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SULFONATE ESTERS AS COUPLING REAGENTS FOR PEPTIDE SYNTHESIS



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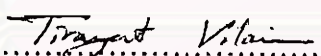
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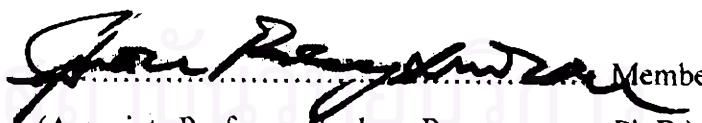
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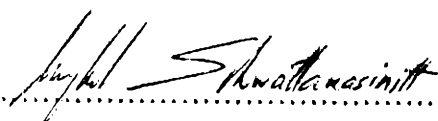
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ขนิษฐา พุดหอม : ซัลโฟเนตเอสเทอร์เพื่อเป็นรีเอเจนต์คู่ควบสำหรับการสังเคราะห์เพปไทด์ : (SULFONATE ESTERS AS COUPLING REAGENTS FOR PEPTIDE SYNTHESIS) อาจารย์ที่ปรึกษา : คร. ชีรยุทธ วิไลวัณย์ ; 196 หน้า. ISBN 974-333-027-5

สามารถสังเคราะห์โคเปปไทด์ที่มีหมู่ปกป้องไนโตรเจนเป็นเทอร์เชียรีบิวทอกซีคาร์บอนิล (Boc) และ 9-ฟลูออรีนิลเมทอกซีคาร์บอนิล (Fmoc) โดยปฏิกิริยาคู่ควบโดยตรงของกรดอะมิโนที่มีหมู่ปกป้องไนโตรเจนและเอสเทอร์ของกรดอะมิโน โดยใช้เอริล 4-ไนโตรเบนซีนซัลโฟเนตเป็นรีเอเจนต์เมื่อมี 1-ไฮดรอกซีเบนโซไตรอะโซลเป็นคะตะลิสต์ ถ้าไม่มีเอสเทอร์ของกรดอะมิโนเป็นนิวคลีโอไฟล์ ผลิตภัณฑ์ที่ได้คือ เอริลเอสเทอร์ของกรดอะมิโนที่มีหมู่ปกป้องไนโตรเจนโดยให้ปริมาณผลผลิตที่ดี จากการทดสอบการเกิดการราซีไมซ์ พบว่ารีเอเจนต์นี้ไม่ทำให้เกิดการราซีไมซ์ในปฏิกิริยาคู่ควบของกรดอะมิโนที่มีหมู่ปกป้องไนโตรเจนประเภทอัลคอกซีคาร์บอนิล แต่เกิดการราซีไมซ์ในกรดอะมิโนที่มีหมู่ปกป้องประเภทเอซิด เอริล 4-ไนโตรเบนซีนซัลโฟเนตนี้เป็นของแข็งที่เสถียร ทำปฏิกิริยาได้รวดเร็ว และการแยกผลิตภัณฑ์ทำได้ง่าย ดังนั้นจึงเป็นรีเอเจนต์ที่น่าจะมีประโยชน์สำหรับการสังเคราะห์เพปไทด์

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ภาควิชา.....เคมี.....
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A number of *N*-*tert*-Butoxycarbonyl (Boc) and *N*-9-fluorenylmethoxycarbonyl (Fmoc) dipeptide esters were prepared by the direct coupling of *N*-protected amino acids and amino acid esters using aryl 4-nitrobenzenesulfonates as coupling reagents in the presence of 1-hydroxybenzotriazole (HOBt) as a catalyst. In the absence of the amino acid esters as external nucleophiles, aryl esters of *N*-protected amino acids were obtained in good yield. Model racemization tests suggested that these reagents provided racemization-free coupling reaction for *N*-alkoxycarbonyl amino acid but not for *N*-acyl amino acid. These reagents are stable crystalline solids, provide fast reaction, the procedure is easy to perform and isolation of the products is simple. Therefore aryl 4-nitrobenzenesulfonates should be generally useful for peptide synthesis.

