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THE UTILISATION OF CYCLOPROPYL COMPOUNDS

IN THE SYNTHESIS OF TROPONOLDS

A thesis

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for the Degree of

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by

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Abstract

The fully regio-controlled synthesis of C_{1a}-C_{12a} mono-seco colchicine **133**, as well as a number of structurally interesting analogues, has been achieved. The key feature employed in our approach to troponoid compounds of this type has been the incorporation of synthetic equivalents for α -tropolone anions **84** and **87** *via* dehydrobrominative ring expansion of C7-substituted 7-bromobicyclo[4.1.0]heptan-2,3- and -3,4-diones respectively.

The hydroxyl functionality present in tropolone **143** has been found to be a suitable progenitor for the C7-acetamido group in mono-seco colchicine **133**. Studies directed towards the enantio-controlled introduction of the C7-acetamide moiety *via* asymmetric reduction of the prochiral ketone **152** are discussed.

Various strategies to effect B-ring closure in mono-seco colchicine **133** and its congeners are presented. The novel preparation and dehydrogenative dimerisation of desacetamido mono-seco colchicine **174** is reported.

An efficient synthesis of the naturally occurring tropone nezukone (**16**) has been accomplished *via* the novel rearrangement of bicyclic methylene cyclopropane **209**. Evidence for the intermediacy of heptafulvenes in this conversion is described.

Glossary of Terms and Abbreviations

Ac ₂ O	acetic anhydride
AcOH	acetic acid
AIBN	α, α' -azoisobutyronitrile
<i>n</i> -BuLi	<i>n</i> -butyllithium
<i>tert</i> -BuLi	<i>tert</i> -butyllithium
<i>m</i> -CPBA	<i>meta</i> -chloroperbenzoic acid
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,5-diazabicyclo[5.4.0]undec-5-ene
DDQ	2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone
DIBAL	diisobutylaluminium hydride
DMAD	dimethylacetylenedicarboxylate
DMAP	4-dimethylaminopyridine
DMP	3,5-dimethylpyrazole
DMSO	dimethylsulphoxide
GASPE	Gate adjusted spin echo
HMPA	hexamethylphosphoric triamide
h.p.l.c.	high pressure liquid chromatography
LiIPCA	lithium isopropylcyclohexylamide
NBS	<i>N</i> -bromosuccinimide
ORTEP	Oak Ridge thermal ellipsoid plot
PDC	pyridinium dichromate
py	pyridine
SFORD	single frequency off resonance decoupled
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride

THF	tetrahydrofuran
t.l.c.	thin layer chromatography
TMS	tetramethylsilane
<i>p</i> -TsoH	<i>para</i> -toluenesulphonic acid
TTFA	thallium tristrifluoroacetate
brine	saturated aqueous sodium chloride solution
NaHCO ₃ solution	saturated aqueous sodium bicarbonate solution
HCl solution	2M aqueous hydrochloric acid solution
H ₂ SO ₄ solution	2M aqueous sulphuric acid solution
Na ₂ S ₂ O ₅	0.1M aqueous sodium <i>meta</i> -bisulphite solution