

Abstract

p-Quinones are a group of compounds which played a vital role in biological processes through their redox system in the respiratory cycles and blood stream. The chemistry of *p*-quinones including their preparations, reactions and different physicochemical properties were dealt with chapter one of this thesis.

Twelve compounds of *p*-amino-quinone were prepared in this work: four were prepared from 1,4-benzoquinone: 2,5-dianilino-1,4-benzoquinone (Ia), 2,5-disulphamethoxazolyl-1,4-benzoquinone (Ib), 2,5-disulphadoxinyl-1,4-benzoquinone (Ic), 2,5-disulphanil amidyl-1,4-benzoquinone (Id); four were prepared from 2,3,5,6-tetrabromo-1,4-benzoquinone: 3,6-dibromo-2,5-dianilino-1,4-benzoquinone (IIa), 3,6-dibromo-2,5-disulphamethoxazolyl-1,4-benzoquinone (IIb), 3,6-dibromo-2,5-disulphadoxinyl-1,4-benzoquinone (IIc), 3,6-dibromo-2,5-disulphanilamidyl-1,4-benzoquinone (IId); four were prepared from 1,4-naphthoquinone: 2-anilino-1,4-naphthoquinone (IIIa), 2-sulphamethoxazolyl-1,4-naphthoquinone (IIIb), 2-sulphadoxinyl-1,4-naphthoquinone (IIIc) and 2-sulphanil amidyl-1,4-naphthoquinone (IIId). The compounds were prepared according to well established literature methods. They are selected based upon the calculated values of their physicochemical properties especially logP when correlated with the substituted groups.

The identities of the prepared compounds were confirmed by infrared IR, ultraviolet-visible UV-VIS and proton-nuclear magnetic resonance $^1\text{H-NMR}$ spectral analysis and chromatographic examination. Physiochemical properties, Mechanisms of the reactions and the appropriate retrosynthetic analysis were given and discussed in chapter three.

الخلاصة

اكتسبت مركبات ال بارا- كينون اهميتها من دورها الحيوي في عملية التنفس داخل جسم الانسان. و لقد تم في هذا البحث تناول كيماء ال بارا- كينون بما فيها تحضيرها ، تفاعالتها و خواصها الفيزيوكيميائية.

تم تحضير ١٢ مركب في هذا المشروع: اربعة مركبات حضرت من ٤,١- بنزوكينون: ٢,٥-ثنائي الانيلينو-١,٤-بنزوكينون، ٢,٥-ثنائي السلفاميثوكسازوليل-١,٤-بنزوكينون، ٢,٥-ثنائي السلفادوكسينيل-١,٤-بنزوكينون، ٢,٥-ثنائي السلفانيل اميديل-١,٤-بنزوكينون؛ اربعة مركبات حضرت من ٦,٣,٢-رياعي البروم-١,٤-بنزوكينون: ٦,٣-ثنائي البروم-٥,٢-ثنائي الانيلينو-١,٤-بنزوكينون، ٣,٦-ثنائي البروم-٥,٢-ثنائي السلفاميثوكسازوليل-١,٤-بنزوكينون، ٣,٦-ثنائي البروم-٥,٢-ثنائي السلفادوكسينيل-١,٤-بنزوكينون، ٣,٦-ثنائي البروم-٥,٢-ثنائي السلفانيل اميديل-١,٤-بنزوكينون؛ اربعة مركبات حضرت من ٤,١- نافثوكينون: ٢-انيلينو-١,٤-نافثوكينون، ٢-سلفاميثوكسازوليل-١,٤-نافثوكينون، ٢-سلفادوكسينيل-١,٤-نافثوكينون، ٢-سلفانيل اميديل-١,٤-نافثوكينون. حضرت هذه المركبات اعتمادا على طرق تحضير مثبتة مسبقا. و تم اختيارها اعتمادا على خواصها الفيزيوكيميائية و خاصةً قيم معامل التوزيع $\log P$.

تم التعرف على البنية التركيبية للمركبات المحضرة عن طريق التحليل الطيفي بواسطة الاشعة تحت الحمراء، الاشعة فوق البنفسجية-الطيف المرئي و الرنين النووي المغنتيسي للهيدروجين بالإضافة الي الطرق الكرومتوغرافية. وضعت ميكانيكية هذه التفاعلات اعتمادا على طريقة التحليل retrosynthetic analysis في الباب الثالث من هذا البحث.