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ลายมือชื่อนิสิต *ทินเรจิก ทุดนอม*
ลายมือชื่ออาจารย์ที่ปรึกษา..... *ธีระยุทธ วิลลาวัณ*
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....



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CONTENTS

	page
Abstract in Thai.....	iv
Abstract in English.....	v
Acknowledgements.....	vi
List of Figures.....	ix
List of Tables.....	xvii
List of Schemes.....	xiv
List of Abbreviations.....	xx
CHAPTER I INTRODUCTION.....	1
Goal of the Research.....	8
CHAPTER II EXPERIMENTAL.....	9
2.1 General.....	9
2.2 Synthesis of Starting Materials.....	10
2.3 Synthesis of Reagents.....	13
2.3.1 Synthesis of Aryl methyl carbonates.....	13
2.3.2 Synthesis of Aryl oxalates.....	15
2.3.3 Synthesis of Aryl p-toluenesulfonates.....	15
2.3.4 Synthesis of Aryl 4-nitrobenzenesulfonates.....	17
2.4 Synthesis of Aryl Esters.....	18
2.4.1 The Study of Effect of Catalysts.....	20
2.4.2 Synthesis of Aryl benzoates.....	21
2.4.3 Synthesis of Aryl esters of <i>N-tert</i> -butoxycarbonyl amino acids.....	22
2.4.4 Synthesis of Aryl esters of <i>N</i> -9-Fluorenylmethoxycarbonyl amino acids.....	25

2.5 Synthesis of Dipeptides by using pentafluorophenyl 4-nitrobenzene-sulfonates (4c) and HOBt.....	35
2.6 The Study of Mechanism.....	44
2.6.1 Synthesis of the mixed carboxylic-sulfonic acid anhydride.....	44
2.6.2 Study of nucleophilic substitution of aryl 4-nitrobenzenesulfonates with various nucleophiles.....	44
2.7 Study of Racemization.....	45
2.7.1 Synthesis of Bz-L-Phe-L-Leu-OMe and Boc-L-Phe-L-Leu-OMe using different peptide coupling reagents.....	45
2.7.2 Investigation of Racemization during coupling.....	47
CHAPTER III RESULTS AND DISCUSSION.....	48
3.1 Synthesis of Reagents.....	48
3.2 Screening the Reagents for Peptide Synthesis.....	50
3.2.1 Reagent Type I: Methyl carbonates.....	50
3.2.2 Reagent Type II: Aryl oxalates.....	52
3.2.3 Reagent Type III: Aryl <i>p</i> -toluenesulfonates.....	52
3.2.4 Reagent Type IV: Aryl 4-nitrobenzenesulfonates.....	55
3.3 Synthesis of Aryl Esters of <i>N</i> -protected amino acid.....	57
3.3.1 Synthesis of Aryl esters of <i>N</i> -Boc protected amino acids.....	57
3.3.2 Synthesis of Aryl esters of <i>N</i> -Fmoc protected amino acids.....	59
3.4 Synthesis of Dipeptides.....	62
3.5 The Study of Mechanism.....	64
3.6 The Study of Racemization.....	68
3.6.1 The study of racemization of <i>N</i> -acyl-protected amino acids.....	68
3.6.2 The study of racemization of urethane-protected amino acids.....	70
CHAPTER IV CONCLUSION.....	73
REFERENCES.....	75
APPENDIX.....	80
VITA.....	196

