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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

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# *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.

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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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# *List of Abbreviations*

| | |
|---|---|
| Ac | acetyl |
| *t*-Bu | *tert*-butyl |
| Boc | *tert*-butoxycarbonyl |
| ºC | 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 |
| *J* | 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 | *N*-methylpyrrolidinone |
| NMR | nuclear magnetic resonance |
| NOESY | nuclear Overhauser effect spectroscopy |
| Nu | nucleophile |
| PMB | *p*-methoxybenzyl |
| PMP | 4-methoxyphenyl |
| ppm | parts per million (in NMR) |
| *p*-TsOH | *para*-toluenesulfonic acid |
| q | quartet (spectral) |
| $R_f$ | retention factor (in chromatography) |
| ROESY | Rotating frame Overhause Effect Spectroscopy |
| rt | room temperature |
| s | singlet (spectral) |
| t | triplet (spectral) |