicose.

Several 4-substituted 1,2-dioxines were also dihydroxylated, followed by reduction of the peroxide bond, providing a convenient route to branched erythritol derivatives, including the important plant sugar 2-C-methyl-erythritol. The cobalt catalysed ring-opening of the peroxy diols produced novel erythrose derivatives in high yield. In addition, the triphenylphosphine induced ring contraction of the peroxy diols is presented, which allowed for the synthesis of novel dihydroxylated tetrahydrofurans in excellent yield. Asymmetric dihydroxylation of the achiral 4-substituted 1,2-dioxines was explored, furnishing optically enriched peroxy diols with varying enantioselectivity depending on the substrate.

The synthesis of novel alkyl and aryl branched erythrono- γ -lactones via oxidation of lactols derived from the acetonide protected peroxy diols is also documented. The utility of this sequence is illustrated by the preparation of potassium 2,3,4-trihydroxy-2-methylbutanoate, a leaf-closing substance of *Leucaena leucocephalam*. Additionally, γ -lactones were prepared from epoxy hydroxy ketones derived from epoxy-1,2-dioxanes, facilitated by a Baeyer-Villiger lactonisation

protocol. The requirements and limitations of this procedure are discussed. The proposed and attempted synthesis of other lactones from 1,2-dioxines was also examined.

Finally, several other general alkene transformations were investigated on 1,2-dioxines including: halo-hydrin formation, phenylselenyl chloride addition, amino-hydroxylation, cyclopropanation, and aziridination, allowing for the preparation of several new classes of functionalised 1,2-dioxines.

In summary, the work presented in this thesis establishes clear and efficient methodology towards several interesting and useful sugar-type core structures from modified 1,2-dioxines.

Declaration

This thesis contains no material that has been accepted for the award of any other degree or diploma in any university or other tertiary institution. To the best of my knowledge it contains no material published or written by another person, except where due reference has been made.

I give my consent for this copy of my thesis being made available for loan and photocopying when deposited in the University Library.

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Antony Vincent Robinson

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Abbreviations

Ac	acetyl
AcOH	acetic acid
Ad	adamantly
Anal. Calcd.	analysis calculated
Bn	benzyl
<i>t</i> -Bu	<i>tert</i> -butyl
CDI	carbonyldiimidazole
Co(SALEN) ₂	<i>N,N'</i> -bis(salicylidene)-ethylenediaminocobalt(II)
CoTPP	5,10,15,20-tetraphenyl-21 <i>H</i> ,23 <i>H</i> -porphine cobalt(II)
Δ	heat
d	days
<i>de</i>	diastereomeric excess
(DHQ) ₂ AQN	1,4- <i>bis</i> (9- <i>O</i> -dihydroquininyl)-anthraquinone
(DHQ) ₂ PHAL	1,4- <i>bis</i> (9- <i>O</i> -dihydroquininyl)-phthalazine
(DHQD) ₂ PHAL	1,4- <i>bis</i> (9- <i>O</i> -dihydroquinidinyl)-phthalazine
(DHQD) ₂ PYR	1,4- <i>bis</i> (9- <i>O</i> -dihydroquinidinyl)-diphenylpyrimidine
DIBALH	diisobutylaluminium hydride
DMP	dimethoxypropane
DMSO	dimethyl sulphoxide
DMT	dimethoxytoluene
<i>ee</i>	enantiomeric excess
equiv.	equivalents
Et	ethyl
EI	Electron Impact
GC	gas chromatography
h	hours
HRMS	high resolution mass spectrometry
<i>hν</i>	light
Hz	hertz
IR	infrared
<i>J</i>	coupling constant
Lit.	literature

M	moles per litre
<i>m</i> -CPBA	<i>meta</i> -chloroperbenzoic acid
<i>m/z</i>	mass to charge ratio
Me	methyl
MeOH	methanol
MHz	megahertz
MIRC	Michael initiated ring closure
mol	mole(s)
mp	melting point
NBS	<i>N</i> -bromosuccinimide
NCS	<i>N</i> -chlorosuccinimide
NMO	<i>N</i> -methylmorpholine- <i>N</i> -oxide
NMR	nuclear magnetic resonance
<i>n</i> -Pr	<i>n</i> -propyl
PDC	pyridinium dichromate
Pd/C	palladium on carbon
<i>p</i> -TSA	<i>para</i> -toluenesulphonic acid
Ph	phenyl
ppm	parts per million
PTAB	phenyltrimethylammonium tribromide
PPTS	pyridinium <i>para</i> -toluenesulphonate
R_f	retention factor
ROESY	Rotating Frame Overhauser Effect Spectroscopy
rt	room temperature
TBS	<i>tert</i> -butyldimethylsilyl
TEA	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilane
TPAP	tetrapropylammonium perruthenate
TPP	5,10,15,20-tetraphenyl-21 <i>H</i> ,23 <i>H</i> -porphine
TPPO	triphenylphosphine oxide