LIST OF FIGURES

	page
Figure 1.1 Example of acidic additives generally used in peptide synthesis.....	3
Figure 3.1 The structure of reagents A-B tested in this study.....	48
Figure 3.2 Restricted rotation around C-N bond in dipeptide containing sarcosine..	64
Figure 3.3 ¹ H NMR spectrum (200 MHz) of Bz-DL-Phe-L-Leu-OMe.....	69
Figure 3.4 ¹ H NMR spectrum (500 MHz) of Boc-DL-Phe-L-Leu-OMe.....	71
Figure 1 ¹ H NMR spectrum (CDCl ₃) of <i>N</i> - <i>tert</i> -butoxycarbonylglycine (Boc-Gly-OH).....	81
Figure 2 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine (Boc-L-Leu-OH).....	82
Figure 3 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-phenylalanine (Boc-L-Phe-OH).....	83
Figure 4 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-DL-phenylalanine (Boc-DL-Phe-OH).....	84
Figure 5 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> -benzoyl-L-phenylalanine (Bz-L-Phe-OH).....	85
Figure 6 ¹ H NMR (DMSO-d ₆) spectrum of <i>N</i> -benzoyl-DL-phenylalanine (Bz-DL-Phe-OH).....	86
Figure 7 ¹ H NMR (D ₂ O) spectrum of L-leucine methyl ester hydrochloride.....	87
Figure 8 ¹ H NMR (CDCl ₃) spectrum of 4-nitrophenyl methyl carbonate (1a).....	88
Figure 9 ¹ H NMR (CDCl ₃) spectrum of benzotriazolyl methyl carbonate (1b).....	89
Figure 10 ¹ H NMR (CDCl ₃) spectrum of bis(4-nitrophenyl) oxalate (2a).....	90
Figure 11 IR spectrum (KBr) of 4-nitrophenyl <i>p</i> -toluenesulfonate (3a).....	91
Figure 12 ¹ H NMR (CDCl ₃) spectrum of 4-nitrophenyl <i>p</i> -toluenesulfonate (3a)....	92
Figure 13 IR spectrum (KBr) of 2,4,5-trichlorophenyl <i>p</i> -toluenesulfonate (3b).....	93

Figure 14	^1H NMR (CDCl_3) spectrum of 2,4,5-trichlorophenyl <i>p</i> -toluenesulfonate (3b).....	94
Figure 15	IR spectrum (KBr) of pentafluorophenyl <i>p</i> -toluenesulfonate (3c).....	95
Figure 16	^1H NMR (CDCl_3) spectrum of pentafluorophenyl <i>p</i> -toluenesulfonate (3c).....	96
Figure 17	IR spectrum (KBr) of pentachlorophenyl <i>p</i> -toluenesulfonate (3d).....	97
Figure 18	^1H NMR (CDCl_3) spectrum of pentachlorophenyl <i>p</i> -toluenesulfonate (3c).....	98
Figure 19	IR spectrum (KBr) of 4-nitrophenyl 4-nitrobenzenesulfonate (4a).....	99
Figure 20	^1H NMR (CDCl_3) spectrum of 4-nitrophenyl 4-nitrobenzenesulfonate (4a).....	100
Figure 21	IR spectrum (KBr) of 2,4,5-trichlorophenyl 4-nitrobenzenesulfonate (4b).....	101
Figure 22	^1H NMR (CDCl_3) spectrum of 2,4,5-trichlorophenyl 4-nitrobenzenesulfonate (4b).....	102
Figure 23	IR spectrum (KBr) of pentafluorophenyl 4-nitrobenzenesulfonate (4c).....	103
Figure 24	^1H NMR (CDCl_3) spectrum of pentafluorophenyl 4-nitrobenzenesulfonate (4c).....	104
Figure 25	IR spectrum (KBr) of pentachlorophenyl 4-nitrobenzenesulfonate (4d).....	105
Figure 26	^1H NMR (CDCl_3) spectrum of pentachlorophenyl 4-nitrobenzenesulfonate (4d).....	106
Figure 27	^1H NMR (CDCl_3) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycine methyl ester.....	107
Figure 28	IR spectrum (KBr) of 4-nitrophenyl benzoate.....	108
Figure 29	^1H NMR (CDCl_3) spectrum of 4-nitrophenyl benzoate.....	109
Figure 30	IR spectrum (KBr) of 2,4,5-trichlorophenyl benzoate.....	110
Figure 31	^1H NMR (CDCl_3) spectrum of 2,4,5-trichlorophenyl benzoate.....	111