بسم الله الرحمن الرحيم

قال تعالى:

(إِنَّ فِي خُلُقِ السَّمَاوَاتِ وَالْأَرْضِ وَاخْتِلَافِ اللَّيلِ وَالنَّهَارِ لَآيَاتٍ لِأُولَئِكَ الَّذِينَ يَذْكُرُونَ
اللهُ قِياماً وَقَعُوداً وَعَلَى جُنُوبِهِمْ وَيَتَفَكَّرُونَ فِي خُلُقِ السَّمَاوَاتِ وَالْأَرْضِ رَبَّنَا مَا خَلَقْتَ هَذَا بَاطِلًا
سَبَحَانَكَ فَقَدْ نَعْلَمُ عَذَابَ النَّارِ)

صدق الله العظيم

الآيات (١٩٠-١٩١) من سورة آل عمران

Dedication

*To my parents, brothers, sisters and friends for
their unconditional support.*

Acknowledgments

Firstly, I would like to express my sincere gratitude to my supervisor Prof. Dr. Ahmed Elsadig Mohammed Saeed for the continuous support of my M.Sc study, for his patience, motivation, and immense knowledge. His guidance helped me in researching and writing of this thesis.

I would like to express my thanks to the staff of chemistry department at Sudan University of Science and technology for their help.

I also place on record, my sense of gratitude to one and all, who directly or indirectly, have lent their hand in this work.

Contents

No	Title	Page. No
	Abstract (English)	i
	Abstract (Arabic)	ii
	اللایة	iii
	Dedication	iv
	Acknowledgments	v
	Contents	vi
	List of tables	x
	List of appendix	xii
	List of abbreviations	xiv

Chapter One Introduction

1.	Introduction	1
1.1.	Definition and structure of Quinones	1
1.2.	Preparation of quinones	1
1.2.1.	<i>p</i> -Benzoquinone	1
1.2.2.	<i>o</i> -Benzoquinone	2
1.2.3.	1,4-Naphthoquinone	3
1.2.4.	1,2-Naphthoquinone	3
1.2.5.	2,6-Naphthoquinone	3
1.2.6.	Anthraquinone	3
1.3.	Quinones reactions	4
1.3.1.	Diels-Alder reaction (electrocyclic addition)	4
1.3.2.	Electrophilic addition to quinones	5
1.3.3.	Nucleophilic addition to quinones	6
1.3.4.	Reduction of quinones	8
1.3.5.	Carbon-Carbon bond formation	10
1.3.5.1.	Alkyl substitution at carbon	10
1.3.5.2.	Cyclization to furan derivatives	11
1.3.6.	Complexes of quinones system	12
1.4.	Spectroscopic properties of quinones	13
1.4.1.	Infrared spectroscopy (IR)	13

1.4.2.	Ultraviolet spectroscopy (UV-VIS)	16
1.4.3.	Nuclear Magnetic Resonance (NMR)	17
1.4.4.	Mass Spectra (MS)	19
1.5.	Biological importance of quinones	23
1.6.	Molecular modeling	25
1.7.	QSAR	25
1.7.1.	Modeling methods	26
1.7.1.1.	Methods for Regression Problems	26
1.7.1.2.	Methods for Classification Problems	26
1.7.2.	Purpose of QSAR	26
1.7.3.	Applications of QSAR	26
1.7.4.	Software for QSAR Development	27
1.7.4.1.	Structure Drawing or File Conversion	27
1.7.4.2.	3D Structure Generation	27
1.7.4.3.	Descriptor Calculation	28
1.7.4.4.	Modeling	28
1.7.4.5	General purpose	28
1.8.	Aim of the project	29

Chapter Two **Material and Methods**

2.	Materials and Methods	30
2.1.	Materials	30
2.1.1.	Chemicals	30
2.1.2.	Solvents	30
2.2.	Thin- layer chromatography (TLC)	30
2.3.	Infra-red spectrophotometer (IR)	30
2.4.	Ultraviolet-visible spectrophotometer (UV-VIS)	31
2.5.	NMR spectrophotometer ($^1\text{H-NMR}$)	31
2.6.	Gas Chromatography/ Mass Spectrometer (GC-MS)	31
2.7.	General equipment	31
2.8.	ACD lab program	31
2.9.	General method of ACD/lab program	31
2.10.	Synthetic methods	32
2.10.1.	Preparation of <i>p</i> -benzoquinone (I)	32
2.10.2.	Preparation of 1:4-naphthoquinone (II)	32
2.10.3.	Preparation of 1:4-naphthoquinone (III)	33

2.10.4.	Preparation of 2,5-diamino-1,4-benzoquinones (Ia-ID) and 3,6-dibromo-2,5-diamino-1,4-benzoquinones (IIa-IIId)	33
2.10.5.	Preparation of 2-amino-1,4-naphthoquinones (IIIa-IIIId)	33
2.10.	Reaction schemes	34

