

## TABLE OF CONTENTS

<b>UNDERGRADUATE THESIS</b>	<b>ii</b>
<b>RATIFICATION PAGE</b>	<b>iv</b>
<b>STATEMENT OF NON-PLAGIARISM</b>	<b>iv</b>
<b>FOREWORD</b>	<b>iv</b>
<b>TABLE OF CONTENTS</b>	<b>v</b>
<b>LIST OF TABLES</b>	<b>iv</b>
<b>LIST OF FIGURES</b>	<b>iv</b>
<b>LIST OF APPENDICES</b>	<b>iv</b>
<b>ABSTRACT</b>	<b>iv</b>
<b>INTISARI</b>	<b>iv</b>
<b>CHAPTER I INTRODUCTION</b>	<b>1</b>
I.1 Background	1
I.2 Objectives	3
I.3 Research benefits	3
<b>CHAPTER II LITERATURE REVIEW AND HYPOTHESES</b>	<b>4</b>
II.1 Literature Review	4
II.1.1 Pyrrole Synthesis	4
II.1.2 One-pot Syntheses	5
II.1.3 Activated Methylene	5
II.1.4 Basicity	6
II.1.5 Reaction Selectivity	7
II.2 Hypotheses	8
II.2.1 Formulation of hypothesis 1	8
II.2.2 Formulation of hypothesis 2	9
II.2.3 Formulation of hypothesis 3	10
II.2.4 Research design	11
<b>CHAPTER III EXPERIMENTAL METHODS</b>	<b>13</b>
III.1 Materials	13
III.2 Equipment	13
III.3 Procedure	14
III.3.1 Purification of Benzylamine	14
III.3.2 Synthesis of 1-(Benzyl)-2,3,4,9-tetrahydro-2-tert-butyl-3-oxo-1H-cyclopenta[b]indole (compound 1)	14
III.3.3 Synthesis of N-(Octyl)-2-(phenylmethylidene)-3-cyano-1H-cyclopenta-[b]pyrrole (compound 2)	15
III.3.4 Synthesis of 2-(tert-Butyl)-3-(cyclopenta[b]indol-3-yl)-1-(benzyl)-pyrrole-3-one (compound 3)	15
<b>CHAPTER IV RESULT AND DISCUSSION</b>	<b>17</b>
IV.1 Synthesis of 1-(Benzyl)-2,3,4,9-tetrahydro-2-tert-butyl-3-oxo-1H-cyclopenta[b]indole (compound 1)	17

IV.2 Synthesis of N-(Octyl)-2-(phenylmethylidene)-3-cyano-1H-cyclopenta-[b]pyrrole (compound 2)	23
IV.3 Synthesis of 2-(tert-Butyl)-3-(cyclopenta[b]indol-3-yl)-1-(benzyl)pyrrole 3-one (compound 3)	26
<b>CHAPTER V CONCLUSION AND RECOMMENDATION</b>	<b>33</b>
V.1 Conclusion	33
V.2 Recommendations	33
<b>REFERENCES</b>	<b>35</b>

## LIST OF TABLES

Table II.1 List of different bases and their pK <sub>b</sub>	7
Table IV.1 List of hydrogens between predicted and obtained spectra of DBU-catalyzed reaction	18
Table IV.2 List of hydrogens between predicted and obtained spectrum of DABCO-catalyzed reaction	20
Table IV.3 List of hydrogens between predicted and obtained spectrum of compound 2	25

## LIST OF FIGURES

Figure I.1 Examples of pyrrole-containing drug candidates: atorvastatin (1), licofelone (2), tolmetin (3), ketorolac (4)	<b>2</b>
Figure I.2 Reaction of D-(+)-Glucose with benzoylacetonitrile and benzylamine	<b>2</b>
Figure I.3 2-hydroxycyclohexanone (left) and glucose (right)	<b>3</b>
Figure II.3 General structure for active methylene compounds, E groups being electron-withdrawing groups	<b>6</b>
Figure II.4 2,2,6,6-tetramethyl-3,5-heptanedione (left), benzoylacetonitrile (center), and 5,5-dimethyl-1,3-cyclohexanedione (right)	<b>6</b>
Figure II.5 Structure of DABCO (left) and DBU (right)	<b>7</b>
Figure II.6 Pyrrole synthesized using aldehyde (top) vs. ketone (bottom)	<b>9</b>
Figure II.7 Reaction scheme with triethylamine as catalyst	<b>10</b>
Figure II.8 Assumed equilibrium of 2-hydroxycyclohexanone dimer/monomer	<b>11</b>
Figure II.9 Proposed reaction mechanism for the synthesis of the target pyrrole	<b>11</b>
Figure IV.1 3 <sup>rd</sup> hour TLC of 5,5-dimethyl-1,3-cyclohexanedione (D), benzylamine (B), DBU (1), DMAP (2), and Et <sub>3</sub> N (3)-catalyzed reactions	<b>18</b>
Figure IV.2 <sup>1</sup> H NMR spectrum of DBU-catalyzed compound 1	<b>19</b>
Figure IV.3 Proposed reaction mechanism for the synthesis of compound 1	<b>20</b>
Figure IV.4 <sup>1</sup> H NMR spectrum of DABCO-catalyzed compound 1	<b>21</b>
Figure IV.5 TLC of crude product of compound 2 against its column fractions using 90:10 of hexane:EtOAc as eluent. From left to right: Crude product, fractions 1, 2, 3, 4, and 5.	<b>23</b>
Figure IV.6 <sup>1</sup> H NMR spectra of compound 2	<b>24</b>
Figure IV.7 Proposed reaction mechanism for the synthesis of compound 2	<b>26</b>
Figure IV.8 TLC of crude product (left) and benzylamine (right) using 90:10 of hexane:EtOAc as eluent	<b>27</b>
Figure IV.9 <sup>1</sup> H NMR spectrum of Et <sub>3</sub> N-catalyzed synthesis of compound 3	<b>28</b>
Figure IV.10 <sup>1</sup> H NMR spectrum of DBU-catalyzed synthesis of compound 3	<b>30</b>
Figure IV.11 <sup>1</sup> H NMR spectrum of DABCO-catalyzed synthesis of compound 3	<b>30</b>
Figure IV.12 <sup>1</sup> H NMR spectrum of KOH-catalyzed synthesis of compound 3	<b>31</b>
Figure IV.13 <sup>1</sup> H NMR spectrum of K <sub>2</sub> CO <sub>3</sub> -catalyzed synthesis of compound 3	<b>31</b>

## LIST OF APPENDICES

<b>Appendix 1</b> Predicted $^1\text{H}$ NMR spectra	39
<b>Appendix 2</b> Reaction data	42