	page
Figure 32 IR spectrum (KBr) of pentafluorophenyl benzoate.....	112
Figure 33 ¹ H NMR (CDCl ₃) spectrum of pentafluorophenyl benzoate.....	113
Figure 34 IR spectrum (KBr) of pentachlorophenyl benzoate.....	114
Figure 35 ¹ H NMR (CDCl ₃) spectrum of pentachlorophenyl benzoate.....	115
Figure 36 IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonylglycine 4-nitrophenyl ester (Boc-Gly-OPnp).....	116
Figure 37 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycine 4-nitrophenyl ester (Boc-Gly-OPnp).....	117
Figure 38 IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonylglycine 2,4,5-trichlorophenyl ester (Boc-Gly-OTcp).....	118
Figure 39 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycine 2,4,5-trichlorophenyl ester (Boc-Gly-OTcp).....	119
Figure 40 IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonylglycine pentafluorophenyl ester (Boc-Gly-OPfp).....	120
Figure 41 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycine pentafluorophenyl ester (Boc-Gly-OPfp).....	121
Figure 42 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycine pentachlorophenyl ester (Boc-Gly-OPcp).....	122
Figure 43 IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine 4-nitrophenyl ester (Boc-L-Leu-OPnp).....	123
Figure 44 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine 4-nitrophenyl ester (Boc-L-Leu-OPnp).....	124
Figure 45 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine 2,4,5-trichlorophenyl ester (Boc-L-Leu-OTcp).....	125
Figure 46 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine pentafluorophenyl ester (Boc-L-Leu-OPfp).....	126
Figure 47 ¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucine pentachlorophenyl ester (Boc-L-Leu-OPcp).....	127

Figure 48	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonylglycine 2,4,5-trichlorophenyl ester (Fmoc-Gly-OTcp).....	128
Figure 49	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonylglycine 2,4,5-trichlorophenyl ester (Fmoc-Gly-OTcp).....	129
Figure 50	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonylglycine pentafluorophenyl ester (Fmoc-Gly-OPfp).....	130
Figure 51	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonylglycine pentafluorophenyl ester (Fmoc-Gly-OPfp).....	131
Figure 52	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valine 2,4,5-trichlorophenyl ester (Fmoc-L-Val-OTcp).....	132
Figure 53	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valine 2,4,5-trichlorophenyl ester (Fmoc-L-Val-OTcp).....	133
Figure 54	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valine pentafluorophenyl ester (Fmoc-L-Val-OPfp).....	134
Figure 55	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valine pentafluorophenyl ester (Fmoc-L-Val-OPfp).....	135
Figure 56	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-methionine 2,4,5-trichlorophenyl ester (Fmoc-L-Met-OTcp).....	136
Figure 57	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L- methionine 2,4,5-trichlorophenyl ester (Fmoc-L-Met-OTcp).....	137
Figure 58	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-methionine pentafluorophenyl ester (Fmoc-L-Met-OPfp).....	138
Figure 59	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L- methionine pentafluorophenyl ester (Fmoc-L-Met-OPfp).....	139
Figure 60	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-phenylalanine 2,4,5-trichlorophenyl ester (Fmoc-L-Phe-OTcp).....	140
Figure 61	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L- phenylalanine 2,4,5-trichlorophenyl ester (Fmoc-L-Phe-OTcp).....	141