Chapter Three Results and Discussion

3.	Results and Discussion	55
3.1.	Analysis of 2-amino-1,4-naphthoquinone	59
3.1.1.	Retro-synthetic disconnection of 2-amino-1,4-naphthoquinone	59
3.1.2.	Mechanism formation of 2-amino-1,4-naphthoquinone	59
3.1.3.	Spectral data of 2-amino-1,4-naphthoquinone interpretation	59
3.1.3.1.	The IR spectrum of 2-amino-1,4-naphthoquinone	59
3.1.3.2.	The ¹ H-NMR spectrum of 2-amino-1,4-naphthoquinone	60
3.1.3.3.	Mass spectrum of 2-amino- <i>p</i> -naphthoquinone compounds	61
3.1.3.4.	UV spectrum of 2-amino-1,4-naphthoquinone	61
3.2.	Analysis of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone	62
3.2.1.	Retro-synthetic disconnection of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone	62
3.2.2.	Mechanism formation of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone	62
3.2.3.a.	Spectral data of 2,5-diamino-1,4-benzoquinone interpretation	63
3.2.3.a.1.	The IR spectrum of 2,5-diamino-1,4-benzoquinone	63
3.2.3.a.2.	The ¹ H-NMR spectrum of 2,5-diamino-1,4-benzoquinone	64
3.2.3.a.3.	Mass spectrum of 2,5-diamino-1,4-benzoquinone	64
3.2.3.a.4.	UV spectrum of 2,5-diamino-1,4-benzoquinone	65
3.2.3.b.	Spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone interpretation	65
3.2.3.b.1.	The IR spectrum of 3,6-dibromo-2,5-diamino-1,4 benzoquinone	65
3.2.3.b.2.	The ¹ H-NMR spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone	65
3.2.3.b.3	Mass spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone	66
3.2.3.b.4.	UV spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone	66
3.3.	Analysis TLC data of prepared <i>p</i> -amino quinones	66
3.3.	Conclusion and recommendation	68

Chapter Four

References

4.	References	69- 73
----	------------	--------

Appendix

4.1.	Examples of ACD/Lab calculated values of some amino- <i>p</i> -quinones derivatives:	74- 79
4.2.	IR spectral data	80- 87
4.3.	UV spectral data	87-92
4.4.	NMR spectral data	92-98
4.5.	MS spectral data	98-104

List of tables

Table No	Title	Page
1.1.	Difference between the electrode potential of the substituted 1,4-naphthoquinone and that substituted 1,4-naphthoquinon	9
1.2.	V CO frequencies in substituted quinones	15
1.3.	N.M.R. spectra (60 MHz) of some <i>p</i> -benzoquinones (δ values)	17
1.4.	N.M.R. spectra (60 MHz) of some naphthaquinones (δ values)	18
2.1.	Chemical names of the synthesized compounds	36
2.1.1.	Chemical name of the synthesized 2,5-diamino-1,4-benzoquinones	36
2.1.2.	Chemical name of the synthesized 3,6-dibromo-2,5-diamino-1,4-benzoquinones	36
2.1.3.	Chemical name of the synthesized 2-amino- <i>p</i> -naphthoquinones	37
2.2.	Reaction conditions	38
2.2.1.	Reaction conditions of 2-amino-1,4-benzoquinone compounds	38
2.2.2.	Reaction conditions of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	39
2.2.3.	Reaction conditions of 2-amino- <i>p</i> -naphthoquinone compounds	40
2.3.	Infrared spectral data of the synthesized compounds	41
2.3.1	Infrared spectral data of 2,5-diamino-1,4-benzoquinone compounds	41
2.3.1	Infrared spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	42
2.3.3	Infrared spectral data of 2-amino- <i>p</i> -naphthoquinone compounds	43
2.3.4	Infrared spectral data of <i>p</i> -quinones	44
2.3.5	Infrared spectral data of amines	44
2.4.	$^1\text{H-NMR}$ Chemical shift of the synthesized compounds	45
2.4.1.	$^1\text{H-NMR}$ Chemical shift of 2,5-diamino-1,4-benzoquinone compounds	45
2.4.2.	$^1\text{H-NMR}$ Chemical shift of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	46
2.4.3.	$^1\text{H-NMR}$ Chemical shift of 2-amino- <i>p</i> -naphthoquinone compounds	47
2.5.	Mass spectral data of the synthesized compounds	48
2.5.1.	Mass spectral data of 2,5-diamino-1,4-benzoquinone compounds	48
2.5.2.	Mass spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	49

2.5.3.	Mass spectral data of 2-amino- <i>p</i> -naphthoquinone compounds	50
2.6.	Ultraviolet-Visible spectral data of the synthesized compounds	51
2.6.1	Ultraviolet-Visible spectral data of 2-amino-1,4-benzoquinone	51
2.6.2	Ultraviolet-Visible spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	51
2.6.3	Ultraviolet-Visible spectral data of 2-amino- <i>p</i> -naphthoquinone compounds	52
2.6.4	Ultraviolet-Visible spectral data of <i>p</i> -quinones	52
2.6.5	Ultraviolet-Visible spectral data of amines	52
2.7.	Thin layer chromatography of the synthesized compounds	53
2.7.1	Thin layer chromatography of 2-amino-1,4-benzoquinone compounds	53
2.7.2	Thin layer chromatography of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds	53
2.7.3	Thin layer chromatography of 2-mino-1,4-naphthoquinone compounds	54
3.1	ACD/Lab results of some amino- <i>p</i> -benzoquinone derivatives	56-58

