

Acknowledgements

Foremost, I would like to thank God (Allah) for giving me guidance in my life and for seeing me through the completion of this thesis.

At the outset, I would like to express my appreciation to my supervisor Assist. Prof. Dr. Riyadh Jaleel Nahi for his supervision, valuable scientific guidance, discussion and suggestion throughout my work.

I would also like to thank the dean of the College of Science, Al-Muthanna University. I would also like to thank the head and the staff members of the department of chemistry. I would also like to thank the staff of central Lab. Mr. Hyder Radhi and Mr. Ahmed Razak for their efforts in the FT-IR and TGA analysis measurements. I would like to thank the chemical store staff specially, Mr. Mohammed Adil.

I would also like to thank Asst. Prof. Dr. Adil Muala Dhumad, Basrah university, collage of Education for pure Sciences, Department of chemistry for the helping in the NMR and GC-MS spectroscopy measurement.

I would also like to thank my brothers and sisters. Thank you for encouraging and praying me during my M.Sc study.

Most importantly, none of this would have been possible without the love, encouragement and constant selfless support from my husband; I greatly value your contribution and deeply appreciate your belief in me.

Zainab / 2019

Abstract

This thesis describes the synthesis, characterization and thermal study of new 1,2,3-triazole derivatives containing 1,3,4-oxadiazole and azo moieties. For the synthesis of the target 1,2,3-triazole derivatives **61-67**, the copper (I) catalyzed azide-alkyne cycloaddition (CuAAC) was the method choice. Since the azide compounds being considered as a substrate for (CuAAC), a series of substituted phenyl azides was synthesized via reaction of diazonium salts with sodium azide, while the commercially available propiolic acid was chosen to be the alkyne function. Choosing of propiolic acid as an alkyne component of click reaction is allowed to functionalize the target 1,2,3-triazole derivatives with a carboxyl group function which can be exploited in different reactions and applications. Having the target 1,2,3-triazole derivatives **61-66**, our efforts focused to exploit their carboxyl function groups for the synthesis of new heterocyclic compounds containing 1,3,4-oxadiazole moieties. A new series of compounds containing on 1,2,3-triazole and 1,3,4-oxadiazole moieties on the same molecule was synthesized through a condensation reaction between the synthesized 1,2,3-triazole derivatives **61-66** and semicarbazide hydrochloride followed by dehydro-cyclization step in the presence of POCl₃. On the other hand, compound **67** was synthesized as an unnatural amino acid containing 1,2,3-triazole ring and is ready for different reactions such as diazonium salts formation. Thus, this unnatural amino acid was exploited in the synthesis of new three azo compounds following the standard procedure that is used in the synthesis of the azo compounds **74-73**. The synthesized compounds introduce the 1,2,3-triazole and azo moieties on the same molecule thereby new applications can be reported. All synthesized compounds were characterized by the FT-IR, ¹H-NMR, ¹³C-NMR and GC-MS spectroscopies. For further investigations, the thermal behavior of the synthesized compounds was studied by TGA and DTG techniques.

List of Contents

Title		page
Acknowledgements		I
Abstract		II
List of Contents		III
List of Tables		VI
List of Figures		VI
List of Schemes		VIII
Appendix		IX
List of Abbreviations		XII
Chapter One: Introduction		
1.1	Heterocyclic Compounds	1
1.1.1	Triazole Ring System: Chemical Structure and Properties	3
1.1.1.1	1,2,3-Triazole Ring System: Chemical Structure and Properties	5
1.1.1.2	Synthesis of 1,4-Disubstituted-1,2,3-Triazole Derivatives	7
1.1.1.2.1	Synthesis of 1,2,3-Triazole Derivatives by Click Reaction	9
1.1.1.3	Applications of 1,4-Disubstituted-1,2,3-Triazole Derivatives	12
1.1.2	Oxadiazole Ring System: Chemical Structure and Properties	12
1.1.2.1	Synthesis of 2,5-Disubstituted-1,3,4-Oxadiazoles	16
1.1.2.2	Importance of 1,3,4-Oxadiazole Derivatives	20
1.2	Azo Compounds: Chemical Structure and Properties	20
1.2.1	Synthesis of Azo Compounds	22
1.2.2	Applications of Azo Compounds	25

