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Studies on the L-proline catalyzed and the borono Mannich reaction

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Studies on the L-proline Catalyzed and the Borono Mannich Reaction

A thesis submitted in fulfillment of the requirements for

the award of the degree

MASTER OF SCIENCE-RESEARCH

from

UNIVERSITY OF WOLLONGONG



By

Qin Yong Mao

University of Wollongong

Department of Chemistry

Wollongong, Australia

August 2007

Declaration

This is to certify that the work reported in this thesis is my own work, conducted in the Chemistry Department at the University of Wollongong. And no part of the thesis has been submitted to any other University or academic institution.

Qin Yong Mao

31/08/2007

Abstract

This thesis describes the results of two independent research projects. The first project is concerned with the synthesis of chiral 1,2-amino alcohols using an organocatalysed Mannich reaction. **Chapter 1** gives an overview of L-proline catalysed Mannich reactions and describes the aims of this project. **Chapter 2** reports the results of this study. These reactions were found to be low yielding and poorly diastereoselective with the model compound propanal and did not work with the desired aldehyde *O*-benzylglycosaldehyde. The stereochemical outcomes of these reactions using NMR analysis were not certain. Future work would require X-ray crystallographic studies to confirm the product relative stereochemistries. This project was thus abandoned and a second project was studied.

Chapter 3 provides an overview of cyclic N-acyliminium ion chemistry.

Chapter 4 describes the results of a study of the borono-Mannich reaction on *N*-acyliminium ions, generated in situ from hemi-aminals derived from chiral 5-hydroxypyrrolidin-2-ones, to prepare substituted pyrrolidinones. The reactions of these *N*-acyliminium ions with boronic acids and other nucleophiles can afford the corresponding substituted pyrrolidinones diastereoselectively. The stereochemical assignments of these products were based on NMR coupling constants. X-ray structures of these compounds would be required in the future to confirm these assignments.

The success of these reactions provided a possible strategy for the synthesis of functionalized pyrrolidinones and other potential glycosidases inhibitors.

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Finally, I dedicate this thesis my grandparents, my parents and my wife.....

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List of Abbreviations

Ac	acetyl
<i>t</i> -Bu	<i>tert</i> -butyl
Boc	<i>tert</i> -butoxycarbonyl
°C	degrees Celsius
COSY	correlation spectroscopy
δ	chemical shift in parts per million downfield from TMS
d	doublet (spectral)
DMSO	dimethylsulfoxide
DMF	dimethylformamide
d.r.	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
Et	ethyl
EtOH	ethanol
Equiv.	Molar equivalents
g	gram(s)
h	hour(s)
HMBC	heteronuclear multiple bond coherence
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
Hz	hertz
<i>J</i>	coupling constant (in NMR)
L	litre(s)
m	multiplet (spectral), milli
M	moles per litre
Me	methyl
MeCN	acetonitrile

MeOH	methanol
MHz	megahertz
min	minute(s)
mmol	millimole(s)
MS	mass spectrometry
m/z	mass to charge ratio (in mass spectrometry)
NMP	<i>N</i> -methylpyrrolidinone
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
Nu	nucleophile
PMB	<i>p</i> -methoxybenzyl
PMP	4-methoxyphenyl
ppm	parts per million (in NMR)
<i>p</i> -TsOH	<i>para</i> -toluenesulfonic acid
q	quartet (spectral)
R_f	retention factor (in chromatography)
ROESY	Rotating frame Overhauser Effect Spectroscopy
rt	room temperature
s	singlet (spectral)
t	triplet (spectral)