List of appendix

Appendix NO.	Title	Page NO.
4.1.	Examples of ACD/Lab calculated values of some amino- <i>p</i> -quinones derivatives	74-79
4.2.	IR spectral data	
1	Appendix (1) IR spectrum of compound (I)	80
2	Appendix (2) IR spectrum of compound (Ia)	80
3	Appendix (3) IR spectrum of compound (Ib)	80
4	Appendix (4) IR spectrum of compound (Ic)	81
5	Appendix (5) IR spectrum of compound (Id)	81
6	Appendix (6) IR spectrum of compound (II)	82
7	Appendix (7) IR spectrum of compound (IIa)	82
8	Appendix (8) IR spectrum of compound (IIb)	83
9	Appendix (9) IR spectrum of compound (IIc)	83
10	Appendix (10) IR spectrum of compound (IId)	84
11	Appendix (11) IR spectrum of compound (III)	84
12	Appendix (12) IR spectrum of compound (IIIa)	85
13	Appendix (13) IR spectrum of compound (IIIb)	85
14	Appendix (14) IR spectrum of compound (IIIc)	86
15	Appendix (15) IR spectrum of compound (IIId)	86
16	Appendix (16) UV spectrum of compound (Ia)	87
17	Appendix (17) UV spectrum of compound (Ib)	87
18	Appendix (18) UV spectrum of compound (Ic)	88
19	Appendix (19) UV spectrum of compound (Id)	88
20	Appendix (20) UV spectrum of compound (II)	88
21	Appendix (21) UV spectrum of compound (IIa)	89
22	Appendix (22) UV spectrum of compound (IIb)	89
23	Appendix (23) UV spectrum of compound (IIc)	89
24	Appendix (24) UV spectrum of compound (IId)	90
25	Appendix (25) UV spectrum of compound (III)	90
26	Appendix (26) UV spectrum of compound (IIIa)	90
27	Appendix (27) UV spectrum of compound (IIIb)	91
28	Appendix (28) UV spectrum of compound (IIIc)	91
29	Appendix (29) UV spectrum of compound (IIId)	92
30	Appendix (30) NMR spectrum of compound (Ia)	92
31	Appendix (31) NMR spectrum of compound (Ib)	93
32	Appendix (32) NMR spectrum of compound (Ic)	93
33	Appendix (33) NMR spectrum of compound (Id)	94
34	Appendix (34) NMR spectrum of compound (IIa)	94

35	Appendix (35) NMR spectrum of compound (IIb)	95
36	Appendix (36) NMR spectrum of compound (IIc)	95
37	Appendix (37) NMR spectrum of compound (IId)	96
38	Appendix (38) NMR spectrum of compound (IIIa)	96
39	Appendix (39) NMR spectrum of compound (IIIb)	97
40	Appendix (40) NMR spectrum of compound (IIIc)	97
41	Appendix (41) NMR spectrum of compound (IIId)	98
42	Appendix (42) MS spectrum of compound (Ia)	98
43	Appendix (43) MS spectrum of compound (Ib)	99
44	Appendix (44) MS spectrum of compound (Ic)	99
45	Appendix (45) MS spectrum of compound (Id)	100
46	Appendix (46) MS spectrum of compound (IIa)	100
47	Appendix (47) MS spectrum of compound (IIb)	101
48	Appendix (48) MS spectrum of compound (IIc)	101
49	Appendix (49) MS spectrum of compound (IId)	102
50	Appendix (50) MS spectrum of compound (IIIa)	102
51	Appendix (51) MS spectrum of compound (IIIb)	103
52	Appendix (52) MS spectrum of compound (IIIc)	103
53	Appendix (53) MS spectrum of compound (IIId)	104

List of abbreviations

BQ	Benzoquinone
DMSO	Dimethylsulfoxide
<i>E</i>	electron withdrawn effect
<i>I</i>	inductive effect
IR	infrared spectroscopy
Lit	literature
logP	logarithmic octanol-water partition coefficient
mL	milliliter
mmol	millimole
M.wt	Molecular weight
NQ	naphthoquinone
ppm	parts per million
Re. Temp	Reaction temperature
Rec. solv	Recrystallization solvent
Re. Time	Reaction time
Rf	Retardation factor
Y%	Yield percentage
α	alpha
β	beta