Figure 62	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>L</i> -phenylalanine pentafluorophenyl ester (Fmoc- <i>L</i> -Phe-OPfp).....	142
Figure 63	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>L</i> -phenylalanine pentafluorophenyl ester (Fmoc- <i>L</i> -Phe-OPfp).....	143
Figure 64	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>D</i> -serine 2,4,5-trichlorophenyl ester (Fmoc- <i>D</i> -Ser(O ^t Bu)-OTcp).....	144
Figure 65	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>D</i> -serine 2,4,5-trichlorophenyl ester (Fmoc- <i>D</i> -Ser (O ^t Bu)-OTcp).....	145
Figure 66	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>D</i> -serine pentafluorophenyl ester (Fmoc- <i>D</i> -Ser (O ^t Bu)-OPfp).....	146
Figure 67	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>D</i> -serine pentafluorophenyl ester (Fmoc- <i>D</i> -Ser (O ^t Bu)-OPfp).....	147
Figure 68	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -serine 2,4,5-trichlorophenyl ester (Fmoc- <i>L</i> -Ser(O ^t Bu)-OTcp).....	148
Figure 69	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -serine 2,4,5-trichlorophenyl ester (Fmoc- <i>L</i> -Ser (O ^t Bu)-OTcp).....	149
Figure 70	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -serine pentafluorophenyl ester (Fmoc- <i>L</i> -Ser (O ^t Bu)-OPfp).....	150
Figure 71	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -serine pentafluorophenyl ester (Fmoc- <i>L</i> -Ser (O ^t Bu)-OPfp).....	151
Figure 72	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>tert</i> -butyl ester)- <i>L</i> -glutamic acid 2,4,5-trichlorophenyl ester (Fmoc- <i>L</i> -Glu(O ^t Bu)-OTcp).....	152

Figure 73	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>tert</i> -butyl ester)-L-glutamic acid 2,4,5-trichlorophenyl ester (Fmoc-L-Glu(O ^t Bu)-OTcp).....	153
Figure 74	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>tert</i> -butyl ester)-L-glutamic acid pentafluorophenyl ester (Fmoc-L-Glu(O ^t Bu)-OPfp).....	154
Figure 75	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>tert</i> -butyl ester)-L-glutamic acid pentafluorophenyl ester (Fmoc-L-Glu(O ^t Bu)-OPfp).....	155
Figure 76	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl-L-lysine 2,4,5-trichlorophenyl ester (Fmoc-L-Lys(Boc)-OTcp).....	156
Figure 77	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl-L-lysine 2,4,5-trichlorophenyl ester (Fmoc-L-Lys(Boc)-OTcp).....	157
Figure 78	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl-L-lysine pentafluorophenyl ester (Fmoc-L-Lys(Boc)-OPfp).....	158
Figure 79	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl-L-lysine pentafluorophenyl ester (Fmoc-L-Lys(Boc)-OPfp).....	159
Figure 80	IR spectrum (neat) of <i>N</i> - <i>tert</i> -butoxycarbonylglycylglycine ethyl ester (Boc-Gly-Gly-OEt).....	160
Figure 81	¹ H NMR (CDCl ₃) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycylglycine ethyl ester (Boc-Gly-Gly-OEt).....	161
Figure 82	IR spectrum (neat) of <i>N</i> - <i>tert</i> -butoxycarbonylglycylalanine methyl ester (Boc-Gly-Ala-OMe).....	162

Figure 83	^1H NMR (CDCl_3) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycylalanine methyl ester (Boc-Gly-Ala-OMe).....	163
Figure 84	IR spectrum (neat) of <i>N</i> - <i>tert</i> -butoxycarbonylglycylsarcosine ethyl ester (Boc-Gly-Sar-OEt).....	164
Figure 85	^1H NMR (CDCl_3) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonylglycylsarcosine ethyl ester (Boc-Gly-Sar-OEt).....	165
Figure 86	IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucylglycine ethyl ester (Boc-L-Leu-Gly-OEt).....	166
Figure 87	^1H NMR (CDCl_3) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucylglycine ethyl ester (Boc-L-Leu-Gly-OEt).....	167
Figure 88	IR spectrum (KBr) of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucyl-L-alanine methyl ester (Boc-L-Leu-L-Ala-OMe).....	168
Figure 89	^1H NMR (CDCl_3) spectrum of <i>N</i> - <i>tert</i> -butoxycarbonyl-L-leucyl-L-alanine methyl ester (Boc-L-Leu-L-Ala-OMe).....	169
Figure 90	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonylglycylglycine ethyl ester (Fmoc-Gly-Gly-OEt).....	170
Figure 91	^1H NMR (CDCl_3) spectrum of <i>N</i> -9-fluorenylmethoxycarbonylglycylglycine ethyl ester (Fmoc-Gly-Gly-OEt).....	171
Figure 92	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valylglycine ethyl ester (Fmoc-L-Val-Gly-OEt).....	172
Figure 93	^1H NMR (CDCl_3) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valylglycine ethyl ester (Fmoc-L-Val-Gly-OEt).....	173
Figure 94	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valyl-L-alanine methyl ester (Fmoc-L-Val-L-Ala-OMe).....	174
Figure 95	^1H NMR (CDCl_3) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valyl-L-alanine methyl ester (Fmoc-L-Val-L-Ala-OMe).....	175
Figure 96	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl-L-valylsarcosine ethyl ester (Fmoc-L-Val-Sar-OEt).....	176