1.3	Objectives of This Study	26
Chapter Two: Experimental part		
2.0	Experimental	27
2.1	Materials and Instruments	27
2.2	Procedures	29
2.2.1	General Procedure for Synthesis of Substituted Phenyl azide	29
2.2.2	General Procedure for Synthesis of 1,2,3-Triazole Derivatives	30
2.2.3	General Procedure for Synthesis of 1,3,4- Oxadiazoles Derivatives	35
2.2.4	General Procedure for Synthesis of Azo Compounds	39
Chapter Three: Results and discussion		
3.1	Synthesis of Substituted Phenyl Azide	42
3.2	Synthesis of 1,2,3-Triazole Derivatives	46
3.3	Synthesis of 1,3,4-Oxadiazole Derivatives	50
3.4.	Synthesis of 1,2,3-Triazole Containing Azo Group	51
Chapter Four: Thermal Stability Study		
4.1	Introduction	54
4.1.1	Thermo Gravimetric (TG) and Derivative Thermal Gravimetry (DTG)	54
4.2	Thermal Stability Study of the Synthesized 1,2,3-Triazole Derivatives	56
4.3	Thermal Stability Study of The Synthesized 1,3,4-Oxadiazole Derivatives	61
4.4	Thermal Stability Study of Azo Compounds	66
Chapter five: Conclusions & Future work		
5.1	Conclusions	70
5.2	Future work	71

References	72
Appendix	85

List of Tables

2.1	Chemicals used with the purity percentage and manufacturing companies.	27
3.1	The most characteristic bands in FT-IR spectra of compounds 54-60	46

List of Figures

1.1	Some of common heterocyclic compounds	2
1.2	Some of heterocycles contain more than one hetero atom	2
1.3	Structure of 1,2,3-triazole and 1,2,4-triazole isomers	4
1.4	Tautomeric forms of 1,2,3-triazole and 1,2,4-triazole isomers	4
1.5	Structures of 1,2,3-triazole classes	6
1.6	Selected contributing structures of an organic azide	12
1.7	Isomeric structures of oxadiazole ring	13
1.8	Some of aromatic systems of 1,3,4-oxadiazole	14
1.9	Different positions of substitution in 1,3,4-oxadiazole	15
1.10	Tautomerism of 2-substituted-1,3,4-oxadiazole	15
1.11	Tautomerism of aromatic azo compounds	21
4.1	TG-DTG curves of compound 62	57
4.2	TG-DTG curves of compound 63	58
4.3	TG-DTG curves of compound 64	59
4.4	TG-DTG curves of compound 65	60
4.5	TG-DTG curves of compound 66	61
4.6	TG-DTG curves of compound 69	62

4.7	TG-DTG curves of compound 70	63
4.8	TG-DTG curves of compound 71	64
4.9	TG-DTG curves of compound 72	65
4.10	TG-DTG curves of compound 73	66
4.11	TG-DTG curves of compound 74	67
4.12	TG-DTG curves of compound 75	68
4.13	TG-DTG curves of compound 76	69

List of Schemes

1.1	Thermal Huisgen cycloaddition	8
1.2	1,3-Dipolar cycloaddition mechanism	9
1.3	A proposed mechanism of click reaction	11
1.4	Thermal synthesis of 1,3,4-oxaziazole derivatives	16
1.5	Synthesis of un substituted 1,3,4-oxaziazole	16
1.6	Cycloaddition reaction of acylhydrazide	17
1.7	Cyclization of Semicarbazones	18
1.8	Cyclization reaction of acylthiosemicarbazides	18
1.9	Dehydration of acylsemicarbazide using POCl ₃	19
1.10	Formation of oxadiazole from acid hydrazide and carboxylic acid	19
1.11	Preparation of diazonium salt	23
1.12	A mechanism for azo coupling reaction	23
1.13	Azo- coupling reaction of α -naphthol	24
1.14	Azo- coupling reaction of <i>m</i> -toluidine	25
3.1	The tow-possible mechanisms of azide formation	43
3.2	Synthesis of series of phenylazide (54-60)	44
3.3	Synthesis of compounds (61-67) via click reaction	47
3.4	Synthesis of compounds (68-73) by cyclodehydration reaction	50
3.5	Synthesis of azo compounds (74-76)	52

Appendix

Figure 1	FT-IR spectroscopy of compound 54 .	85
Figure 2	FT-IR spectroscopy of compound 55 .	85
Figure 3	FT-IR spectroscopy of compound 56 .	86
Figure 4	FT-IR spectroscopy of compound 57 .	86
Figure 5	FT-IR spectroscopy of compound 58 .	87
Figure 6	FT-IR spectroscopy of compound 59 .	87
Figure 7	FT-IR spectroscopy of compound 60 .	88
Figure 8	FT-IR spectroscopy of compound 61 .	88
Figure 9	FT-IR spectroscopy of compound 62 .	89
Figure 10	FT-IR spectroscopy of compound 63 .	89
Figure 11	FT-IR spectroscopy of compound 64 .	90
Figure 12	FT-IR spectroscopy of compound 65 .	90
Figure 13	FT-IR spectroscopy of compound 66 .	91
Figure 14	FT-IR spectroscopy of compound 67 .	91
Figure 15	FT-IR spectroscopy of compound 68 .	92
Figure 16	FT-IR spectroscopy of compound 69 .	92
Figure 17	FT-IR spectroscopy of compound 70 .	93
Figure 18	FT-IR spectroscopy of compound 71 .	93
Figure 19	FT-IR spectroscopy of compound 72 .	94
Figure 20	FT-IR spectroscopy of compound 73 .	94
Figure 21	FT-IR spectroscopy of compound 74 .	95
Figure 22	FT-IR spectroscopy of compound 75 .	95
Figure 23	FT-IR spectroscopy of compound 76 .	96

Figure 24	¹ H-NMR spectrum of compound 61 .	96
Figure 25	¹ H-NMR spectrum of compound 62 .	97
Figure 26	¹ H-NMR spectrum of compound 63 .	97
Figure 27	¹ H-NMR spectrum of compound 64 .	98
Figure 28	¹ H-NMR spectrum of compound 65 .	98
Figure 29	¹ H-NMR spectrum of compound 66 .	99
Figure 30	¹ H-NMR spectrum of compound 68 .	99
Figure 31	¹ H-NMR spectrum of compound 69 .	100
Figure 32	¹ H-NMR spectrum of compound 70 .	100
Figure 33	¹ H-NMR spectrum of compound 71 .	101
Figure 34	¹ H-NMR spectrum of compound 72 .	101
Figure 35	¹ H-NMR spectrum of compound 73 .	102
Figure 36	¹ H-NMR spectrum of compound 74 .	102
Figure 37	¹ H-NMR spectrum of compound 75 .	103
Figure 38	¹ H-NMR spectrum of compound 76 .	103
Figure 39	¹³ C-NMR spectrum of compound 62 .	104
Figure 40	¹³ C-NMR spectrum of compound 69 .	104
Figure 41	¹³ C-NMR spectrum of compound 71 .	105
Figure 42	¹³ C-NMR spectrum of compound 73 .	105
Figure 43	¹³ C-NMR spectrum of compound 75 .	106
Figure 44	GC-MS spectrum of compound 61 .	106
Figure 45	GC-MS spectrum of compound 62 .	107
Figure 46	GC-MS spectrum of compound 63 .	107
Figure 47	GC-MS spectrum of compound 64 .	108

Figure 48	GC-MS spectrum of compound 65 .	108
Figure 49	GC-MS spectrum of compound 66 .	109
Figure 50	GC-MS spectrum of compound 68 .	109
Figure 51	GC-MS spectrum of compound 69 .	110
Figure 52	GC-MS spectrum of compound 70 .	110
Figure 53	GC-MS spectrum of compound 71 .	111
Figure 54	GC-MS spectrum of compound 73 .	111
Figure 55	GC-MS spectrum of compound 74 .	112
Figure 56	GC-MS spectrum of compound 75 .	112
Figure 57	GC-MS spectrum of compound 76 .	113

List of Abbreviations

<i>t</i> -Bu	Tert-Butyl
°C	Degrees Celcius
¹³ C-NMR	Carbon nuclear magnetic resonance
CuAAC	Copper-catalyzed azide-alkyne cycloaddition
cm	Centimetre
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
DMAD	Dimethyl acetylene dicarboxylate
DSC	Differential scanning calorimetry
DTA	Differential thermal analysis
DTG	Derivative thermal gravimetry
FMO	Frontier molecular orbitals
FT-IR	Fourier transforms infrared
HIV	Human immunodeficiency virus
GC-MS	Gas chromatography-mass
HUMO	Highest occupied molecular orbital
LOMO	Lowest unoccupied molecular orbital
¹ H-NMR	Proton nuclear magnetic resonance
HPMS-EI	High preference GC-MS spectrometry-electron impact
mL	Mili Liters
mmol	Mili mole
M.p	Melting point
<i>m</i>	Meta

MS	GC-MS spectrometry
m	Multiple
NMR	Nuclear magnetic resonance
s	Singlet
TGA	Thermogravimetric analysis
TMA	Thermomechanical analysis
<i>o</i>	Ortho
<i>p</i>	Para