Figure 97	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>L</i> -valylsarcosine ethyl ester (Fmoc- <i>L</i> -Val-Sar-OEt).....	177
Figure 98	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>L</i> -phenylalanyl-glycine ethyl ester (Fmoc- <i>L</i> -Phe-Gly-OEt).....	178
Figure 99	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>L</i> -phenylalanylglycine ethyl ester (Fmoc- <i>L</i> -Phe-Gly-OEt).....	179
Figure 100	IR spectrum (neat) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl- <i>L</i> -lysylsarcosine ethyl ester (Fmoc- <i>L</i> -Lys(Boc)-Sar-OEt).....	180
Figure 101	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl- <i>L</i> -lysylsarcosine ethyl ester (Fmoc- <i>L</i> -Lys(Boc)-Sar-OEt).....	181
Figure 102	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -seryl- <i>L</i> -leucine methyl ester (Fmoc- <i>L</i> -Ser(<i>O</i> ^{<i>t</i>} Bu)- <i>L</i> -Leu-OMe).....	182
Figure 103	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl-(<i>O</i> - <i>t</i> -butyl)- <i>L</i> -seryl- <i>L</i> -leucine methyl ester (Fmoc- <i>L</i> -Ser(<i>O</i> ^{<i>t</i>} Bu)- <i>L</i> -Leu-OMe).....	183
Figure 104	IR spectrum (KBr) of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> ^{<i>in</i>} - <i>tert</i> -butoxycarbonyltryptophanylglycineglycine ethyl ester (Fmoc-Trp(Boc)-Gly-OEt).....	184
Figure 105	¹ H NMR (CDCl ₃) spectrum of <i>N</i> -9-fluorenylmethoxycarbonyl- <i>N</i> ^{<i>in</i>} - <i>tert</i> -butoxycarbonyltryptophanylglycineglycine ethyl ester (Fmoc-Trp(Boc)-Gly-OEt).....	185
Figure 106	IR spectrum (neat) of benzoic anhydride from reaction of tosyl chloride with benzoic acid (a) and from DCC-mediated coupling of benzoic acid (b).....	186
Figure 107	¹ H NMR (CDCl ₃) spectrum of 4-nitrobenzenesulfonyl piperidine.....	187
Figure 108	¹ H NMR (CDCl ₃) spectrum of 4-nitrobenzenesulfonyl morpholine.....	188
Figure 109	¹ H NMR (CDCl ₃) spectrum of Bz-Phe-Leu-OMe obtained from different peptide coupling reagents.....	189

- Figure 110 ^1H NMR (CDCl_3) spectrum of Bz-Phe-Leu-OMe obtained from reagent (4c)+HOBT as coupling reagent under various conditions.....191
- Figure 111 ^1H NMR (CDCl_3) spectrum of Boc-Phe-Leu-OMe obtained from different peptide coupling reagents.....194



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LIST OF TABLES

	page
Table 3.1 Physical data of reagents.....	49
Table 3.2 Reaction of (2a) with benzoic acid under various conditions.....	52
Table 3.3 Reaction of aryl <i>p</i> -toluenesulfonates with benzoic acid.....	53
Table 3.4 Effect of catalysts in sulfonation reaction.....	54
Table 3.5 Effect of the amounts of HOBt.H ₂ O in catalysing carboxylic acid activation reaction.....	55
Table 3.6 Reaction of benzoic acid with aryl 4-nitrobenzenesulfonates.....	56
Table 3.7 Aryl esters of <i>N</i> -Boc protected amino acids from aryl 4-nitrobenzene- sulfonates.....	58
Table 3.8 Aryl esters of <i>N</i> -Fmoc protected amino acids from reagent (4b) and (4c).....	61
Table 3.9 Dipeptides from reagent (4c) with HOBt.....	63
Table 3.10 Reaction of reagent (4b) with various nucleophiles in DMF.....	66
Table 3.11 Racemization during the coupling of Bz-L-Phe-OH with L-Leu-OMe.....	69
Table 3.12 Racemization during the coupling of Bz-L-Phe-OH with L-Leu-OMe using reagent (4c)+HOBt under various conditions.....	70
Table 3.13 Racemization during the coupling Boc-L-Phe-OH with L-Leu-OMe.....	71

LIST OF SCHEMES

	page
Scheme 1.1 Mechanism of carboxyl group activation by DCC.....	1
Scheme 1.2 The role of HOBt in DCC-mediated coupling reaction.....	3
Scheme 1.3 Mechanism of carboxyl group activation by A-B reagent.....	4
Scheme 1.4 Mechanism of BOP reagent in peptide coupling.....	6
Scheme 3.1 Reaction of Boc-Gly-OH with reagent (1b).....	50
Scheme 3.2 A proposed mechanism of reaction of Boc-Gly-OH with reagent (1b).....	51
Scheme 3.3 The mechanism of the Fmoc group removal.....	60
Scheme 3.4 The mechanism of aryl sulfonate as peptide coupling reagent <i>via</i> the formation of a mixed carboxylic-sulfonic acid anhydride.....	64
Scheme 3.5 The mechanism of aryl sulfonate as peptide coupling reagent <i>via</i> S_NAr mechanism.....	65
Scheme 3.6 Reaction of benzoic acid with tosyl chloride.....	65
Scheme 3.7 A proposed mechanism of reagent (4b) with morpholine in the presence of HOBt.....	67
Scheme 3.8 Racemization of peptide by oxazolone intermediate.....	68

LIST OF ABBREVIATIONS

Ala	alanine
Anal. Calcd.	Analysis calculation
Boc	<i>tert</i> -butoxycarbonyl
Boc ₂ O	di- <i>t</i> -butyl dicarbonate
br	broad
Bz	benzoyl
cm ⁻¹	unit of wavenumber
d	doublet
DCC	<i>N,N</i> -dicyclohexylcarbodiimide
DCU	dicyclohexylurea
DIEA	<i>N,N</i> -diisopropyl- <i>N</i> -ethylamine
DMAP	4-dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
Fmoc	<i>N</i> -9-fluorenylmethoxycarbonyl
Glu(O ^t Bu)	(<i>tert</i> -butyl ester)glutamic acid
Gly	glycine
HOBt	1-hydroxybenzotriazole
Leu	leucine
Lys(Boc)	(<i>N</i> - ϵ - <i>tert</i> -butoxycarbonyl)lysine
m	multiplet
mg	milligram
MHz	megahertz
mL	milliliter
Phe	phenylalanine
ppm	part per million
s	singlet
Sar	sarcosine

Ser(O ^t Bu)	(<i>O</i> - <i>t</i> -butyl)serine
t	triplet
TLC	Thin Layer Chromatography
Trp(Boc)	(<i>N</i> ^{trp} - <i>tert</i> -butoxycarbonyl)tryptophane
Val	valine
°C	degree celcius
δ	chemical shift
λ _{max}	the wavelength at maximum absorption



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